UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 20-F

(Mark one)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report

Commission file number 001-37710

HUTCHMED (CHINA) LIMITED

(Exact name of Registrant as specified in its charter)

N/A

(Translation of Registrant's name into English)

Cayman Islands

(Jurisdiction of incorporation or organization)

48th Floor, Cheung Kong Center
2 Queen's Road Central
Hong Kong
+852 2121 8200

(Address of principal executive offices)

Dr. Weiguo Su
Chief Executive Officer and Chief Scientific Officer
Level 18, The Metropolis Tower
10 Metropolis Drive
Hunghom, Kowloon
Hong Kong
Telephone: +852 2121 8200
Facsimile: +852 2121 8281

(Name, telephone, email and/or facsimile number and address of Company contact person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
American depositary shares, each representing five ordinary shares, par value $0.10 per share	HCM	Nasdaq Global Select Market
Ordinary shares, par value $0.10 per share*		Nasdaq Global Select Market*

*Not for trading, but only in connection with the listing of American depositary shares on the Nasdaq Global Select Market

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the Annual Report:
864,775,340 ordinary shares were issued and outstanding as of December 31, 2022.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

☒ Yes ☐ No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

☐ Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

☒ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

☒ Yes ☐ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Emerging growth company ☐

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 13(a) of the Exchange Act. ☐

†The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepare or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☒ International Financial Reporting Standards as issued by the International Accounting Standards Board ☐ Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

☐ Item 17 ☐ Item 18

If this is an Annual Report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

☐ Yes ☒ No

(APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS)
Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court.

☐ Yes ☐ No

HUTCHMED (China) Limited
Table of Contents

INTRODUCTION

This annual report on Form 20-F contains our audited consolidated statements of operations data for the years ended December 31, 2022, 2021 and 2020 and our audited consolidated balance sheet data as of December 31, 2022 and 2021. Our consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP.

This annual report also includes audited consolidated income statement data for the years ended December 31, 2022, 2021 and 2020 and the audited consolidated statements of financial position data as of December 31, 2022 and 2021 for our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, and audited consolidated income statement data for the period from January 1, 2021 to September 28, 2021 and the year ended December 31, 2020 and the audited consolidated statements of financial position data as of September 28, 2021 of Hutchison Baiyunshan when it was our non-consolidated joint venture. On September 28, 2021, we completed the disposal of our entire interest in Hutchison Baiyunshan, which was our non-core and over-the-counter drug joint venture business. The financial statements of each of Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan have been prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standard Board, or IASB.

Unless the context requires otherwise, references herein to the "company," "HUTCHMED," "we," "us" and "our" refer to HUTCHMED (China) Limited, a holding company incorporated in the Cayman Islands, and its consolidated subsidiaries and joint ventures, some of which, as noted below, are incorporated and operate in the PRC. "HUTCHMED Holdings" refers to HUTCHMED Holdings Limited, a subsidiary of the Company and a holding company incorporated in the Cayman Islands. "HUTCHMED Limited" refers to "HUTCHMED Limited", a subsidiary of HUTCHMED Holdings which is incorporated in the PRC and through which we operate our Oncology/Immunology operations in China. Our other principal operating subsidiaries for our Oncology/Immunology operations are HUTCHMED International Corporation (incorporated in Delaware), HUTCHMED Holdings (HK) Limited (incorporated in Hong Kong) and HUTCHMED (Suzhou) Limited (incorporated and operates in the PRC). "Hutchison Sinopharm" refers to Hutchison Whampoa Sinopharm Pharmaceuticals (Shanghai) Company Limited, our PRC-incorporated joint venture with Sinopharm through which we operate our principal consolidated joint venture. See Item 4. "Information on the Company—C. Organizational Structure" for a diagram illustrating our corporate structure.

Conventions Used in this Annual Report

Unless otherwise indicated, references in this annual report to:

- "ADRs" are to the American depositary receipts, which evidence our ADSs;
- "ADSs" are to our American depositary shares, each of which represents five ordinary shares;
- "China" or "PRC" refers to the People's Republic of China including Hong Kong and Macau and, only for the purpose of this annual report, excluding Taiwan; and only in the context of describing PRC rules, laws, regulations, regulatory authority, and any PRC entities or citizens under such rules, laws and regulations and other legal or tax matters in this annual report, excludes Taiwan, Hong Kong, and Macau; the legal and operational risks associated with operating in China also apply to our operations in Hong Kong;
- "CK Hutchison" are to CK Hutchison Holdings Limited, a company incorporated in the Cayman Islands and listed on the Hong Kong Stock Exchange, and the ultimate parent company of our largest shareholder, Hutchison Healthcare Holdings Limited;
- "E.U." are to the European Union;
- "Guangzhou Baiyunshan" are to Guangzhou Baiyunshan Pharmaceutical Holdings Company Limited, a leading China-based pharmaceutical company listed on the Shanghai Stock Exchange and the Hong Kong Stock Exchange;
- "Hain Celestial" are to The Hain Celestial Group, Inc., a Nasdaq-listed, natural and organic food and personal care products company;
- "HK$" or "HK dollar" are to the legal currency of the Hong Kong Special Administrative Region;

- "Hutchison Baiyunshan" are to Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited, which was our non-consolidated joint venture with Guangzhou Baiyunshan in which we indirectly held a 50% interest through a holding company until our disposal of such interest on September 28, 2021 (this interest was previously held through a holding company in which we have a 80% interest);

- "HUTCHMED Science Nutrition" are to HUTCHMED Science Nutrition Limited, our wholly owned subsidiary;

- "Hutchison Hain Organic" are to Hutchison Hain Organic Holdings Limited, our joint venture with Hain Celestial in which we have a 50% interest;

- "Hutchison Healthcare" are to Hutchison Healthcare Limited, our wholly owned subsidiary;

- "HUTCHMED Limited", our PRC-incorporated subsidiary through which we operate our Oncology/Immunology operations in China and in which we have a 99.8% interest;

- "HUTCHMED Holdings" are to HUTCHMED Holdings Limited, our subsidiary incorporated in the Cayman Islands in which we have a 99.8% interest and which is the indirect holding company of HUTCHMED Limited;

- "Hutchison Sinopharm" are to Hutchison Whampoa Sinopharm Pharmaceuticals (Shanghai) Company Limited, our PRC-incorporated joint venture with Sinopharm in which we have a 50.9% interest and through which we operate our principal consolidated joint venture;

- "ordinary shares" or "shares" are to our ordinary shares, par value $0.10 per share;

- "RMB" or "renminbi" are to the legal currency of the PRC;

- "SEHK" are to The Stock Exchange of Hong Kong Limited, or the Hong Kong Stock Exchange;

- "Shanghai Hutchison Pharmaceuticals" are to Shanghai Hutchison Pharmaceuticals Limited, our non-consolidated joint venture with Shanghai Pharmaceuticals in which we have a 50% interest;

- "Shanghai Pharmaceuticals" are to Shanghai Pharmaceuticals Holding Co., Ltd., a leading pharmaceutical company in China listed on the Shanghai Stock Exchange and the Hong Kong Stock Exchange;

- "Sinopharm" are to Sinopharm Group Co. Ltd., a leading distributor of pharmaceutical and healthcare products and a leading supply chain service provider in China listed on the Hong Kong Stock Exchange;

- "U.S." or "United States" are to the United States of America;

- "$" or "U.S. dollars" are to the legal currency of the United States; and

- "£" or "pound sterling" are to the legal currency of the United Kingdom.

References in this annual report to our "Oncology/Immunology" operations are to all activities related to oncology/immunology, including sales, marketing, manufacturing and research and development with respect to our drugs and drug candidates, and references to our "Other Ventures" are to all of our other businesses.

Our reporting currency is the U.S. dollar. In addition, this annual report also contains translations of certain foreign currency amounts into dollars for the convenience of the reader. Unless otherwise stated, all translations of pound sterling into U.S. dollars were made at £1.00 to $1.21, all translations of RMB into U.S. dollars were made at RMB6.96 to $1.00 and all translations of HK dollars into U.S. dollars were made at HK$7.8 to $1.00, which are the exchange rates used in our audited consolidated financial statements as of December 31, 2022. We make no representation that the pound sterling, HK dollar or U.S. dollar amounts referred to in this annual report could have been or could be converted into U.S. dollars, pounds sterling or HK dollars, as the case may be, at any particular rate or at all.

Trademarks and Service Marks

We own or have been licensed rights to trademarks, service marks and trade names for use in connection with the operation of our business, including, but not limited to, the trademarks “Hutchison”, “Chi-Med”, “Hutchison China MediTech”, “HUTCHMED”, “Elunate”, “Sulanda”, “Orpathys”, “Tazverik” and the logos used by HUTCHMED Limited. All other trademarks, service marks or trade names appearing in this annual report that are not identified as marks owned by us are the property of their respective owners.

Solely for convenience, the trademarks, service marks and trade names referred to in this annual report are listed without the ®, ™ and (sm) symbols, but we will assert, to the fullest extent under applicable law, our applicable rights in these trademarks, service marks and trade names.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This annual report contains forward-looking statements made under the “safe harbor” provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The words “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “goal,” “intend,” “may,” “might,” “objective,” “plan,” “potential,” “predict,” “project,” “positioned,” “seek,” “should,” “target,” “will,” “would,” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are based on current expectations, estimates, forecasts and projections about our business and the industry in which we operate and management’s beliefs and assumptions, are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors. These forward-looking statements include statements regarding:

- the initiation, timing, progress and results of our or our collaboration partners’ pre-clinical and clinical studies, and our research and development programs;
- our or our collaboration partners’ ability to advance our drug candidates into, and/or successfully complete, clinical studies;
- the timing of regulatory filings and the likelihood of favorable regulatory outcomes and approvals;
- regulatory developments in China, the United States and other countries;
- the ability of our oncology drug sales team to effectively develop and execute promotional and marketing activities to support the marketing and sales of our approved drug candidates;
- the timing, progress and results of our commercial launches, the rate and degree of market acceptance and potential market for any of our approved drug candidates;
- the pricing and reimbursement of our and our joint ventures’ products and our approved drug candidates;
- our ability to contract on commercially reasonable terms with contract research organizations, or CROs, third-party suppliers and manufacturers;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our or our joint ventures’ products and our drug candidates;
- the ability of third parties with whom we contract to successfully conduct, supervise and monitor clinical studies for our drug candidates;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to obtain additional funding for our operations;

- the potential benefits of our collaborations and our ability to enter into future collaboration arrangements;
- the ability and willingness of our collaborators to actively pursue development activities under our collaboration agreements;
- our receipt of milestone or royalty payments, service payments and manufacturing costs pursuant to our strategic alliances with AstraZeneca AB (publ), or AstraZeneca, Lilly (Shanghai) Management Company Limited, or Eli Lilly and Takeda Pharmaceuticals International AG, or Takeda;
- our financial performance;
- our ability to attract and retain key scientific and management personnel;
- our relationship with our joint venture and collaboration partners;
- developments relating to our competitors and our industry, including competing drug products;
- changes in our tax status or the tax laws in the jurisdictions that we operate;
- developments in our business strategies and business plans; and
- the extent of the impact of the COVID-19 pandemic, including the duration, spread, severity of the COVID-19 pandemic, the duration and scope of related government orders and restrictions and the extent of the impact of the COVID-19 pandemic on the global economy.

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. As a result, any or all of our forward-looking statements in this annual report may turn out to be inaccurate. We have included important factors in the cautionary statements included in this annual report on Form 20-F, particularly in the section of this annual report on Form 20-F titled "Risk Factors," that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Moreover, we operate in a highly competitive and rapidly changing environment in which new risks often emerge. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make.

You should read this annual report and the documents that we reference herein and have filed as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained herein are made as of the date of the filing of this annual report, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

In addition, this annual report contains statistical data and estimates that we have obtained from industry publications and reports generated by third-party market research firms. Although we believe that the publications, reports and surveys are reliable, we have not independently verified the data and cannot guarantee the accuracy or completeness of such data. You are cautioned not to give undue weight to this data. Such data involves risks and uncertainties and are subject to change based on various factors, including those discussed above.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. Reserved.

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors.

HUTCHMED (China) Limited is a Cayman Islands holding company which conducts its operations in China through its PRC subsidiaries (our corporate group does not include any variable interest entities). We face various legal and operational risks and uncertainties as a company with substantial operations in China. The PRC government has significant authority to exert influence on the ability of a company with substantial operations in China, like us, to conduct its business, accept foreign investments or be listed on a U.S. stock exchange. For example, we face risks associated with PRC regulatory approvals of offshore offerings, anti-monopoly regulatory actions, cybersecurity, data privacy and from U.S. regulators if there is a lack of inspection from the U.S. Public Company Accounting Oversight Board, or PCAOB, on our auditors, which is further discussed below under "—Holding Foreign Companies Accountable Act" and in various risk factors in this section. The PRC government may also intervene with or influence our operations as the government deems appropriate to further regulatory, political and societal goals. The PRC government publishes from time to time new policies that can significantly affect our industry in which we operate and we cannot rule out the possibility that it will in the future further release regulations or policies regarding our industry that could adversely affect our business, financial condition and results of operations. Any such action, once taken by the PRC government, could cause the value of our ADSs and ordinary shares to significantly decline or in extreme cases, become worthless.

Holding Foreign Companies Accountable Act

Pursuant to the Holding Foreign Companies Accountable Act, or the HFCAA if the SEC determines that we have filed audit reports issued by a registered public accounting firm that has not been subject to inspections by the PCAOB for two consecutive years, the SEC will prohibit our shares or the ADSs from being traded on a national securities exchange or in the over-the-counter trading market in the United States. On December 16, 2021, the PCAOB issued a report to notify the SEC of its determination that the PCAOB was unable to inspect or investigate completely registered public accounting firms headquartered in mainland China and Hong Kong, including our auditor. In March 2022, the SEC conclusively listed us as a Commission-Identified Issuer under the HFCAA following the filing of our annual report on Form 20-F for the fiscal year ended December 31, 2021. On December 15, 2022, the PCAOB issued a report that vacated its December 16, 2021 determination and removed mainland China and Hong Kong from the list of jurisdictions where it is unable to inspect or investigate completely registered public accounting firms. For this reason, we do not expect to be identified as a Commission-Identified Issuer under the HFCAA after we file this annual report on Form 20-F. Each year, the PCAOB will determine whether it can inspect and investigate completely audit firms in mainland China and Hong Kong, among other jurisdictions. If PCAOB determines in the future that it no longer has full access to inspect and investigate completely accounting firms in mainland China and Hong Kong and we continue to use an accounting firm headquartered in one of these jurisdictions to issue an audit report on our financial statements filed with the Securities and Exchange Commission, we would be identified as a Commission-Identified Issuer following the filing of the annual report on Form 20-F for the relevant fiscal year. There can be no assurance that we would not be identified as a Commission-Identified Issuer for any future fiscal year, and if we were so identified for two consecutive years, we would become subject to the prohibition on trading under the HFCAA. See Item 3.D. “Risk Factors—Risks Relating to our ADSs—The PCAOB had historically been unable to inspect our auditor in relation to their audit work performed for our financial statements and the inability of the PCAOB to conduct inspections of our auditor in the past has deprived our investors with the benefits of such inspections.” And Item 3.D. “ Risk Factors—Risks Relating to our ADSs—Our ADSs may be prohibited from trading in the United States under the HFCAA in the future if the PCAOB is unable to inspect or investigate completely auditors located in China. The delisting of the ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment.”

Permissions, Approvals, Licenses and Permits Required from the PRC Authorities for Our Operations and for the Offering of Our Securities to Foreign Investors

We conduct our business primarily through our subsidiaries and joint ventures in China. Our operations in China are governed by PRC laws and regulations. As of the date of this annual report, we and our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, have obtained the requisite permissions, approvals, licenses and permits from the PRC government authorities that are material for the business operations of our subsidiaries and our joint ventures in China, including, among others, pharmaceutical manufacturing permits, business licenses, drug registration certificates and pharmaceutical distribution permits and no such material permission or approval has been denied. For a detailed discussion on the licenses and permits we and our non-consolidated joint venture are required to obtain as a pharmaceutical company operating in China, see Item 4.B. “Business Overview—Certificates and Permits”, “Business Overview—Regulations—Government Regulation of Pharmaceutical Product Development and Approval,” “Business Overview—Regulations—Coverage and Reimbursement” and “Business Overview—Regulations—Other Healthcare Laws.” Given the uncertainties of interpretation and implementation of relevant laws and regulations and the enforcement practice by relevant government authorities, we may be required to obtain additional requisite permissions, approvals, licenses, permits and filings for the operation of our business in the future. See also “Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs—Pharmaceutical companies in China are required to comply with extensive regulations and hold a number of permits and licenses to carry on their business. Our and our joint ventures’ ability to obtain and maintain these regulatory approvals is uncertain, and future government regulation may impose additional burdens on our operations.”

Furthermore, in connection with our historical issuance of securities to foreign investors, under currently effective PRC laws, regulations and regulatory rules, as of the date of this annual report, we and our non-consolidated joint venture are not currently required to obtain permissions from the China Securities Regulatory Commission (the "CSRC"), and we have not received any formal notice from any PRC authority indicating that we should apply for or are otherwise subject to cybersecurity review or security assessment. In addition, we and our non-consolidated joint venture have not been asked to obtain such permissions by any PRC authority or received any denial to do so. However, the PRC government has recently indicated an intent to exert more oversight and control over offerings that are conducted overseas and/or foreign investment in China-based issuers. For example, the CSRC published the Trial Measures and Listing Guidelines (defined below) on February 17, 2023, designed to regulate overseas securities offerings by PRC domestic companies. Given the recent nature of the introduction of the Trial Measures and Listing Guidelines, and the fact that the Trial Measures and Listing Guidelines are not due to become effective until March 31, 2023, there remains significant uncertainty as to the enactment, interpretation and implementation of regulatory requirements related to overseas securities offerings and other capital markets activities.

If (i) we mistakenly conclude that certain regulatory filings, permissions and approvals are not required or (ii) applicable laws, regulations, or interpretations change and (iii) we are required to obtain such filings, permissions or approvals in the future, but fail to receive or maintain such filings, permissions or approvals, we may face sanctions by the CSRC, the Cyberspace Administration of China (the "CAC") or other PRC regulatory agencies. In addition, rules and regulations in China can change quickly with little advance notice. These regulatory agencies may impose fines and penalties on our operations in China, limit our operations in China, limit our ability to pay dividends outside of China, limit our ability to list on stock exchanges outside of China or offer our securities to foreign investors or take other actions that could have a material adverse effect on our business, financial condition, results of operations and prospects, as well as the trading price of our securities. Our non-consolidated joint venture faces the same risks as well. See also "Other Risks and Risks Relating to Doing Business in China—The PRC government exerts substantial influence over the manner in which we conduct our business activities. Its oversight and discretion over our business could result in a material adverse change in our operations and the value of our ordinary shares and ADSs. Changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system could materially and adversely affect us." and "—The PRC government may intervene in our offerings conducted overseas or on foreign investment in China-based issuers, which could result in a material change in our operations and our ordinary shares and ADSs could decline in value or become worthless."

Cash Flows Through Our Organization

HUTCHMED (China) Limited is a Cayman Islands incorporated holding company with no material operations of its own. We conduct our operations primarily in China through our PRC subsidiaries and PRC joint ventures, collectively referred to as the Onshore Entities below. HUTCHMED (China) Limited has an indirect equity ownership interest in all Onshore Entities through offshore Hong Kong-incorporated holding companies, and it has received funding through various capital markets transactions (e.g., offerings and private placements of equity securities). We also fund our operations through cash flows generated and dividend payments from our Oncology/Immunology and Other Ventures operations (substantially all of which have been generated in China), service and milestone and upfront payments from our collaboration partners to our PRC subsidiaries, and bank loans to our subsidiaries.

We utilize a portion of our funds outside of China to support the operations of our subsidiaries in China through capital contributions and/or shareholder loans, which are the only methods by which we can fund our subsidiaries under PRC laws and regulations. Such capital contributions and shareholder loans are subject to the satisfaction of applicable government registration and approval requirements in China and limitations on the amount of shareholder loans relative to the amount of total capital contributions. If such subsidiaries generate sufficient income, they may repay shareholder loans or distribute retained earnings through cash dividends as determined by their respective board of directors. Our PRC subsidiaries are permitted to pay dividends only out of their retained earnings, if any, as determined in accordance with PRC accounting standards and regulations. Furthermore, our PRC subsidiaries are required to make appropriations to certain statutory reserve funds or may make appropriations to certain discretionary funds, which are not distributable as cash dividends except in the event of a solvent liquidation of the companies. The amount of any repayment of shareholder loans or dividend payments can be distributed to our various offshore subsidiaries through our offshore Hong Kong-incorporated holding companies. For more information, see Item 3.D. "Risk Factors—Other Risks and Risks Relating to Doing Business in China—Restrictions on currency exchange may limit our ability to receive and use our revenue effectively." and Item 4.B. "Business Overview—Regulations—PRC Regulation of Foreign Currency Exchange, Offshore Investment and State-Owned Assets—Regulation on Investment in Foreign invested Enterprises." Our joint ventures in China do not require intra-group funding as they have been profitable. Service and milestone and upfront payments from our collaboration partners are received directly by our PRC subsidiaries and reinvested into their operations.

For the years ended December 31, 2022, 2021 and 2020, HUTCHMED provided funds to its PRC subsidiaries of $310.0 million, $230.0 million and $188.0 million, respectively, of which $100.0 million, $100.0 million and $40.0 million, respectively, were in the form of capital contributions and $210.0 million, $130.0 million and $148.0 million, respectively, were in the form of shareholder loans. Additionally, during the years ended December 31, 2022 and 2021, shareholder loans of approximately $3.4 million and $2.0 million was repaid by a PRC subsidiary, respectively. There were no transfers of assets other than transfers of cash to/from PRC subsidiaries in 2022, 2021 and 2020.

For the years ended December 31, 2022, 2021 and 2020, the respective Hong Kong immediate holding company of our onshore non-consolidated joint ventures (Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan prior to its divestment in September 2021) received dividends totaling approximately $43.7 million, $49.9 million and $86.7 million, respectively. These dividends were subject to a 5% withholding tax upon distribution from the onshore non-consolidated joint ventures to their respective Hong Kong immediate holding company.

HUTCHMED also conducts operations outside of China through subsidiaries in the U.S. and E.U. Such subsidiaries have entered into service agreements with our PRC subsidiaries pursuant to which cash is transferred by our PRC subsidiaries to support their operations via the settlement of service invoices based on actual activities.

We have comprehensive cash management policies in place, including specific policies with respect to fund transfers through our organization. Our management regularly monitors the liquidity position and funding requirements of our subsidiaries and joint ventures. When funding is required by our operations in China, a thorough assessment is performed on the purpose of the funding (e.g., R&D investment, capital expenditures, etc.), the amount of funding and the form of injection (i.e., shareholder loans or capital contributions). Conversely, when a dividend distribution is to be made by an onshore joint venture, a similar assessment is performed on the cash flow forecast, sufficiency of funds and related factors. All necessary approvals are obtained at the chairman and chief executive officer levels and the board of directors for the relevant entities prior to any transfer. All such transfers and distributions are reviewed and approved by the relevant authorities where necessary, including the State Administration of Foreign Exchange, or SAFE, and the State Administration for Market Regulations, or SAMR. Our cash management policies and procedures also govern the management of any funds that are not yet required by our operations. Such funds are retained by our subsidiaries outside of China mainly in the form of short-term investments, such as time deposits with major banks in Hong Kong.

We have never declared or paid dividends on our ordinary shares. There have been no transfers, dividends or distributions made to U.S. investors to date. We currently expect to retain all future earnings for use in the operation and expansion of our business and do not have any present plan to pay any dividends. The declaration and payment of any dividends in the future will be determined by our board of directors in its discretion, and will depend on a number of factors, including our earnings, capital requirements, overall financial condition, and contractual restrictions. See Item 8. "Financial Information—A.8 Dividend Policy" and Item 3.D. "Risk Factors—Risks Relating to Our ADSs—We do not currently intend to pay dividends on our securities, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of the ADSs."

You should carefully consider all of the information in this annual report before making an investment in the ADSs. Below please find a summary of the principal risks and uncertainties we face, organized under relevant headings. In particular, as we are a China-based company incorporated in the Cayman Islands, you should pay special attention to subsections headed "Item 3. Key Information-3.D. Risk Factors-Other Risks and Risks Related to Doing Business in China."

The following summarizes some, but not all, of the risks provided below. Please carefully consider all of the information discussed in this Item 3.D. "Risk Factors" in this annual report for a more thorough description of these and other risks.

Risks Relating to Our Financial Position and Need for Capital

- Risks relating to our need for additional funding
- Risks relating to our existing and future indebtedness

Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates

- Risks relating to our approach to the discovery and development of drug candidates and the lengthy, expensive and uncertain clinical development process

- Risks relating to expediting regulatory review, obtaining and maintaining regulatory approval and ongoing regulatory review for our drug candidates
- Risks relating to the commercialization of our drug candidates
- Risks relating to undesirable side effects of our drug candidates
- Risks relating to competition in discovering, developing and commercializing drugs
- Risks relating to our collaboration partners with respect to clinical trials, marketing and distribution
- Risks relating to our international operations

Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs

- Risks relating to obtaining and maintaining permits and licenses for our and our joint ventures' pharmaceutical operations in China
- Risks relating to leveraging our Other Ventures' prescription drug business to commercialize our internally developed drug candidates
- Risks relating to competition in selling our approved, internally developed drugs and drugs of our Other Ventures
- Risks relating to maintaining and enhancing the brand recognition of our drugs
- Risks relating to the availability of reimbursement of our drugs, the lack of which could diminish our sales or profitability
- Risks relating to counterfeit products in China
- Risks relating to rapid changes in the pharmaceutical industry rendering our products obsolete
- Risks relating to cultivating or sourcing raw materials
- Risks relating to adverse publicity of us, our joint ventures or our products

Risks Relating to Our Dependence on Third Parties

- Risks relating to disagreements with current or future collaboration partners which we rely on for certain drug development activities including the conducting of clinical trials
- Risks relating to relying on third party suppliers for the active pharmaceutical ingredients in our drug candidate and drug products
- Risks relating to our collaboration partners or our CROs' failure to comply with regulatory requirements pertaining to clinical trials
- Risks relating to our collaboration partners, principal investigators, CROs and other third-party contractors and consultants engaging in misconduct or other improper activities
- Risks relating to relying on third parties to construct our new manufacturing facility in Shanghai
- Risks relating to relying on distributors for logistics and distributions services

- Risks relating to the availability of benefits currently enjoyed by virtue of our association with CK Hutchison

Other Risks and Risks Relating to Doing Business in China

- Risks relating to COVID-19
- Risks relating to compliance with privacy and cybersecurity laws, information security policies and contractual obligations related to data privacy and security and any information technology or data security failures
- Risks relating to product liability claims or lawsuits
- Risks relating to liabilities under anti-corruption laws, environmental, health and safety laws and laws relating to equity incentive plans
- Risks relating to changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system, China's currency exchange limits and PRC government tax incentives or treatment

Risks Relating to Intellectual Property

- Risks relating to our, our joint ventures and our collaboration partners' abilities to protect and enforce intellectual property rights and maintain confidentiality of trade secrets
- Risks relating to infringing upon third parties' intellectual property rights

Risks Relating to our ADSs

- Risks relating to being delisted from the Nasdaq if the PCAOB is unable to inspect or investigate completely auditors located in China in the future
- Risks relating to our largest shareholder which may limit the ability of other shareholders to influence corporate matters

You should carefully consider the following risk factors in addition to the other information set forth in this annual report. If any of the following risks were actually to occur, our company's business, financial condition and results of operations prospects could be adversely affected and the value of our ADSs would likely suffer.

Risks Relating to Our Financial Position and Need for Capital

We may need substantial additional funding for our product development programs and commercialization efforts. If we are unable to raise capital on acceptable terms when needed, we could incur losses and be forced to delay, reduce or eliminate such efforts.

We expect to incur significant expenses in connection with our ongoing activities, particularly as we or our collaboration partners advance the clinical development of our clinical drug candidates which are currently in active or completed clinical studies in various countries. We will incur significant expenses as we continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other future drug candidates. In addition, we have incurred and expect to continue to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution in China for Sulanda (surufatinib), our unpartnered drug product approved in China in December 2020, and any of our other unpartnered drug candidates that may be approved in the future. In particular, the costs that may be required for the manufacture of any drug candidate that receives regulatory approval may be substantial as we may have to modify or increase the production capacity at our current manufacturing facilities or contract with third-party manufacturers. We may also incur expenses as we create additional infrastructure, such as our new manufacturing facility under construction in Shanghai. Accordingly, we may need to obtain substantial funding in connection with our continuing operations through public or private equity offerings, debt financings, collaborations or licensing arrangements or other sources. If we are unable to raise capital when needed or on attractive terms, we could incur losses and be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Our net cash used in operating activities was $62.1 million, $204.2 million and $268.6 million for the years ended December 31, 2020, 2021 and 2022, respectively. We believe, however, that our expected cash flow from operations, including dividends from our Other Ventures and milestone and other payments from our collaboration partners, our cash and cash equivalents and short-term investments as well as our unutilized bank facilities as of December 31, 2022, will enable us to fund our operating expenses, debt service and capital expenditure requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the number and development requirements of the drug candidates we pursue;
- the scope, progress, timing, results and costs of researching and developing our drug candidates, and conducting pre-clinical and clinical trials;
- the cost, timing and outcome of regulatory review of our drug candidates;
- the cost and timing of commercialization activities, including product manufacturing, marketing, sales and distribution, for our drug candidates for which we have received regulatory approval;
- the amount and timing of any upfront milestone or royalty payments, service payments and reimbursement of manufacturing costs from our collaboration partners, with whom we cooperate with respect to the development and potential commercialization of certain of our drug candidates;
- the cash received from commercial sales of drug candidates for which we have received regulatory approval;
- our ability to establish and maintain strategic partnerships, collaboration, licensing or other arrangements and the financial terms of such agreements;
- the cost, timing and outcome of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the costs of operating as a public company listed in Hong Kong, the United States and United Kingdom.

Identifying potential drug candidates and conducting pre-clinical testing and clinical trials is a time-consuming, expensive and uncertain process that may take years to complete, and our commercial revenue will be derived from sales of products that will not be commercially available unless and until we receive regulatory approval. We may never generate the necessary data or results required for certain drug candidates to obtain regulatory approval, and even if approved, they may not achieve commercial success. Accordingly, we will need to continue to rely on financing to achieve our business objectives. Adequate financing may not be available to us on acceptable terms, or at all.

Raising capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to technologies or drug candidates.

We expect to finance our cash needs in part through cash flow from our operations, including dividends from our Other Ventures, and we may also rely on raising capital through a combination of public or private equity offerings, debt financings and/or license and development agreements with collaboration partners. In addition, we may seek capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise capital through the sale of equity or convertible debt securities (including potential further listings on other stock exchanges), the ownership interest of our shareholders may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect the rights of our existing shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. Additional debt financing would also result in increased fixed payment obligations.

In addition, if we raise funds through collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us. We may also lose control of the development of drug candidates, such as the pace and scope of clinical trials, as a result of such third-party arrangements. If we are unable to raise funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

Our outstanding indebtedness combined with current and future financial obligations and contractual commitments, including any additional indebtedness beyond our current facilities with HSBC and Bank of China could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, and prepayment and repayment fees and penalties, thereby reducing money available to fund working capital, capital expenditures, product development and other general corporate purposes;

- increasing our vulnerability to adverse changes in general economic, industry and market conditions;

- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;

- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and

- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and short-term investments. Nevertheless, we may not have sufficient funds, and may be unable to arrange for financing, to pay the amounts due under our existing debt. Failure to make payments or comply with other covenants under our existing debt instruments could result in an event of default and acceleration of amounts due.

We have historically incurred significant net operating cash outflows, and may continue to experience net cash outflow from operating activities.

Investment in biopharmaceutical drug development is highly speculative. It entails substantial upfront expenditures and significant risk that a drug candidate might fail to gain regulatory approval or become commercially viable. We continue to incur significant expenses related to our ongoing operations. For a detailed discussion of our net cash used in operating activities, see Item 5.B. "Operating and Financial Review and Prospects", "Liquidity and Capital Resources." We expect to incur significant expenses, particularly research and development expenses, for the foreseeable future as we expand our development of, and seek regulatory approvals for, our drug candidates. Typically, it takes many years to develop one new drug from the drug discovery stage to the time it is available for treating patients. Our ability to improve our cash flow depends on a number of variables, including the number and scope of our drug development programs and the associated costs of those programs, the cost of commercializing any approved products, our ability to generate revenues and the timing and amount of milestones and other payments we make or receive through arrangements with third parties. Our failure to generate positive cash flow from operations may adversely affect our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. There is no assurance that we will be able to generate sufficient net cash inflows from operating activities, which could have adverse effects on our long-term viability.

We face risks with our short-term investments and in collecting our accounts receivables.

Our short-term investments are bank deposits with maturities of more than three months but less than one year. Our short-term investments were $634.2 million and $317.7 million as of December 31, 2021 and 2022, respectively, and are placed with major financial institutions. These investments may earn yields substantially lower than expected. Failure to realize the benefits we expected from these investments may materially and adversely affect our business and financial results. To date, we have experienced no loss or lack of access to our invested cash or cash equivalents; however, we can provide no assurance that access to our invested cash and cash equivalents will not be impacted by adverse conditions in the financial and credit markets.

Our accounts receivable balance, net of allowance for credit losses, totaled $83.6 million and $98.0 million as of December 31, 2021 and 2022, respectively. We have policies and procedures in place to ensure that sales are made to customers with an appropriate credit history. We perform periodic credit evaluations of our customers and monitor risk factors and forward-looking information, such as country risk, when determining credit limits for customers. However, there can be no assurance such policies and procedures will effectively limit our credit risk and enable us to avoid losses, which could adversely affect our financial condition and results of operations. In addition, amounts due to us are not covered by collateral or credit insurance. If we fail to collect all or part of such accounts receivable in a timely manner, or at all, our financial condition may be materially and adversely affected.

Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates

Historically, our in-house research and development division, which is included in our Oncology/Immunology operations, has not generated significant profits or has operated at a net loss. Our future profitability is dependent on the successful commercialization of our drug candidates.

To date, fruquintinib, surufatinib and savolitinib (marketed as Elunate, Sulanda and Orpathys, respectively in China) are our only internally developed drug candidates that have been approved for sale in China. We do not expect our Oncology/Immunology operations to be significantly profitable unless and until we generate substantial revenues from Elunate, Sulanda and Orpathys and can successfully commercialize our other drug products. We expect to incur significant sales and marketing costs as we prepare to commercialize our drug candidates.

Successful commercialization of our drug candidates is subject to many risks. Elunate is marketed in collaboration with our partner, Eli Lilly. Beginning in October 2020, we assumed responsibility for the development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in China. Sulanda is marketed by us without the support of a collaboration partner. Orpathys is marketed in collaboration with our partner, AstraZeneca. Elunate, Sulanda and Orpathys are the first innovative oncology drugs we, as an organization, have commercialized, and there is no guarantee that we will be able to successfully commercialize them or any of our other drug candidates for their approved indications. There are numerous examples of failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us. There are many factors that could cause the commercialization of Elunate, Sulanda, Orpathys or our other drug products to be unsuccessful, including a number of factors that are outside our control. In the case of Elunate, for example, the third-line metastatic colorectal cancer, or mCRC, patient population in China may be smaller than we estimate or physicians may be unwilling to prescribe, or patients may be unwilling to take, Elunate for a variety of reasons. Additionally, any negative development for fruquintinib, surufatinib or savolitinib in clinical development in additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Elunate, Sulanda or Orpathys in China and globally. For example, in April 2022, the FDA issued a Complete Response Letter ("CRL") regarding the NDA for surufatinib for the treatment of non-pancreatic neuroendocrine tumors (NETs) and pancreatic NETs and determined that the data package submitted does not support an approval in the U.S. at the time. We have subsequently withdrawn our submission to the FDA and the EMA for surufatinib. Thus, significant uncertainty remains regarding the commercial potential of Elunate, Sulanda and Orpathys.

We may not achieve profitability after generating revenues from Elunate, Sulanda, Orpathys and/or our other drug candidates, if ever. If the commercialization of Elunate, Sulanda, Orpathys and/or our other drug candidates is unsuccessful or perceived as disappointing, our stock price could decline significantly and the long-term success of the product and our company could be harmed.

All of our drug candidates, other than fruquintinib, surufatinib and savolitinib for approved indications in China, are still in development. If we are unable to obtain regulatory approval and ultimately commercialize our drug candidates, or if we experience significant delays in doing so, our business will be materially harmed.

All of our drug candidates are still in development, including fruquintinib, surufatinib and savolitinib which have been approved in China for the treatment of third-line mCRC, non-pancreatic NETs and advanced pancreatic NETs, and non-small cell lung cancer, or NSCLC, respectively, but are still in development in the United States and other jurisdictions for these and other indications.

Although we receive certain payments from our collaboration partners, including upfront payments and payments for achieving certain development, regulatory or commercial milestones, for certain of our drug candidates, our ability to generate revenue from our drug candidates is dependent on their receipt of regulatory approval for and successful commercialization of such products, which may never occur. Each of our drug candidates in development will require additional pre-clinical and/or clinical trials, regulatory approval in multiple jurisdictions, manufacturing supply, substantial investment and significant marketing efforts before we generate any revenue from product sales. The success of our drug candidates will depend on several factors, including the following:

- successful completion of pre-clinical and/or clinical trials;
- successful enrollment in, and completion of, clinical trials;
- receipt of regulatory approvals from applicable regulatory authorities for planned clinical trials, future clinical trials, drug registrations or post-approval trials;
- successful completion of all safety studies required to obtain regulatory approval and/or fulfillment of post-approval requirements in the United States, China and other jurisdictions for our drug candidates;
- adapting our commercial manufacturing capabilities to the specifications for our drug candidates for clinical supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drug candidates;
- launching commercial sales of our drug candidates, if and when approved, whether alone or in collaboration with others;

- acceptance of the drug candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims; and
- maintaining a continued acceptable safety profile of the drug candidates following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates, which would materially harm our business.

Our primary approach to the discovery and development of drug candidates focuses on the inhibition of kinases, some of which are unproven.

A primary focus of our research and development efforts is on identifying kinase targets for which drug compounds previously developed by others affecting those targets have been unsuccessful due to limited selectivity, off-target toxicity and other problems. We then work to engineer drug candidates which have the potential to have superior efficacy, safety and other features as compared to such prior drug compounds. We also focus on developing drug compounds with the potential to be global best-in-class/next-generation therapies for validated kinase targets.

Even if we are able to develop compounds that successfully target the relevant kinases in pre-clinical studies, we may not succeed in demonstrating safety and efficacy of the drug candidates in clinical trials. Even if we are able to demonstrate safety and efficacy of compounds in certain indications in certain jurisdictions, we may not succeed in demonstrating the same in other indications or same indications in other jurisdictions. As a result, our efforts may not result in the discovery or development of drugs that are commercially viable or are superior to existing drugs or other therapies on the market. While the results of pre-clinical studies, early-stage clinical trials as well as clinical trials in certain indications have suggested that certain of our drug candidates may successfully inhibit kinases and may have significant utility in several cancer indications, potentially in combination with other cancer drugs, chemotherapy and immunotherapies, we have not yet demonstrated efficacy and safety for many of our drug candidates in later stage clinical trials.

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we must limit our research programs to specific drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. In addition, if we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements when it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

The regulatory approval processes of the U.S. Food and Drug Administration, or FDA, National Medical Products Administration of China, or NMPA, and comparable authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our ability to generate revenue will be materially impaired.

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA, NMPA and other regulatory agencies in the United States and China and by comparable regulatory authorities in other countries. Securing regulatory approval requires the submission of extensive pre-clinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate’s safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

The process of obtaining regulatory approvals in the United States, China and other countries is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted New Drug Application, or NDA, pre-market approval or equivalent application types, may cause delays in the approval or rejection of an application. The FDA, NMPA and comparable regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional pre-clinical, clinical or other studies. Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA, NMPA or comparable regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, NMPA or comparable regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, NMPA or comparable regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA, NMPA or comparable regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA, NMPA or comparable regulatory authorities may fail to approve the manufacturing processes for our clinical and commercial supplies;
- the approval policies or regulations of the FDA, NMPA or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- the FDA, NMPA or comparable regulatory authority may prioritize treatments for emerging health crises, such as COVID-19, resulting in delays for our drug candidates;
- the FDA, NMPA or comparable regulatory authorities may restrict the use of our products to a narrow population; and
- our collaboration partners or CROs that are retained to conduct the clinical trials of our drug candidates may take actions that materially and adversely impact the clinical trials.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

Furthermore, even though the NMPA has granted approval for fruquintinib and surufatinib for use in third-line mCRC and NET patients, respectively, and approval for savolitinib for lung cancer with MET exon 14 skipping alterations, we are still subject to substantial, ongoing regulatory requirements. See "—Even if we receive regulatory approval for our drug candidates, we are subject to ongoing obligations and continued regulatory review, which may result in significant additional expense."

If the FDA, NMPA or another regulatory agency revokes its approval of, or if safety, efficacy, manufacturing or supply issues arise with, any therapeutic that we use in combination with our drug candidates, we may be unable to market such drug candidate or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.

We are currently developing combination therapies using our savolitinib, fruquintinib, surufatinib and other drug candidates with various immunotherapies, targeted therapies and/or other therapies. For example, we are currently developing savolitinib in combination with immunotherapy (Imfinzi) and targeted therapy (Tagrisso). However, we did not develop and we do not manufacture or sell Imfinzi, Tagrisso or any other therapeutic we use in combination with our drug candidates. We may also seek to develop our drug candidates in combination with other therapeutics in the future.

If the FDA, NMPA or another regulatory agency revokes its approval, or does not grant approval, of any of these and other therapeutics we use in combination with our drug candidates, we will not be able to market our drug candidates in combination with such therapeutics. If safety or efficacy issues arise with these or other therapeutics that we seek to combine with our drug candidates in the future, we may experience significant regulatory delays, and we may be required to redesign or terminate the applicable clinical trials. In addition, if manufacturing or other issues result in a supply shortage of these or any other combination therapeutics, we may not be able to complete clinical development of savolitinib, fruquintinib, surufatinib and/or any other of our drug candidates on our current timeline or at all.

Even if one or more of our drug candidates were to receive regulatory approval for use in combination with a therapeutic, we would continue to be subject to the risk that the FDA, NMPA or another regulatory agency could revoke its approval of the combination therapeutic, or that safety, efficacy, manufacturing or supply issues could arise with one of these combination therapeutics. This could result in Orpathys, Elunate, Sulanda or one of our other products being removed from the market or being less successful commercially.

We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current drug candidates, and will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market drugs or are pursuing the development of therapies in the field of kinase inhibition for cancer and other diseases. Some of these competitive drugs and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Specifically, there are a large number of companies developing or marketing treatments for cancer and immunological diseases, including many major pharmaceutical and biotechnology companies.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA, NMPA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Clinical development involves a lengthy and expensive process with an uncertain outcome.

There is a risk of failure for each of our drug candidates. It is difficult to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining regulatory approval from regulatory authorities for the sale of any drug candidate, we or our collaboration partners must complete pre-clinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement and can take many years to complete. The outcomes of pre-clinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain regulatory approval of their drug candidates. Our current or future clinical trials may not be successful.

Commencing each of our clinical trials is subject to finalizing the trial design based on ongoing discussions with the FDA, NMPA or other regulatory authorities. The FDA, NMPA and other regulatory authorities could change their position on the acceptability of our trial designs or clinical endpoints, which could require us to complete additional clinical trials or impose approval conditions that we do not currently expect. Successful completion of our clinical trials is a prerequisite to submitting an NDA or analogous filing to the FDA, NMPA or other regulatory authorities for each drug candidate and, consequently, the ultimate approval and commercial marketing of our drug candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all.

We and our collaboration partners may incur additional costs or experience delays in completing our pre-clinical or clinical trials, or ultimately be unable to complete the development and commercialization of our drug candidates.

We and our collaboration partners, including AstraZeneca, Eli Lilly, BeiGene Ltd., or BeiGene, Inmagene Biopharmaceuticals Co. Ltd., or Inmagene, Innovent Biologics (Suzhou) Co., Inc., or Innovent, Genor Biopharma Co. Ltd., or Genor, Shanghai Junshi Biosciences Co. Ltd., or Junshi and Epizyme, Inc. (a subsidiary of Ipsen Pharma SAS), or Epizyme, and Takeda may experience delays in completing our pre-clinical or clinical trials, and numerous unforeseen events could arise during, or as a result of, future clinical trials, which could delay or prevent us from receiving regulatory approval, including:

- regulators, institutional review boards, or IRBs, ethics committees or the China Human Genetic Resources Administration Office may not authorize us or our investigators to commence or conduct a clinical trial at a prospective trial site;

- we may experience delays in reaching, or we may fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, who conduct clinical trials on behalf of us and our collaboration partners, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- clinical trials may produce negative or inconclusive results, and we or our collaboration partners may decide, or regulators may require us or them, to conduct additional clinical trials or we may decide to abandon drug development programs;

- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- third-party contractors used in our clinical trials may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we or our collaboration partners add new clinical trial sites or investigators;

- we or our collaboration partners may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- the cost of clinical trials of our drug candidates may be greater than we anticipate;

- the supply or quality of our drug candidates, companion diagnostics, if any, or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate; and

- our drug candidates may have undesirable side effects or unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports may arise from pre-clinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our drug candidates.

We could encounter regulatory delays if a clinical trial is suspended or terminated by us or our collaboration partners, by, as applicable, the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, which is an independent group of experts that is formed to monitor clinical trials while ongoing, or by the FDA, NMPA or other regulatory authorities. Such authorities may impose a suspension or termination due to a number of factors, including: a failure to conduct the clinical trial in accordance with regulatory requirements or the applicable clinical protocols, inspection of the clinical trial operations or trial site by the FDA, NMPA or other regulatory authorities that results in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the FDA, NMPA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

If we or our collaboration partners are required to conduct additional clinical trials or other testing of our drug candidates beyond those that are currently contemplated, if we or our collaboration partners are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining regulatory approval for our drug candidates;

- not obtain regulatory approval at all;

- obtain approval for indications or patient populations that are not as broad as intended or desired;

- be subject to post-marketing testing requirements; or

- have the drug removed from the market after obtaining regulatory approval.

Our drug development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant pre-clinical study or clinical trial delays also could allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and prospects significantly.

If we or our collaboration partners experience delays or difficulties in the enrollment of patients in clinical trials, the progress of such clinical trials and our receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaboration partners may not be able to initiate or continue clinical trials for our drug candidates if we or our collaboration partners are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, NMPA or similar regulatory authorities. In particular, we and our collaboration partners have designed many of our clinical trials, and expect to design future trials, to include some patients with the applicable genomic alteration that causes the disease with a view to assessing possible early evidence of potential therapeutic effect. Genomically defined diseases, however, may have relatively low prevalence, and it may be difficult to identify patients with the applicable genomic alteration. In addition, for many of our trials, we focus on enrolling patients who have failed their first or second-line treatments, which limits the total size of the patient population available for such trials. The inability to enroll a sufficient number of patients with the applicable genomic alteration or that meet other applicable criteria for our clinical trials would result in significant delays and could require us or our collaboration partners to abandon one or more clinical trials altogether.

In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the total size and nature of the relevant patient population;
- the design and eligibility criteria for the clinical trial in question;
- the availability of an appropriate genomic screening test/companion diagnostic;
- the perceived risks and benefits of the drug candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the availability of competing therapies which are undergoing clinical trials;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients ; and
- the impact of the spread of infectious diseases, including but not limited to the duration and scope of related government orders and restrictions.

Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which could cause the value of our company to decline and limit our ability to obtain financing.

Our drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if any.

Undesirable side effects caused by our drug candidates could cause us or our collaboration partners to interrupt, delay or halt clinical trials or could cause regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA or other regulatory authorities. In particular, as is the case with all oncology drugs, it is likely that there may be side effects, for example, hand-foot syndrome, associated with the use of certain of our drug candidates. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA, NMPA or comparable regulatory authorities could order us to cease further development of or deny approval of our drug candidates for some or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our drug candidates could cause undesirable side effects related to off-target toxicity. Many of the currently approved tyrosine kinase inhibitors or TKIs have been associated with off-target toxicities because they affect multiple kinases. While we believe that the kinase selectivity of our drug candidates has the potential to significantly improve the unfavorable adverse off-target toxicity issues, if patients were to experience off-target toxicity, we may not be able to achieve an effective dosage level, receive approval to market, or achieve the commercial success we anticipate with respect to any of our drug candidates, which could prevent us from ever generating revenue or achieving profitability. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

Clinical trials assess a sample of the potential patient population. With a limited number of patients and duration of exposure, rare and severe side effects of our drug candidates may only be uncovered with a significantly larger number of patients exposed to the drug candidate. If our drug candidates receive regulatory approval and we or others identify undesirable side effects caused by such drug candidates (or any other similar drugs) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such drug candidates;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contra-indication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such drug candidates are distributed or administered, conduct additional clinical trials or change the labeling of the drug candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such drug candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our drug candidates; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected drug candidates and could substantially increase the costs of commercializing our drug candidates, if approved, and significantly impact our ability to successfully commercialize our drug candidates and generate revenue.

We and our collaboration partners have conducted and intend to conduct additional clinical trials for certain of our drug candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations or may require additional U.S.-based trials.

We and our collaboration partners have conducted, currently are conducting and intend in the future to conduct, clinical trials outside the United States, particularly in China where our Oncology/Immunology operations are headquartered as well as in other jurisdictions such as Australia, Japan, South Korea, the U.K., and various European countries.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted by qualified investigators in accordance with current good clinical practices, or GCPs, including review and approval by an independent ethics committee and receipt of informed consent from trial patients. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical trial conducted outside of the United States must be representative of the population for which we intend to seek approval in the United States. In addition, while these clinical trials are subject to applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also comply with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials conducted outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our ability to develop and market these or other drug candidates in the United States. In April 2022, we received a CRL from the FDA regarding the NDA for surufatinib for the treatment of pancreatic NETs and non-pancreatic NETs. The FDA determined that the current data package, based on two positive Phase III trials in China and one bridging study in the U.S., does not support an approval in the U.S. at this time. The CRL indicated that a multi-regional clinical trial is required for U.S. approval. We have subsequently withdrawn our submission to the FDA and the EMA for surufatinib.

In addition, there are risks inherent in conducting clinical trials in jurisdictions outside the United States including:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange fluctuations;
- manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- the risk that patient populations in such trials are not considered representative as compared to patient populations in the United States and other markets.

If we are unable to obtain and/or maintain priority review by the NMPA, fast track designation by the FDA, or another expedited registration pathway for our drug candidates, the time and cost we incur to obtain regulatory approvals may increase. Even if we receive such approvals, they may not lead to a faster development, review or approval process.

Under the Breakthrough Therapy Drug Review Procedures (For Trial Implementation), the Review and Approval Procedures for Conditional Approval of Drug Marketing Applications (For Trial Implementation), and the Priority Review and Approval Procedures for Drug Marketing Authorization (For Trial Implementation), the NMPA (or, where applicable, the National Health Commission, or the NHC) may grant priority review approval (i) to innovative drugs or new improved drugs undergoing clinical trials that are used to prevent and treat diseases that are seriously life-threatening or which seriously affect quality of life for which there is no effective prevention or treatment, or for which there is sufficient evidence to show obvious clinical advantages compared with existing treatments, (ii) to drugs undergoing clinical trials which meet the conditions for conditional approval specified in the Technical Guidelines for Conditional Approval of Drugs, (iii) to innovative drugs and new improved drugs which are in shortage, prevent and treat major infectious diseases and rare diseases, (iv) to new varieties, dosage forms and specifications that meet the physiological characteristics of children, (v) to vaccines (including innovative vaccines) urgently needed for control and prevention of diseases, and (vi) under other circumstances stipulated by the NMPA. Priority review provides a fast track process for drug registration. We have received priority review status for a number of our drug candidates, including for example fruquintinib for the treatment of advanced colorectal cancer, or CRC, savolitinib for the treatment of NSCLC and surufatinib for the treatment of advanced NET. We anticipate that we may seek priority review for certain of our other drug candidates in the future.

In the United States, if a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, we may apply for fast track designation by the FDA. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot be sure that the FDA would decide to grant it. We have sought and will likely continue to seek fast track designation for some of our drug candidates. For example, in June 2020, the FDA granted fast track designation to fruquintinib for metastatic CRC. Even if we receive fast track designation for a drug candidate, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

A failure to obtain and/or maintain priority review, fast track designation or any other form of expedited development, review or approval for our drug candidates would result in a longer time period to commercialization of such drug candidate, could increase the cost of development of such drug candidate and could harm our competitive position in the marketplace. In addition, even if we obtain priority review, there is no guarantee that we will experience a faster review or approval compared to non-accelerated registration pathways or that a drug candidate will ultimately be approved for sale.

Although we have obtained orphan drug designation for surufatinib for the treatment of pancreatic NETs in the United States, we may not be able to obtain or maintain the benefits associated with orphan drug status, including market exclusivity.

Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as affecting fewer than 200,000 individuals in the United States. We have obtained orphan drug designation from the FDA for surufatinib for the treatment of pancreatic NETs. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a seven-year period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same molecule for the same indication for that time period. We can provide no assurance that another drug will not receive marketing approval prior to our product candidates. Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, even after a drug is granted orphan exclusivity and approved, the FDA can subsequently approve another drug for the same condition before the expiration of the seven-year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Even if we receive regulatory approval for our drug candidates, we are subject to ongoing obligations and continued regulatory review, which may result in significant additional expense.

If the FDA, NMPA or a comparable regulatory authority approves any of our drug candidates, we will continue to be subject to extensive and ongoing regulatory requirements. For example, even though the NMPA has granted approval of fruquintinib, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for fruquintinib continue to be subject to the NMPA's oversight. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing processes.

Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-approval testing, sometimes referred to as Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the drug. In addition, regulatory policies may change or additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with any of our drugs that receive regulatory approval.

Once a drug is approved by the FDA, NMPA or a comparable regulatory authority for marketing, it is possible that there could be a subsequent discovery of previously unknown problems with the drug, including problems with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements. If any of the foregoing occurs with respect to our drug products, it may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA, NMPA or comparable regulatory authority to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug license approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources and could generate negative publicity. If we or our collaborators are not able to maintain regulatory compliance, regulatory approval that has been obtained may be lost and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

The incidence and prevalence for target patient populations of our drug candidates are based on estimates and third-party sources. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations for particular diseases based on various third-party sources and internally generated analysis and use such estimates in making decisions regarding our drug development strategy, including determining indications on which to focus in pre-clinical or clinical trials.

These estimates may be inaccurate or based on imprecise data. For example, the total addressable market opportunity will depend on, among other things, their acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the addressable markets may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the expertise of the members of our research and development team, as well as the other principal members of our management, including Weiguo Su, Ph.D., our Chief Executive Officer, Chief Scientific Officer and director. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time with three months' prior written notice. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified management, scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We have operations internationally and are subject to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects.

We have been involved in clinical and non-clinical development internationally for over a decade. Conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- applicable trade laws, tariffs, export quotas, custom duties or other trade restrictions and any changes to them;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

There can be no assurance that we will effectively manage the increased complexity without experiencing operating inefficiencies or control deficiencies. Such increased complexity may also lead to decisions to reposition our international operations to align them with our overall and evolving business strategy, including with our recent strategic change to focus on path to profitability. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We may be restricted from transferring our scientific data abroad.

On March 17, 2018, the General Office of the State Council promulgated the Measures for the Management of Scientific Data, or the Scientific Data Measures, which provides a broad definition of scientific data and relevant rules for the management of scientific data. According to the Scientific Data Measures, enterprises in China must seek governmental approval before any scientific data involving a state secret may be transferred abroad or to foreign parties. Further, any researcher conducting research funded at least in part by the Chinese government is required to submit relevant scientific data for management by the entity to which such researcher is affiliated before such data may be published in any foreign academic journal. Given that the term state secret is not clearly defined in the Scientific Data Measures, if and to the extent our research and development of drug candidates will be subject to the Scientific Data Measures and any subsequent laws as required by the relevant government authorities, we cannot assure you that we can always obtain relevant approvals for sending scientific data (such as the results of our pre-clinical studies or clinical trials conducted within China) abroad or to our foreign partners in China. The PRC Personal Information Protection Law, effective November 2021, provides that where a personal information processor needs to provide personal information outside the territory of the PRC due to business or other needs, it shall meet any of the following conditions: (i) it shall pass the security evaluation organized by the Cyberspace Administration of China ("CAC") in accordance with the provisions of Article 40 thereof, (ii) it shall have been certified by a specialized agency for protection of personal information in accordance with the provisions of the CAC, (iii) it shall enter into a contract with the overseas recipient under the standard contract formulated by the CAC, specifying the rights and obligations of both parties, or (iv) it shall meet other conditions prescribed by laws, administrative regulations or the CAC. If we are unable to obtain necessary approvals or meet the necessary requirements in a timely manner, or at all, our research and development of drug candidates may be hindered, which may materially and adversely affect our business, results of operations, financial conditions and prospects. If the relevant government authorities consider the transmission of our scientific data to be in violation of the requirements under the Scientific Data Measures, we may be subject to fines and other administrative penalties imposed by those government authorities.

If we expand our existing compassionate-use program or participate in additional compassionate-use programs, discrepancies among the regulations in different countries may lead to increased risk of adverse drug reactions and serious adverse events arising from the use of our drug candidates.

Compassionate-use programs are regulatory programs that facilitate access to investigational drugs for the treatment of patients with serious or immediately life-threatening diseases or conditions that lack therapeutic alternatives. Currently, there is no unified approach or standard practice to regulate compassionate-use programs or access to investigational drugs across countries. In China, the PRC Drug Administration Law provides that drugs in clinical trials intended for the treatment of serious life-threatening diseases without existing effective treatments may, upon review and informed consent, be administered to patients with the same conditions within the institution conducting the clinical trials, provided that such drugs may be beneficial as indicated by medical observation and such practice is in conformity with ethical principles. On May 9, 2022, the NMPA published the draft PRC Drug Administration Implementation Regulations for comment, of which Article 100 states that (i) with respect to experimental drugs undergoing clinical trials for treatment of seriously life-threatening diseases for which there is no effective treatment, compassionate-use thereof may be proposed by physician to patient if the patient cannot participate in the clinical trial of the drug and, based on medical analysis of the patient's condition, the physician believes that benefits of use may outweigh risks, and (ii) compassionate-use of experimental drugs should follow the principles of patients' voluntary requests, medical ethics and informed consent, and following review and approval by an ethics committee, experimental drugs can be administered in institutions conducting clinical trials by physicians with use or training experience in experimental drugs on patients with the same conditions as subjects receiving treatment by experimental drugs in clinical trials thereof. In the United States, compassionate-use programs are limited to patients who have a life-threatening disease or serious disease or condition, who may gain access to an investigational medical product for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. Additionally, the U.S. Right to Try Act provides a separate pathway for patients with a life-threatening disease or condition who have exhausted all other treatment options and who are unable to participate in clinical trials to access investigational drugs that have passed Phase I clinical trials under a more expedited process.

The regulatory discrepancy for compassionate-use programs among countries may lead to uneven patient entry criteria and protocols for compassionate use programs. This may create increased risk of serious adverse events because of enrolled patients' advanced disease or comorbidities. In addition, because the products in compassionate-use programs are investigational drugs, many of which are still in experimental stages, patients in compassionate-use program may exhibit adverse drug reactions from using these products. We currently have named patient programs in Hong Kong for compassionate use of fruquintinib, surufatinib and savolitinib, an expanded access program in the United States for compassionate use of surufatinib and have enlisted fruquintinib in the Macau Government Hospital Named Patient drug formulary. Although we have enrolled a limited number of patients in each of our current programs, we may be subject to the risk of enrolled patients exhibiting adverse drug reactions or serious adverse events being produced from the use of our drug products, particularly if we expand such programs or establish or participate in additional compassionate-use programs. Such occurrences can potentially lead to clinical holds of our ongoing clinical trials or complicate the determination of the safety profile of a drug candidate under regulatory review for commercial marketing, or expose us to tort liability.

Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs

Pharmaceutical companies in China are required to comply with extensive regulations and hold a number of permits and licenses to carry on their business. Our and our joint ventures' ability to obtain and maintain these regulatory approvals is uncertain, and future government regulation may impose additional burdens on our operations.

The pharmaceutical industry in China is subject to extensive government regulation and supervision. The regulatory framework addresses all aspects of operations in the pharmaceutical industry, including approval, production, distribution, advertising, licensing and certification requirements and procedures, periodic renewal and reassessment processes, registration of new drugs and environmental protection. Violation of applicable laws and regulations may materially and adversely affect our business. In order to manufacture and distribute pharmaceutical products in China, we and our joint ventures are required to, among other things:

- obtain a pharmaceutical manufacturing permit for each production facility from the NMPA;
- obtain a drug registration certificate, which includes a drug approval number, from the NMPA for each drug manufactured by us;
- obtain a pharmaceutical distribution permit from the NMPA; and
- renew the pharmaceutical manufacturing permits, the pharmaceutical distribution permits, drug registration certificates, among other requirements.

If we or our joint ventures are unable to obtain or renew such permits or any other permits or licenses required for our or their operations, we will not be able to engage in the manufacture and distribution of our products and our business may be adversely affected.

The regulatory framework regarding the pharmaceutical industry in China is subject to change and amendment from time to time. Any such change or amendment could materially and adversely impact our business, financial condition and results of operations. The PRC government has introduced various reforms to the Chinese healthcare system in recent years and may continue to do so, with an overall objective to expand basic medical insurance coverage and improve the quality and reliability of healthcare services. Specific upcoming regulatory and policy changes remain uncertain. The implementing measures to be issued may not be sufficiently effective to achieve the stated goals and, as a result, we may not be able to benefit from such reform to the level we expect, if at all. Moreover, the reform could give rise to regulatory developments, such as more burdensome administrative procedures, which may have an adverse effect on our business and prospects.

For further information regarding government regulation in China and other jurisdictions, see Item 4.B. "Business Overview—Regulations—Government Regulation of Pharmaceutical Product Development and Approval," "Business Overview—Regulations—Coverage and Reimbursement" and "Business Overview—Regulations—Other Healthcare Laws."

As a significant portion of the operations of our Other Ventures is conducted through joint ventures, we are dependent on the success of our joint ventures, our receipt of dividends or other payments from our joint ventures for cash to fund our operations, and our investments in our joint ventures are subject to liquidity risk.

We are party to a joint venture agreement with Shanghai Pharmaceuticals, relating to our non-consolidated joint venture namely, Shanghai Hutchison Pharmaceuticals, which forms part of the operations of our Other Ventures. Our equity in earnings of such non-consolidated joint venture, net of tax, was $33.5 million, $44.7 million and $49.7 million for the years ended December 31, 2020, 2021 and 2022, respectively, as recorded in our consolidated financial statements. As such, our results of operations and financial performance have been, and will continue to be, affected by the financial performance of such joint venture as well as any other equity investees we have or may have in the future. We may also be required to recognize an impairment charge in our consolidated financial statements if there is a decline in the fair market value of our investments in such businesses below their carrying amounts for whatever reason that is determined to be other-than-temporary. Furthermore, we have consolidated joint ventures with each of Sinopharm and Hain Celestial which accounted for substantially all of our Other Ventures' consolidated revenue for the years ended December 31, 2020, 2021 and 2022.

As a result, our ability to fund our operations and pay our expenses or to make future dividend payments, if any, is largely dependent on the earnings of our joint ventures and the payment of those earnings to us in the form of dividends. Payments to us by our joint ventures will be contingent upon our joint ventures' earnings and other business considerations and may be subject to statutory or contractual restrictions. Each joint venture's ability to distribute dividends to us is subject to approval by their respective boards of directors, which in the case of Shanghai Hutchison Pharmaceuticals is comprised of an equal number of representatives from each party. Furthermore, our ability to promptly sell one or more of our interests in our joint ventures in response to changing corporate strategy or economic, financial and investment conditions is limited. The market for such investments can be affected by various factors, such as general economic and market conditions, availability of financing, interest rates and investor demand, many of which are beyond our control. If we determine to sell any of our joint venture investments, we cannot predict if we will be successful or whether any price or other terms offered by a prospective purchaser would be acceptable to us.

Operationally, our joint venture partners have certain responsibilities and/or certain rights to exercise control or influence over operations and decision-making under the joint venture arrangements. Therefore, the success of our joint ventures depends on the efforts and abilities of our joint venture parties. For example, we appoint the general managers of Hutchison Sinopharm and Shanghai Hutchison Pharmaceuticals pursuant to the respective joint venture agreements governing these entities and therefore oversee the day-to-day management of these joint ventures. However, we still rely on our joint venture partners Sinopharm and Shanghai Pharmaceuticals to provide certain distribution and logistics services. See "—Risks Relating to Our Dependence on Third Parties—Joint ventures form an important part of our Other Ventures, and our ability to manage and develop the businesses conducted by these joint ventures depends in part on our relationship with our joint venture partners" for more information.

We may not be successful in building a commercial team to successfully manufacture, sell and market our approved drugs, and we may not be able to generate any revenue from such products.

We have leveraged our experience operating our prescription drugs business to commercialize certain of our approved, internally developed drug candidates in China. We must adapt our know-how to build a specific oncology and/or immunology focused sales and marketing team. As of December 31, 2022, we had an oncology commercial team with over 860 staff in mainland China to support the commercialization of Elunate, Sulanda, Orpathys and our other drug candidates, if approved. There are risks involved in establishing an in-house oncology commercial team. For example, recruiting and/or training a sales force to detail our approved drug candidates is time consuming and could delay any drug launch. Factors that may inhibit our efforts to commercialize our drug candidates include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- our inability to effectively manage the expansion of our operations and train additional qualified personnel in the relevant areas of oncology and/or immunology;
- the inability of our sales personnel to obtain access to physicians or educate adequate numbers of physicians who then prescribe any future drugs; and

- the lack of complementary drugs to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines.

In such case, our business, results of operations, financial condition and prospects will be materially and adversely affected.

We face substantial competition in selling our approved, internally developed drugs and the drugs of our Other Ventures.

The marketed drugs developed and sold by our Oncology/Immunology operations and the prescription drugs business which is part of our Other Ventures' operations face substantial competition in the pharmaceutical industry in China, which is characterized by a number of established, large pharmaceutical companies, as well as smaller emerging pharmaceutical companies, engaged in the development, production, marketing or sales of prescription drugs, in particular cardiovascular drugs. The identities of the key competitors with respect to drugs sold by our Oncology/Immunology and Other Ventures operations vary by product and, in certain cases, competitors have greater financial resources than us and may elect to focus these resources on developing, importing or in-licensing and marketing products in the PRC that are substitutes for our products and may have broader sales and marketing infrastructure with which to do so.

Such drugs may compete against products that have lower prices, superior performance, greater ease of administration or other advantages compared to our products. In some circumstances, price competition may drive our competitors to conduct illegal manufacturing processes to lower their manufacturing costs. Increased competition may result in price reductions, reduced margins and loss of market share, whether achieved by either legal or illegal means, any of which could materially and adversely affect our profit margins. We and our joint ventures may not be able to compete effectively against current and future competitors.

If we are not able to maintain and enhance brand recognition of our drugs to maintain a competitive advantage, our reputation, business and operating results may be harmed.

We believe that market awareness of our products sold through our Oncology/Immunology and Other Ventures operations, which include our joint ventures' branded products, such as Shang Yao, and the brands of third-party products which are distributed through our joint ventures, has contributed significantly to our success. We also believe that maintaining and enhancing such brands is critical to maintaining our competitive advantage. Although the sales and marketing staff of such businesses will continue to further promote such brands to remain competitive, they may not be successful. If we or our joint ventures are unable to further enhance brand recognition and increase awareness of such products, or are compelled to incur excessive marketing and promotion expenses in order to maintain brand awareness, our business and results of operations may be materially and adversely affected. Furthermore, our results of operations could be adversely affected if the Shang Yao brand, or the brands of any other products, or our reputation, are impaired by certain actions taken by our joint venture partners, distributors, competitors or relevant regulatory authorities.

Reimbursement may not be available for the products currently sold through our Oncology/Immunology and Other Ventures operations or our drug candidates in China, the United States or other countries, which could diminish our sales or affect our profitability.

The regulations that govern pricing and reimbursement for pharmaceuticals vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after regulatory approval is granted. In some foreign markets, pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Furthermore, once marketed and sold, government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Adverse pricing reimbursement levels may hinder market acceptance of our drug candidates or other products sold by us.

In China, for example, the Ministry of Human Resources and Social Security of the PRC or provincial or local human resources and social security authorities, together with other government authorities, review the inclusion or removal of drugs from the Medicines Catalogue for the National Basic Medical Insurance, Labor Injury Insurance and Childbirth System in China, or the National Reimbursement Drug List, or NRDL, or provincial or local medical insurance catalogues for the National Medical Insurance Program, and the category under which a drug will be classified, both of which affect the amounts reimbursable to program participants for their purchases of those medicines. These determinations are made based on a number of factors, including price and efficacy. Depending on the category under which a drug is classified in the provincial medicine catalogue, a National Medical Insurance Program participant residing in that province can be reimbursed for the full cost of Category A medicine and for the majority of the cost of a Category B medicine. In some instances, if the price range designated by the local or provincial government decreases, it may adversely affect our business and could reduce our total revenue, and if our revenue falls below production costs, we may stop manufacturing certain products. In November 2019 and January 2022, Elunate and Sulanda were added to China's NRDL as a Category B medicine, respectively. Orpathys has been added as a Category B medicine in the updated NRDL, effective from March 1, 2023.

In addition, in order to access certain local or provincial-level markets, our joint ventures are periodically required to enter into competitive bidding processes for She Xiang Bao Xin (the best-selling product of our Shanghai Hutchison Pharmaceuticals joint venture) and other products with a pre-defined price range. The competitive bidding in effect sets price ceilings for those products, thereby limiting our profitability.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs which may affect reimbursement rates of our drug candidates if approved. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, was passed, which substantially changed the way health care is financed by both governmental and private insurers. The Affordable Care Act, among other things, established a new Medicare Part D coverage gap discount program, in which, effective 2019, manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted.

Modifications to or repeal of all or certain provisions of the Affordable Care Act had been expected based on statements made by former President Trump and certain members of Congress. However, President Biden has indicated that his healthcare policy will build on the Affordable Care Act and that his administration will prioritize comprehensive drug pricing reform. We cannot predict the ultimate content, timing or effect of any changes to the Affordable Care Act or other federal and state reform efforts. Several U.S. states have also enacted laws to control drug pricing or require manufacturers to disclose information about drug pricing. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results. We expect that additional U.S. state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures. We expect that the pharmaceutical industry will experience pricing pressures due to the increasing influence of managed care (and related implementation of managed care strategies to control utilization), consolidation in drug distribution industry, additional federal and state legislative and regulatory proposals to regulate pricing of drugs, limit coverage of drugs or reduce reimbursement for drugs, public scrutiny and recent regulatory initiatives to control the price of pharmaceuticals through government negotiations of drug prices in Medicare Part D and, eventually Medicare Part B, and importation of cheaper products from abroad.

Moreover, eligibility for reimbursement in the United States does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim U.S. reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by U.S. government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors in the United States often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

Sales of our generic prescription drugs sold through our Other Ventures rely on the ability to win tender bids for the medicine purchases of hospitals in China.

Our prescription drugs business markets to hospitals in China that may make bulk purchases of a medicine only if that medicine is selected under a government-administered tender process that was initiated in 2018 and aimed at driving consolidation in the fragmented generic prescription drug market in China. Pursuant to this process, major cities bulk-buy certain generic drugs together, forcing companies to bid for contracts and driving down prices. The process was later expanded nationwide to cover more cities and drugs. This process, which only applies to generic prescription drugs, may reduce our Other Ventures' product portfolio as some of our third-party generic drug partners may fail to win bids.

Periodically, a bidding process is organized on a provincial or municipal basis. Whether a drug manufacturer is invited to participate in the tender depends on the level of interest that hospitals have in purchasing this drug. The interest of a hospital in a medicine is evidenced by:

- the inclusion of this medicine on the hospital's formulary, which establishes the scope of drug physicians at this hospital may prescribe to their patients, and

- the willingness of physicians at this hospital to prescribe a particular drug to their patients.

We believe that effective marketing efforts are critical in making and keeping hospitals interested in purchasing the prescription drugs sold through our Other Ventures so that we and our joint ventures are invited to submit the products to the tender. Even if we and our joint ventures are invited to do so, competitors may be able to substantially reduce the price of their products or services. If competitors are able to offer lower prices, our and our joint ventures' ability to win tender bids during the hospital tender process will be materially affected, and could reduce our total revenue or decrease our profit.

Counterfeit products could negatively impact our revenue, brand reputation, business and results of operations.

Our products are subject to competition from counterfeit products, especially counterfeit pharmaceuticals which are manufactured without proper licenses or approvals and are fraudulently mislabeled with respect to their content and/or manufacturer. Counterfeiters may illegally manufacture and market products under our or our joint venture's brand names, the brand names of the third-party products we or they sell, or those of our or their competitors. Counterfeit pharmaceuticals are generally sold at lower prices than the authentic products due to their low production costs, and in some cases are very similar in appearance to the authentic products. Counterfeit pharmaceuticals may or may not have the same chemical content as their authentic counterparts. If counterfeit pharmaceuticals illegally sold under our or our joint ventures' brand names or the brand names of third-party products we or they sell result in adverse side effects to consumers, we or our joint ventures may be associated with any negative publicity resulting from such incidents. In addition, consumers may buy counterfeit pharmaceuticals that are in direct competition with products sold through our Oncology/Immunology and Other Ventures operations, which could have an adverse impact on our revenue, business and results of operations. The proliferation of counterfeit pharmaceuticals in China and globally may grow in the future. Any such increase in the sales and production of counterfeit pharmaceuticals in China, or the technological capabilities of the counterfeiters, could negatively impact our revenue, brand reputation, business and results of operations.

Rapid changes in the pharmaceutical industry may render our Other Ventures' products or our internally developed drugs and drug candidates obsolete.

Future technological improvements by our competitors and continual product developments in the pharmaceutical market may render our and our joint ventures' existing products, our or their third-party licensed products or our drug candidates obsolete or affect our viability and competitiveness. Therefore, our future success will largely depend on our and our joint ventures' ability to:

- improve existing products;

- develop innovative drug candidates;

- diversify the product and drug candidate portfolio;

- license diverse third-party products; and
- develop new and competitively priced products which meet the requirements of the constantly changing market.

If we or our joint ventures fail to respond to this environment by improving our existing products, licensing new third-party products or developing new drug candidates in a timely fashion, or if such new or improved products do not achieve adequate market acceptance, our business and profitability may be materially and adversely affected.

Certain of our joint ventures' principal products involve the cultivation or sourcing of key raw materials including botanical products, and any quality control or supply failure or price fluctuations could adversely affect our ability to manufacture our products and/or could materially and adversely affect our operating results.

The key raw materials used in the manufacturing process of certain of our joint ventures' principal products are medicinal herbs whose properties are related to the regions and climatic conditions in which they are grown. Access to quality raw materials and products necessary for the manufacture of our products is not guaranteed. We rely on materials sourced from third-party growers and suppliers. The availability, quality and prices of these raw materials are dependent on and closely affected by weather conditions and other seasonal factors which have an impact on the yields of the harvests each year. The quality, in some instances, also depends on the operations of third-party growers or suppliers. There is a risk that such growers or suppliers sell or attempt to sell us or our joint ventures raw materials which are not authentic. If there is any supply interruption for an indeterminate period of time, our joint ventures may not be able to identify and obtain alternative supplies that comply with our quality standards in a timely manner. Any supply disruption could adversely affect our ability to satisfy demand for our products, and materially and adversely affect our product sales and operating results. Moreover, any use by us or our joint ventures of unauthentic materials illegally sold to us by third-party growers or suppliers in our or our joint ventures' products may result in adverse side effects to the consumers, negative publicity, or product liability claims against us or our joint ventures, any of which may materially and adversely affect our operating results.

The prices of necessary raw materials and products may be subject to price fluctuations according to market conditions, and any sudden increases in demand in the case of a widespread illness such as COVID-19, SARS, MERS or avian flu may impact the costs of production. Raw material price fluctuations could increase the cost to manufacture our products and adversely affect our operating results.

Adverse publicity associated with our company, our joint ventures or our or their products or third-party licensed products or similar products manufactured by our competitors could have a material adverse effect on our results of operations.

Sales of our and our joint ventures' products are highly dependent upon market perceptions of the safety and quality of such products, including proprietary products and third-party products we and they distribute. Concerns over the safety of biopharmaceutical products manufactured in China could have an adverse effect on the reputation of our industry and the sale of such products, including products manufactured or distributed by us and our joint ventures.

We and our joint ventures could be adversely affected if any of our or our joint ventures' products, third-party licensed products or any similar products manufactured by other companies prove to be, or are alleged to be, harmful to patients. Any negative publicity associated with severe adverse reactions or other adverse effects resulting from patients' use or misuse of our and our joint ventures' products or any similar products manufactured by other companies could also have a material adverse impact on our results of operations. We and our joint ventures have not, to date, experienced any significant quality control or safety problems. If in the future we or our joint ventures become involved in incidents of the type described above, such problems could severely and adversely impact our financial position and reputation.

We are dependent on our joint ventures' production facilities in Shanghai, China, our manufacturing facility in Suzhou, China and third-party manufacturing facilities for the manufacture of the principal products of our joint ventures and our own drug candidates and products.

The principal products sold by our Other Ventures are mainly produced or expected to be produced at our joint ventures' manufacturing facilities in Shanghai, China. Our commercial supplies of Elunate and Sulanda sold by our Oncology/Immunology operations are manufactured at our manufacturing facility in Suzhou, China. We outsourced the manufacturing of active pharmaceutical ingredients and finished product of Orpathys to a third-party manufacturer based in Shanghai, China. Until construction of our new manufacturing facility in Shanghai is completed and it receives the requisite government approvals, we have no back-up manufacturing facility for fruquintinib and surufatinib, and our ability to produce such drugs will be negatively impacted if we experience any significant production problems at our Suzhou facility. A significant disruption at our, our joint ventures' and/or our contract manufacturer's facilities, even on a short-term basis, could impair our and/or our joint ventures' ability to timely produce and ship products, which could have a material adverse effect on our business, financial position and results of operations.

Our, our joint ventures' and our contract manufacturer's manufacturing operations are vulnerable to interruption and damage from natural and other types of disasters, including earthquake, fire, floods, environmental accidents, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our, our joint ventures' or our contract manufacturer's business at these facilities would be materially impaired. In addition, the nature of our production and research activities could cause significant delays in our programs and make it difficult for us to recover from a disaster or switch to other contract manufacturers. We and our joint ventures maintain insurance for business interruptions to cover some of our potential losses; however, such disasters could still disrupt our operations and thereby result in substantial costs and diversion of resources.

In addition, our, our joint ventures' and our contract manufacturer's production process requires a continuous supply of electricity. We and they have encountered power shortages historically due to restricted power supply to industrial users during summers when the usage of electricity is high and supply is limited or as a result of damage to the electricity supply network. Because the duration of those power shortages was brief, they had no material impact on our or their operations. Interruptions of electricity supply could result in lengthy production shutdowns, increased costs associated with restarting production and the loss of production in progress. Any major suspension or termination of electricity or other unexpected business interruptions could have a material adverse impact on our business, financial condition and results of operations.

We may engage in strategic transactions, including acquisitions, investments, joint ventures or divestitures that may have an adverse effect on our business. If we engage in a strategic transaction, there is no assurance that the transaction will be consummated.

We may pursue transactions as part of our business strategy, including continuing to actively evaluate non-core assets divestment opportunities. We are considering alternative ways to divest non-core businesses in our Other Ventures segment, including Shanghai Hutchison Pharmaceuticals for which we have started the process for a share reform. For more information, please refer to Item 4.A. "History and Development of the Company."

Acquisitions and investments involve numerous risks such as difficulties in finding suitable partners or acquisition candidates, difficulties in obtaining financing on favorable terms, if at all, the assumption of certain known and unknown liabilities of acquired companies and difficulties in integrating operations, services, products and personnel. Divestitures also involve numerous risks. Any divestiture could result in a dilutive impact to our future earnings and significant write-offs, including those related to goodwill and other intangible assets, which could have a material adverse effect on our results of operations and financial condition. Divestitures could involve additional risks, including difficulties in the separation of operations, services, products and personnel, the diversion of management's attention from other business concerns, the disruption of our business and the potential loss of key employees.

We may not complete strategic transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the expected benefits of any transaction. We may not be successful in managing these or any other significant risks that we encounter if we engage in a strategic transaction. If we are not successful in managing the risks, uncertainties and potential disruptions, a strategic transaction could have a negative impact on our business, results of operations or financial position.

Risks Relating to Our Dependence on Third Parties

Disagreements or disputes with our current or future collaboration partners, the amendment of any collaboration agreement or the termination of any collaboration arrangement, could cause delays in our product development and materially and adversely affect our business.

Our collaborations, including those with our oncology drug partners AstraZeneca and Eli Lilly and our in-licensing arrangement with Epizyme, and expected collaborations, including with Takeda and any future collaborations that we enter into may not be successful. Disagreements or disputes between parties to a collaboration arrangement regarding issues such as clinical development and commercialization, intellectual property ownership and transfer, clinical supply of drug candidates or products, cost allocation and other matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement. In addition, we or our partners may seek to amend the terms of one or more our collaboration agreements to adjust, among other things, the respective roles of our company and our collaboration partners as circumstances change. Our interests may not always be aligned with those of our collaboration partners, for instance, we may be much smaller than our collaboration partners and because they or their affiliates may sell competing products. This may result in potential conflicts between our collaborators and us on matters that we may not be able to resolve on favorable terms or at all.

Collaborations with pharmaceutical or biotechnology companies and other third parties, including our existing agreements with AstraZeneca, Eli Lilly and Takeda, are often terminable by the other party for any reason with certain advance notice. Any such termination or expiration would adversely affect us financially and could harm our business reputation. For instance, in the event one of the strategic alliances with a current collaborator is terminated, we may require significant time and resources to secure a new collaboration partner, if we are able to secure such an arrangement at all. As noted in the following risk factor, establishing new collaboration arrangements can be challenging and time-consuming. The loss of existing or future collaboration arrangements would not only delay or potentially terminate the possible development or commercialization of products we may derive from our technologies, but it may also delay or terminate our ability to test specific target candidates.

We rely on our collaborations with third parties for certain of our drug development activities, and, if we are unable to establish new collaborations when desired on commercially attractive terms or at all, we may have to alter our development and commercialization plans.

Certain of our drug development programs and the potential commercialization of certain drug candidates rely on collaborations, such as savolitinib with AstraZeneca and fruquintinib with Eli Lilly for China and with Takeda outside of China. In the future, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of our other drug candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, NMPA or similar regulatory authorities outside the United States and China, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our drug candidate. The terms of any additional collaboration or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or eventually close the deal. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate drug revenue. In January 2023, we entered into a license agreement with a subsidiary of Takeda to further the global development, commercialization and manufacture of fruquintinib outside of mainland China, Hong Kong and Macau. The deal is subject to customary closing conditions, including completion of antitrust regulatory clearance. If the transaction contemplated by this license agreement is not consummated or is delayed, our expectations regarding future revenues, research and development costs, other operating expenses and operating cash flows associated with the development and commercialization of fruquintinib would be materially affected. For additional information regarding the fruquintinib collaboration with Takeda, please refer to “Business—Our Clinical Pipeline—3. Fruquintinib (HMPL-013), VEGFR 1, 2 and 3 Inhibitor—Overview of Elunate Commercial Launch.

The third-party vendors upon whom we rely for the supply of the active pharmaceutical ingredients used in some of our drug candidates and drug products are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The active pharmaceutical ingredients used in some of our drug candidates and products are supplied to us from third-party vendors. Our ability to successfully develop our drug candidates, and to supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the active pharmaceutical ingredients for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. We currently obtain active pharmaceutical ingredients for each of our drug candidates from a limited number of suppliers. For example, a single supplier based in Shanghai manufactures and provides us active pharmaceutical ingredient for savolitinib. In the event any of our current suppliers of such active pharmaceutical ingredient cease operations for any reason, it may lead to an interruption in our production and supply of the product.

For all of our drug candidates and products, we aim to identify and qualify a manufacturer to provide such active pharmaceutical ingredient prior to submission of an NDA to the FDA and/or NMPA. We are not certain, however, that our current supply arrangements will be able to meet our demand, either because of the nature of our agreements with third party suppliers, our limited experience with third party suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess third party vendors’ ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the active pharmaceutical ingredients used in our drug candidates and products, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such alternative arrangements would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the active pharmaceutical ingredients used in our drug candidates and products, any interruption or delay in the supply of components or materials, or our inability to obtain such active pharmaceutical ingredient from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development and commercialization efforts, which could harm our business, results of operations, financial condition and prospects.

We and our collaborators rely, and expect to continue to rely, on third parties to conduct certain of our clinical trials for our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be harmed.

We do not have the ability to independently conduct large-scale clinical trials. We and our collaboration partners rely, and expect to continue to rely, on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support certain clinical trials for our drug candidates. Nevertheless, we and our collaboration partners (as applicable) will be responsible for ensuring that each clinical trial is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of clinical trials for our drug candidates, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

Although we or our collaboration partners design the clinical trials for our drug candidates, CROs conduct most of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, are outside of our direct control. Our reliance on third parties to conduct clinical trials results in less control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially and adversely affect the willingness or ability of third parties to conduct our and our collaboration partners' clinical trials and may subject us or them to unexpected cost increases that are beyond our or their control.

If any of our and our collaboration partners' relationships with these third-party CROs terminate, we or they may not be able to enter into arrangements with alternative CROs on reasonable terms or at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We, our collaboration partners or our CROs may fail to comply with the regulatory requirements pertaining to clinical trials, which could result in fines, adverse publicity and civil or criminal sanctions.

We, our collaboration partners and our CROs are required to comply with regulations for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the NMPA and comparable foreign regulatory authorities for any drugs in clinical development. In the United States, the FDA regulates GCP through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, our collaboration partners or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require additional clinical trials before approving the marketing applications for the relevant drug candidate. We cannot assure you that, upon inspection, the FDA or other applicable regulatory authority will determine that any of the future clinical trials for our drug candidates will comply with GCPs. In addition, clinical trials must be conducted with drug candidates produced under applicable manufacturing regulations. Our failure or the failure of our collaboration partners or CROs to comply with these regulations may require us or them to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We are also required to register applicable clinical trials and post certain results of completed clinical trials on a U.S. government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil sanctions.

Our collaboration partners, principal investigators, CROs and other third-party contractor and consultants may engage in misconduct or other improper activities.

We are exposed to the risk that collaboration partners, principal investigators, CROs and other third-party contractor and consultants may engage in fraudulent or other illegal activity with respect to our business. Their misconduct could include intentional, reckless and/or negligent conduct or unauthorized activity that violates NMPA, FDA or other regulations, including but not limited to those laws requiring the reporting of true, complete and accurate information. In addition, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of insurance, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. We may not be able to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, our collaboration partners, principal investigators, CROs and other third-party contractor and consultants, and we and/or such other parties are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, contractual damages, reputational harm, diminished profits and future earnings and disruption of our operations.

Joint ventures form an important part of our Other Ventures, and our ability to manage and develop the businesses conducted by these joint ventures depends in part on our relationship with our joint venture partners.

We are party to joint venture agreements with each of Shanghai Pharmaceuticals, Sinopharm and Hain Celestial, which together form a major portion of our Other Ventures. Under these arrangements, our joint venture partners have certain operational responsibilities and/or certain rights to exercise control or influence over operations and decision-making.

Our equity interests in these operating companies do not provide us with the unilateral ability to control actions which require shareholder approval. In addition, under the joint venture contracts for these entities, the consent of the directors nominated by our joint venture partners is required for the passing of resolutions in relation to certain matters concerning the operations of these companies. As a result, although we participate in the management and nominate the management and run the day-to-day operations of our joint ventures, Hutchison Sinopharm, Hutchison Hain Organic and Shanghai Hutchison Pharmaceuticals, we may not be able to secure the consent of our joint venture partners to pursue activities or strategic objectives that are beneficial to or that facilitate our overall business strategies. Furthermore, disagreements or disputes which arise between us and our joint venture partners may potentially require legal action to resolve and hinder the smooth operation of our Other Ventures or adversely affect our financial condition, results of operations and prospects.

We are relying on third parties to construct our new manufacturing facility in Shanghai. Any delays in completing and receiving regulatory approvals for our new Shanghai facility, or any disruptions to the third parties' performance of their obligations, could reduce or restrict our production capacity for the drug candidates used in our clinical trials or our commercial supply for any drug candidates which are approved.

We are contracting with third parties to construct our new manufacturing facility in Shanghai. The new facility is expected to be a 55,000 square meter large-scale facility with a production capacity estimated to be five times that of our existing manufacturing plant in Suzhou. The first phase will be primarily for small molecule production, with production capacity expected to be able to produce 250 million tablets and capsules per year. The second phase is expected to include expansion into large molecule production. Third parties will be responsible for the construction of the buildings, including the production lines and other production facilities within such buildings.

We cannot assure you that we will not experience any disruptions to the third parties' performance of their obligations, and there could be delays in completing and receiving regulatory approvals for our new manufacturing facility. If the construction of our manufacturing facility or our production lines encounter unanticipated delays or incur additional expenses than expected, if regulatory evaluation and/or approval of our new manufacturing facility is delayed, or if our third party contracts are terminated or adversely affected, our manufacturing capacity of our drug candidates may be limited, which would delay or limit our development and commercialization activities and our opportunities for growth. Cost overruns associated with constructing or maintaining our Shanghai facility could also require us to raise additional funds from other sources. Any disruption that impedes our ability to manufacture our drug candidates in a timely manner could materially adversely affect our business, financial condition, results of operations and prospects.

We and our joint ventures rely on our distributors for logistics and distribution services.

We and our joint ventures rely on distributors to perform certain operational activities, including invoicing, logistics and delivery of the products we and they market to the end customers. Because we and our joint ventures rely on third-party distributors, we have less control than if we handled distribution logistics directly and can be adversely impacted by the actions of our distributors. Any disruption of our distribution network, including failure to renew existing distribution agreements with desired distributors, could negatively affect our ability to effectively sell our products and materially and adversely affect the business, financial condition and results of operations of us and our joint ventures.

There is no assurance that the benefits currently enjoyed by virtue of our association with CK Hutchison will continue to be available.

Historically, we have relied on the reputation and experience of, and support provided by, our founding shareholder, a wholly owned subsidiary of CK Hutchison, to advance our joint ventures and collaborations in China and elsewhere. CK Hutchison is interested in approximately 38.5% of our total outstanding share capital as of February 15, 2023. We believe that CK Hutchison group's reputation in China has given us an advantage in negotiating collaborations and obtaining opportunities.

We also benefit from sharing certain services with the CK Hutchison group including, among others, legal and regulatory services, company secretarial support services, tax and internal audit services, participation in the CK Hutchison group's pension, medical and insurance plans, participation in the CK Hutchison group's procurement projects with third-party vendors/suppliers, other staff benefits and staff training services, company functions and activities and operation advisory and support services. We pay a management fee to an affiliate of CK Hutchison for the provision of such services. In each of the years ended December 31, 2020, 2021 and 2022, we paid a management fee of approximately $1.0 million, $1.0 million and $1.0 million respectively. In addition, we benefit from the fact that two retail chains affiliated with the CK Hutchison group, PARKnSHOP and Watsons, sell certain of our Other Ventures' products in their stores throughout Hong Kong and in other Asian countries. For the years ended December 31, 2020, 2021 and 2022, sales of our products to members of the CK Hutchison group amounted to $5.5 million, $4.3 million and $3.6 million, respectively.

Our business also depends on certain intellectual property rights licensed to us by the CK Hutchison group. See "—Risks Relating to Intellectual Property—We and our joint ventures are dependent on trademark and other intellectual property rights licensed from others. If we lose our licenses for any of our products, we or our joint ventures may not be able to continue developing such products or may be required to change the way we market such products" for more information on risks associated with such intellectual property licensed to us.

There can be no assurance the CK Hutchison group will continue to provide the same benefits or support that they have provided to our business historically. Such benefit or support may no longer be available to us, in particular, if CK Hutchison's ownership interest in our company significantly decreases in the future.

Other Risks and Risks Relating to Doing Business in China

The COVID-19 pandemic and other adverse public health developments could materially and adversely affect our business.

In December 2019, an outbreak of a novel strain of coronavirus (COVID-19) was reported and has since spread around the world. In March 2020, the World Health Organization declared the COVID-19 outbreak a global pandemic. After the initial outbreak of COVID-19, from time to time, some instances of COVID-19 or its variants infections have emerged, such as the infections caused by the Omicron variants emerged in late 2021 and spread across the globe including in China in early 2022. In response to the pandemic and the evolving strands of different variants, many governments around the world implemented a variety of measures to reduce the spread of COVID-19, including travel restrictions and bans, instructions to residents to practice social distancing, quarantine advisories, shelter-in-place orders and required closures of non-essential businesses. Such restrictive measures and the outbreak of COVID-19 itself have in the past negatively impacted and may continue to negatively impact our operations, given the disruption they may have on the manufacturing and supply chain, our sales and marketing and clinical trial operations and those of our collaboration partners, and the ability to advance our research and development activities and pursue development of any of our drug candidates, each of which could have an adverse impact on our business and our financial results. For instance, COVID-19 had an impact on our research, clinical studies and our commercial activities in 2022 because of hospital lockdowns, travel restrictions and disruptions in logistics. Our clinical sites in Shanghai were particularly affected during April and May in 2022, and in response, we put in place measures to reduce the disruptions, including online patient follow-up and the retention of core research teams on-site to maintain critical activities. Although the restrictive measures related to the COVID-19 pandemic have gradually been lifted around the world, including in China starting from December 2022, and we expect the travel, social and economic activities to gradually normalize and the impact of COVID-19 to be reduced in the regions we operate, the COVID-19 pandemic or any other adverse public health developments may continue to have a negatively impact on our business, our clinical trials, our research programs, healthcare systems or the global economy as a whole, which could have a material adverse effect on our business, financial condition and results of operations and cash flows.

We are subject to stringent privacy and cybersecurity laws, information security policies and contractual obligations related to data privacy and security, and we may be exposed to risks related to our management of the medical data of subjects enrolled in our clinical trials and other personal or sensitive information.

We routinely receive, collect, generate, store, process, transmit and maintain medical data, treatment records and other personal details of the subjects enrolled in our clinical trials, along with other personal or sensitive information. As such, we are subject to the relevant local, state, national and international data protection and privacy laws, directives regulations, and standards that apply to the collection, use, retention, protection, disclosure, transfer and other processing of personal data in the various jurisdictions in which we operate and conduct our clinical trials. We are also subject to contractual obligations regarding the processing of personal data. Legal requirements regarding data protection and privacy continue to evolve and may result in ever-increasing public scrutiny and escalating levels of enforcement and sanctions and increased costs of compliance. Failure to comply with any of these laws could result in enforcement action against us, including investigations, civil and criminal enforcement action, fines, imprisonment of company officers and public censure, claims for damages by customers and other affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

Data protection and privacy laws and regulations generally require clinical trial sponsors and operators and their personnel to protect the privacy of their enrolled subjects and prohibit unauthorized disclosure of personal information. We have established procedures to protect the confidentiality of medical records and personal data of subjects enrolled in our clinical trials. Access to clinical trial data has been strictly limited to authorized personnel only according to the relevant rules and regulations. External parties involved in clinical trials are also required to comply with all relevant data protection and confidentiality requirements. Data are to be used only for the intended use, as agreed by the patients and consistent with the patients' informed consent form. While we have adopted security policies and measures to protect our proprietary data and patients' privacy, personal patient information could be subject to leaks caused by hacking activities, human error, employee misconduct or negligence or system breakdown. We also cooperate with third parties including collaboration partners, principal investigators, hospitals, CROs and other third-party contractor and consultants for our clinical trials and operations. Any leakage or abuse of patient data by our third-party partners may be perceived by the patients as a result of our failure. Furthermore, any change in applicable laws and regulations could affect our ability to use medical data and subject us to liability for the use of such data for previously permitted purposes. For instance, we may be subject to additional regulations, laws and policies adopted by the PRC government to apply more stringent social and ethical standards in data privacy resulting from the increased global focus on this area. Any failure or perceived failure by us to prevent information security breaches or to comply with privacy policies or privacy-related legal obligations, or any compromise of information security that results in the unauthorized release or transfer of personally identifiable information or other patient data, could cause our customers to lose trust in us and could expose us to regulatory action and legal claims.

There are numerous U.S. federal and state laws and regulations relating to the privacy and security of personal information. In particular, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended, establish privacy and security standards that limit the use and disclosure of individually identifiable health information (known as "protected health information"), require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information, and create breach reporting obligations in cases of certain unauthorized uses or disclosures. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can require complex factual and statistical analyses and may be subject to changing interpretations. Although we take measures to protect sensitive data from unauthorized access, use or disclosure, and whenever possible contractually require third-party partners to do the same, our information technology and infrastructure and those of our third-party partners may be vulnerable to attacks by hackers or viruses or breached due to employee error, malfeasance or other malicious or inadvertent disruptions. Any such breach or interruption could compromise those networks and the information stored there could be accessed by unauthorized parties, manipulated, publicly disclosed, lost or stolen. Any such access, breach, or other loss of information relating to our information technology and infrastructure or that of our third-party partners may subject us to liability including legal claims or proceedings and liability under federal or state laws that protect the privacy of personal information, such as HIPAA, the Health Information Technology for Economic and Clinical Health ("HITECH") Act, and regulatory penalties. If we or a third-party partner suffers a breach, we may need to send breach notifications to affected individuals and, if 500 or more individuals were affected, also notify the Secretary of the Department of Health and Human Services. Breach notifications may separately be required under applicable state breach notification laws, which may include notifications to affected individuals, and for extensive breaches, to the media, credit reporting agencies, and/or State Attorneys General. Such notices could harm our reputation and our ability to compete and could potentially attract enforcement scrutiny from governmental authorities.

Regulatory authorities in China have implemented a number of legislative and regulatory proposals concerning data protection. The PRC Cyber Security Law, which became effective in June 2017, created China's first national-level data protection for "network operators," which may include all organizations in China that provide services over the internet or another information network. The PRC Data Security Law, which took effect in September 2021, provides for a security review procedure for the data activities that may affect national security. The PRC Personal Information Protection Law, which took effect from November 2021, provides the circumstances under which a personal information processor could process personal information and the requirements for such circumstances. The PRC Personal Information Protection Law clarifies the scope of application, the definition of personal information and sensitive personal information, the legal basis of personal information processing and the basic requirements of notice and consent. The Measures for Cybersecurity Review, which took effect on February 15, 2022, provides that critical information infrastructure operators that purchase network products and services and online platform operators engaging in data processing activities that affect or may affect national security shall be subject to the cybersecurity review, and elaborates the factors to be considered when assessing the national security risks of the relevant activities. The Measures for Cybersecurity Review further stipulates that online platform operators holding personal information of over one million users shall apply with the Cybersecurity Review Office for a cybersecurity review before any public listing in a foreign country. As of the date of this annual report, we have not received any formal notice from any PRC cybersecurity regulator that we should apply for or otherwise be subject to the cybersecurity review, or subject to any investigation or received any inquiry, notice or sanction on cybersecurity review. The exact scope of "critical information infrastructure operators" under the current regulatory regime remains unclear, and the PRC government authorities may have wide discretion in the interpretation and enforcement of the applicable laws. Therefore, it is uncertain whether we would be deemed to be a critical information infrastructure operator under PRC law. If we are deemed to be a critical information infrastructure operator under the PRC cybersecurity laws and regulations, we may be subject to obligations in addition to what we have fulfilled under the PRC cybersecurity laws and regulations. In addition, on November 14, 2021, the Data Security Management Measures (Draft for Comments) was published by the CAC for public comments, which provides that data processors conducting the following activities shall apply for cybersecurity review: (i) a merger, reorganization or division of online platform operators that have acquired a large number of data resources related to national security, economic development or public interests which affect or may affect national security; (ii) a listing abroad when the data processor processes over one million users' personal information; (iii) a listing in Hong Kong which affects or may affect national security; or (iv) other data processing activities that affect or may affect national security. It also requires data processors processing important data or listed outside China to carry out a data security assessment annually by itself or through a third party data security service provider and submit an assessment report to the local agency of the CAC. As there are still uncertainties regarding the further enactment of new laws and regulations as well as the revision, interpretation and implementation of those existing laws and regulations, we cannot assure you that we will be able to comply with such regulations in all respects.

The Measures on Security Assessment of Cross-border Data Transfer, or the Security Assessment Measures, were published on July 7, 2022, and became effective on September 1, 2022. The Security Assessment Measures specify that data controllers and/or critical information infrastructure operators will be subject to security assessment under the following circumstances: (i) data controllers exporting important data (which, under the Security Assessment Measures, is defined as data which if tampered with, damaged, leaked, or if obtained or used illegally may endanger national security, the economy, social stability, and public health and safety, etc.), (ii) critical information infrastructure operators or data controllers processing the personal information of one million people or more exporting personal information, (iii) data controllers who have exported the personal information of 100,000 people or the sensitive personal information of 10,000 people since January 1 of the previous year, or (iv) other situations provided for by the CAC that require a security assessment. As of the date of this annual report, we have not received any formal notice from any PRC cybersecurity regulator that the Company should apply for or otherwise be subject to security assessment, or subject to any investigation or received any inquiry, notice or sanction on security assessment. PRC government authorities may have wide discretion in the interpretation and enforcement of the Security Assessment Measures, including whether we have exported "important data" as defined thereunder, and thus there is uncertainty as to whether we may be subject to security assessment. Further, drafts of some of these measures have now been published, including the Measures on Security Assessment for Individual Information Cross-border Transfer (Draft for Comments) in June 2019, which may, upon enactment, require security review before transferring human health-related data out of China.

In addition, certain industry-specific laws and regulations affect the collection and transfer of personal data in China. For example, the Regulations of the PRC on the Administration of Human Genetic Resources, or HGR Regulations, which became effective and implemented on July 1, 2019, stipulates that use of Chinese human genetic resources, or HGR, for the purposes of carrying out collaborative international scientific research shall be approved by the administrative department of science and technology under the State Council, with which the two parties shall file the type, quantity and usage of the human genetic resources, to be used before clinical trials. However, no approval is required for "international collaboration in clinical trials" that do not involve the export of HGR materials; the two parties to the international collaboration shall file the type, quantity and usage of the HGR to be used with the administrative department of science and technology under the State Council before clinical trials. The PRC Biosecurity Law, which took effect on April 15, 2021, stipulates that foreign organizations and individuals, as well as institutions they establish or are the actual controllers of, must not collect or preserve HGR within the territory of China and must not provide China's HGR to overseas. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices, potentially resulting in confiscation of HGR samples and associated data and administrative fines, penalties and negative publicity.

Our clinical trial programs may implicate European data privacy laws, including the General Data Protection Regulation, or the GDPR, and local laws further implementing or supplementing the GDPR. The GDPR implements more stringent operational requirements for processors and controllers of personal data including requirements for such companies to be able to ensure and be able to demonstrate compliance with the GDPR. If our or our third-party partners' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher. In addition to statutory enforcement, non-compliance can lead to compensation claims by affected individuals, negative publicity and a potential loss of business. We are also subject to European laws on personal data export, as we may transfer personal data from the E.U. (or U.K.) to other jurisdictions which are not considered by the European Commission to offer "adequate" protection of personal data (such as Hong Kong or the United States). Following the Schrems II decision of the European Court of Justice in 2020, there has been intensified focus on exports of personal data which do not meet the high standards of protection expected by the E.U. Certain supervisory authorities in the E.U. have now begun to take enforcement action in this area, ordering restrictions on certain transfers of personal data to third countries such as the United States. These changes could require us to make operational changes and could increase costs and may lead to governmental enforcement actions, litigation, fines and penalties or adverse publicity that could have an adverse effect on our business.

We believe, to the best of our knowledge, our business operations do not violate any of the above laws and regulations currently in force in all material aspects. We have been taking and will continue to take reasonable measures to comply with applicable data privacy, data protection and cybersecurity laws. We cannot guarantee the effectiveness of the measures undertaken by us and business partners, and such measures may still be determined as insufficient, improper, or even as user-privacy invasive, by the relevant authorities, which may result in penalties against us. Complying with all applicable laws, regulations, standards and obligations relating to data privacy, security, and transfers may cause us to incur substantial operational costs or require us to modify our data processing practices and processes. To the extent that we need to alter our business model or practices to adapt to these announcement and provisions and future regulations, laws and policies, we could incur additional expenses. We cannot assure you we can adapt our operations to it in a timely manner. Non-compliance could result in proceedings against us by data protection authorities, governmental entities or others, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, penalties, judgments and negative publicity. In addition, if our practices are not consistent or viewed as not consistent with legal and regulatory requirements, including changes in laws, regulations and standards or new interpretations or applications of existing laws, regulations and standards, we may become subject to audits, inquiries, whistleblower complaints, adverse media coverage, investigations, loss of export privileges, severe criminal or civil sanctions and reputational damage. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Product liability claims or lawsuits could cause us, our collaborators or our joint ventures to incur substantial liabilities.

We, our collaborators and our joint ventures face an inherent risk of product liability exposure related to the use of our drug candidates in clinical trials, sales of our or our joint ventures' products or the products we or they license from third parties. If we, our collaborators and our joint ventures cannot successfully defend against claims that the use of such drug candidates in our clinical trials or any products sold by us or our joint ventures, including fruquintinib, surufatinib, savolitinib and/or any of our drug candidates which receive regulatory approval, caused injuries, we, our collaborators and our joint ventures could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our and our joint ventures' products;

- significant negative media attention and reputational damage;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any drug candidates that we may develop.

Our principal insurance policies cover product liability for fruquintinib, surufatinib, savolitinib, certain prescription drugs and health supplements, property loss due to accidents or natural disasters and adverse events in clinical trials. Existing PRC laws and regulations do not require us, our collaborators or our joint ventures to have, nor do we or they, maintain liability insurance to cover product liability claims except with respect to fruquintinib, surufatinib, savolitinib, certain prescription drugs and health supplements, and liability with respect to our oncology and immunology clinical trials. Any litigation might, result in substantial costs and diversion of resources. While we maintain liability insurance for clinical trials and products, this insurance may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products that we or our collaborators develop.

We and our joint ventures may be exposed to liabilities under the U.S. Foreign Corrupt Practices Act, or FCPA, U.S. healthcare fraud and abuse laws, the Bribery Act 2010 of the United Kingdom, or U.K. Bribery Act, and Chinese anti-corruption laws, and any determination that we have violated these laws could have a material adverse effect on our business or our reputation.

In the day-to-day conduct of our business, we and our joint ventures are in frequent contact with persons who may be considered government officials under applicable anti-corruption, anti-bribery and anti-kickback laws, which include doctors at public hospitals in China and elsewhere. Therefore, we and our joint ventures are subject to risk of violations under the FCPA, the U.K. Bribery Act, and other laws in the countries where we do business. We and our joint ventures have operations in China, agreements with third parties in China, and we and our joint ventures make most of our sales in China. The PRC laws and regulations also strictly prohibit bribery of government officials. Our and our joint ventures' activities in China create the risk of unauthorized payments or offers of payments by the directors, employees, representatives, distributors, consultants or agents of our company or our joint ventures, even though they may not always be subject to our control. It is our policy to implement safeguards to discourage these practices by our and our joint ventures' employees and third parties. We have implemented and adopted policies designed by the R&D-based Pharmaceutical Association Committee, an industry association representing approximately 40 global biopharmaceutical companies, to ensure compliance by us and our joint ventures and our and their directors, officers, employees, representatives, distributors, consultants and agents with the anti-corruption laws and regulations. We cannot assure you, however, that our existing safeguards are sufficient or that our or our joint ventures' directors, officers, employees, representatives, distributors, consultants and agents have not engaged and will not engage in conduct for which we may be held responsible, nor can we assure you that our business partners have not engaged and will not engage in conduct that could materially affect their ability to perform their contractual obligations to us or even result in our being held liable for such conduct. Violations of the FCPA, the U.K. Bribery Act or Chinese anti-corruption laws may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could have a material adverse effect on our business, reputation, financial condition, cash flows and results of operations.

If we begin to commercialize products in the United States and secure governmental reimbursement of our products, we also will be subject to the risk of violating U.S. federal and state healthcare fraud and abuse laws, including the Anti-Kickback Statute and the False Claims Act. These laws broadly prohibit providing or receiving kickbacks in connection with government-reimbursed healthcare items or services, as well submitting or causing the submission of false or fraudulent claims to government healthcare programs. Violations of these laws may result in severe criminal or civil sanctions and other administrative sanctions, which could have a material adverse effect on our business, reputation, financial condition, cash flows and results of operations.

Ensuring that our and our joint ventures' future business arrangements with third parties comply with applicable laws could also involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our or our joint ventures' operations were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment and exclusion from government funded healthcare programs, any of which could substantially disrupt our operations. If the physicians, hospitals or other providers or entities with whom we and our joint ventures do business are found not to be in compliance with applicable laws, they may also be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

If we or our joint ventures fail to comply with environmental, health and safety laws and regulations, we or they could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and our joint ventures are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemical materials. Our operations also produce hazardous waste products. We and our joint ventures are therefore subject to PRC laws and regulations concerning the discharge of waste water, gaseous waste and solid waste during our manufacturing processes. We and our joint ventures are required to establish and maintain facilities to dispose of waste and report the volume of waste to the relevant government authorities, which conduct scheduled or unscheduled inspections of our facilities and treatment of such discharge. We and our joint ventures may not at all times comply fully with environmental regulations. Any violation of these regulations may result in substantial fines, criminal sanctions, revocations of operating permits, shutdown of our facilities and obligation to take corrective measures. We and our joint ventures generally contract with third parties for the disposal of these materials and waste. We and our joint ventures cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials, we and/or our joint ventures could be held liable for any resulting damages, and any liability could exceed our resources. We and/or our joint ventures also could incur significant costs associated with civil or criminal fines and penalties.

Although we and our joint ventures maintain workers' compensation insurance to cover costs and expenses incurred due to on-the-job injuries to our employees and third-party liability insurance for injuries caused by unexpected seepage, pollution or contamination, this insurance may not provide adequate coverage against potential liabilities. Furthermore, the PRC government may take steps towards the adoption of more stringent environmental regulations. Due to the possibility of unanticipated regulatory or other developments, the amount and timing of future environmental expenditures may vary substantially from those currently anticipated. If there is any unanticipated change in the environmental regulations, we and our joint ventures may need to incur substantial capital expenditures to install, replace, upgrade or supplement our equipment or make operational changes to limit any adverse impact or potential adverse impact on the environment in order to comply with new environmental protection laws and regulations. If such costs become prohibitively expensive, we may be forced to cease certain aspects of our or our joint ventures' business operations.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

We are heavily dependent on critical, complex and interdependent information technology systems, including internet-based systems, to support our business processes. Our information technology system security is continuously reviewed, maintained and upgraded in response to possible security breach incidents. Despite the implementation of these measures, our information technology systems and those of third parties with which we contract are vulnerable to damage from external or internal security incidents, breakdowns, malicious intrusions, cybercrimes, including State-sponsored cybercrimes, malware, misplaced or lost data, programming or human errors or other similar events. System failures, accidents or security breaches could cause interruptions in our operations and could result in inappropriately accessed, tampered with, modified or stolen scientific data or a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. Such event could significantly harm our Oncology/Immunology operations, including resulting in the loss of clinical trial data which could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Such events could also lead to the loss of important information such as trade secrets or other intellectual property and could accelerate the development or manufacturing of competing products by third parties. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our research and development programs and the development of our drug candidates could be delayed.

We have granted, and may continue to grant, options, long-term incentive scheme ("LTIP") awards and other types of awards under our Option Schemes and our LTIP, or collectively the Schemes, which may result in increased share-based compensation expenses and give rise to potential employment related disputes.

We have adopted the Options Schemes for the purpose of granting share-based compensation awards to certain management, directors, employees and other eligible grantees as a means to retain, incentivize, reward, remunerate, compensate and/or provide benefits to eligible grantees. We recognized share-based compensation expenses of $19.6 million, $42.0 million and $30.6 million for the years ended December 31, 2020, 2021 and 2022, respectively, in our consolidated financial statements in accordance with U.S. GAAP.

We believe the granting of share-based compensation is of significant importance to our ability to attract and retain key personnel and employees, and we will continue to grant share-based compensation in the future. As a result, our expenses associated with share-based compensation may increase, which may have an adverse effect on our results of operations. We may re-evaluate the vesting schedules, exercise price or other key terms applicable to the grants under our currently effective Schemes from time to time, which may result in a substantial change in our share-based compensation expenses in the reporting periods. In addition, we could in the future become involved in disputes or legal proceedings with our employees or former employees on employment related matters (including disputes on the entitlement of options, awards and other share-based compensation or in connection with the employees' incentive or compensation arrangements). If such disputes or legal proceedings arise, there can be no assurance that we will prevail in them, and in any event defending against these disputes or legal proceedings could cause us to incur legal and other costs. Any adverse outcome of these disputes or legal proceedings could have a material adverse effect on our reputation, business and results of operations.

For more information on the Schemes, please refer to Item 6.B. "Directors, Senior Management and Employees," "Compensation," "Equity Compensation Schemes and Other Benefit Plans."

The PRC's economic, political and social conditions, as well as governmental policies, could affect the business environment and financial markets in China, our ability to operate our business, our liquidity and our access to capital.

Substantially all of our and our joint ventures' business operations are conducted in China. Accordingly, our results of operations, financial condition and prospects are subject to economic, political and legal developments in China to a significant degree. China's economy differs from the economies of developed countries in many respects, including with respect to the amount of government involvement, level of development, growth rate, control of foreign exchange and allocation of resources. If the business environment in China deteriorates from the perspective of domestic or international investors, our or our joint ventures' business in China may also be adversely affected.

Although the PRC government has implemented measures emphasizing the utilization of market forces for economic reform, the reduction of state ownership of productive assets, and the establishment of improved corporate governance in business enterprises, a substantial portion of productive assets in China is still owned by the government. In addition, the PRC government continues to play a significant role in regulating industry development by imposing industrial policies. The PRC government also exercises significant control over China's economic growth by allocating resources, controlling payment of foreign currency-denominated obligations, setting monetary policy, regulating financial services and institutions and providing preferential treatment to particular industries or companies. See also "The PRC government exerts substantial influence over the manner in which we conduct our business activities. Its oversight and discretion over our business could result in a material adverse change in our operations and the value of our ordinary shares and ADSs. Changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system could materially and adversely affect us. In addition, rules and regulations in China can change quickly with little advance notice."

While the PRC economy has experienced significant growth in the past 40 years, growth has been uneven across different regions and among various economic sectors of China. The PRC government has implemented various measures to encourage economic development and guide the allocation of resources. Some of these measures benefit the overall PRC economy, but may have a negative effect on us or our joint ventures. For example, our financial condition and results of operations may be adversely affected by government control over capital investments or changes in tax regulations that are applicable to us or our joint ventures.

Besides policies directly related to its economic development, the PRC government may also impose other policies from time to time that may affect our ability to operate our business and the general business environment in China. For example, in response to the COVID-19 outbreak, the PRC government implemented a series of policies to contain the spread of the virus which may have negatively impacted various aspects of our operations. Since December 2022, the PRC government started to gradually lift the restrictive measures under such policies and we expect the travel, social and economic activities in the regions we operate will normalize. See also “The COVID-19 pandemic and other adverse public health developments could materially and adversely affect our business.”

The PRC government exerts substantial influence over the manner in which we conduct our business activities. Its oversight and discretion over our business could result in a material adverse change in our operations and the value of our ordinary shares and ADSs. Changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system could materially and adversely affect us. In addition, rules and regulations in China can change quickly with little advance notice.

We conduct a substantial portion of our business through our subsidiaries and joint ventures in China. PRC laws and regulations govern our and their operations in China. The Chinese government has exercised and continues to exercise substantial control over virtually every sector of the Chinese economy through regulation and state ownership. For example, the PRC government has recently published new policies that significantly affected certain industries such as the education and internet industries, and we cannot rule out the possibility that it will in the future release regulations or policies regarding our industry that could adversely affect our business, financial condition and results of operations. See also “The PRC’s economic, political and social conditions, as well as governmental policies, could affect the business environment and financial markets in China, our ability to operate our business, our liquidity and our access to capital” and “The PRC government may intervene in our offerings conducted overseas or on foreign investment in China-based issuers, which could result in a material change in our operations and our ordinary shares and ADSs could decline in value or become worthless.”

Our ability to operate in China may be harmed by changes in its laws and regulations. The central or local governments may impose new, stricter regulations or interpretations of existing regulations that would require additional expenditures and efforts on our part to ensure our compliance with such regulations or interpretations. For instance, regulations introduced by the NMPA concerning drug inspection, investigation, evidence collection and disposal are relatively new, and because of the limited volume of published judicial decisions, which are non-binding in nature, the interpretation and enforcement of these laws and regulations are uncertain. In addition, the implementation of laws and regulations may be in part based on government policies and internal rules that are subject to the interpretation and discretion of different government agencies (some of which are not published on a timely basis or at all) that may have a retroactive effect. As a result, we may not be aware of our, our collaboration partners’ or our joint ventures’ violation of these policies and rules until sometime after the violation. The imposition of new regulations or interpretations of existing regulations can occur quickly with little advance notice. We may incur penalties for any failure to comply with PRC laws and regulations. In addition, any litigation in China, regardless of outcome, may be protracted and result in substantial costs and diversion of resources and management attention. Since PRC administrative and court authorities have significant discretion in interpreting and implementing statutory and contractual terms, it may be more difficult to evaluate the outcome of administrative and court proceedings and the level of legal protection we enjoy than in more developed legal systems.

For further information regarding government regulation in China and other jurisdictions, see Item 4.B. “Business Overview—Regulations—Government Regulation of Pharmaceutical Product Development and Approval—PRC Regulation of Pharmaceutical Product Development and Approval,” “Business Overview—Regulations—Coverage and Reimbursement—PRC Coverage and Reimbursement” and “Business Overview—Regulations—Other Healthcare Laws—Other PRC Healthcare Laws.”

The PRC government has increasingly strengthened oversight in offerings conducted overseas or on foreign investment in China-based issuers, which could result in a material change in our operations and our ordinary shares and ADSs could decline in value or become worthless.

The PRC government has recently indicated an intent to take actions to exert more oversight and control over offerings that are conducted overseas and/or foreign investment in China-based issuers. For example, on July 6, 2021, the relevant PRC government authorities made public the Opinions on Strictly Scrutinizing Illegal Securities Activities in Accordance with the Law, or the Opinions. These Opinions emphasized the need to strengthen the administration over illegal securities activities and the supervision of overseas listings by China-based companies and proposed to take effective measures, such as promoting the construction of relevant regulatory systems to deal with the risks and incidents faced by China-based overseas-listed companies.

On December 24, 2021, the CSRC issued the Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) and the Administrative Measures for the Filing of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments), collectively the Draft Overseas Listing Regulations, for public comment until January 23, 2022.

Following issuance of the Draft Overseas Listing Regulations, on February 17, 2023, the CSRC issued the Notice on Filing Arrangements for Overseas Securities Offering and Listing by Domestic Companies (the "**CSRC Filing Notice**"), stating that the CSRC has published the Trial Administrative Measures of Overseas Securities Offering and Listing by Domestic Companies (the "**Trial Measures**") and five supporting guidelines (the "**Listing Guidelines**"), collectively the Trial Measures and Listing Guidelines. Among others, the Trial Measures and Listing Guidelines provide that overseas offerings and listings by PRC domestic companies shall:

(i) require submission of relevant materials that contain a filing report and a legal opinion, providing truthful, accurate and complete information on matters including but not limited to the shareholders of the issuer. Where the filing documents are complete and in compliance with stipulated requirements, the CSRC shall, within 20 working days after receipt of filing documents, conclude the filing procedure and publish filing results on the CSRC website. Where filing documents are incomplete or do not conform to stipulated requirements, the CSRC shall request supplementation and amendment thereto within five working days after receipt of the filing documents. The issuer should then complete supplementation and amendment within 30 working days;

(ii) abide by laws, administrative regulations and relevant state rules concerning foreign investment in China, state-owned asset administration, industry regulation and outbound investment, and shall not disrupt the PRC domestic market order, harm state or public interests or undermine the lawful rights and interests of PRC domestic investors;

(iii) abide by national secrecy laws and relevant provisions. Necessary measures shall be taken to fulfill confidentiality obligations. Divulgence of state secrets or working secrets of government agencies is strictly prohibited. Provision of personal information and important data, etc., to overseas parties in relation to overseas offering and listing of PRC domestic companies shall be in compliance with applicable laws, administrative regulations and relevant state rules; and

(iv) be made in strict compliance with relevant laws, administrative regulations and rules concerning national security in the spheres of foreign investment, cybersecurity, data security, etc., and issuers shall duly fulfill their obligations to protect national security. If the intended overseas offering and listing necessitates a national security review, relevant security review procedures shall be completed according to the law before the application for such offering and listing is submitted to any overseas parties such as securities regulatory agencies and trading venues;

The Trial Measures will come into effect on March 31, 2023. PRC domestic companies seeking to offer and list securities (which, for the purposes of the Trial Measures, are defined thereunder as equity shares, depository receipts, corporate bonds convertible to equity shares, and other equity securities that are offered and listed overseas, either directly or indirectly, by PRC domestic companies) in overseas markets, either via direct or indirect means, must file with the CSRC within three working days after their application for an overseas listing is submitted.

The Trial Measures provide that where a PRC domestic company seeks to indirectly offer and list securities in overseas markets, the issuer shall designate a major domestic operating entity, which shall, as the domestic entity responsible, file with the CSRC. The Trial Measures stipulate that an overseas listing will be determined as "indirect" if the issuer meets both of the following conditions: (1) 50% or more of any of the issuer's operating revenue, total profit, total assets or net assets as documented in its audited consolidated financial statements for the most recent accounting year are accounted for by PRC domestic companies ("**Condition I**"), and (2) the main parts of the issuer's business activities are conducted in the PRC, or its main places of business are located in the PRC, or the senior managers in charge of its business operations and management are mostly Chinese citizens or domiciled in the PRC ("**Condition II**"); whether Chinese citizens from Taiwan, Hong Kong, and Macau are included in the foregoing specification is not specified. The determination as to whether or not an overseas offering and listing by PRC domestic companies is indirect shall be made on a 'substance over form' basis; the Listing Guidelines further stipulate that if an issuer not satisfying Condition I submits an application for issuance and listing in overseas markets in accordance with relevant non-PRC issuance regulations requiring such issuer to disclose risk factors mainly related to the PRC, the securities firm(s) and the issuer's PRC counsel should follow the principle of 'substance over form' in order to identify and argue whether the issuer should complete a filing under the Trial Measures.

Subsequent securities offerings of an issuer in (i) the same overseas market where it has previously offered and listed securities, and (ii) an overseas market other than one where the issuer has previously offered and listed securities shall be filed with the CSRC within three working days after offerings are completed. Additionally, the Trial Measures stipulate that after an issuer has offered and listed securities in an overseas market, the issuer shall submit a report to the CSRC within three working days after the occurrence and public disclosure of (i) a change of control thereof, (ii) investigations of or sanctions imposed on the issuer by overseas securities regulators or relevant competent authorities, (iii) changes of listing status or transfers of listing segment, and (iv) a voluntary or mandatory delisting.

The CSRC Filing Notice states that, beginning from March 31, 2023, PRC domestic enterprises which have already issued and listed securities overseas and fall within the scope of filing under the Trial Measures shall be considered "existing enterprises" ("**Existing Listed Enterprises**"). Existing Listed Enterprises are not required to complete filings immediately; rather, Existing Listed Enterprises should complete filings if they are subsequently involved in matters require filings, such as follow-on financing activities, in accordance with the Trial Measures.

There is a possibility that we may be deemed as an Existing Listed Enterprise as defined under the CSRC Filing Notice, and that future offerings of listed securities or listings outside China by us may be subject to CSRC filing requirements in accordance with the Trial Measures. Given that the Trial Measures and Listing Guidelines have been introduced recently, and that there remain substantial uncertainties surrounding the enforcement thereof, we cannot assure you that, if required, we would be able to complete the filings and fully comply with the relevant new rules on a timely basis, if at all. Further, as of the date of this annual report, the aforementioned Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) issued on December 24, 2021 remain in draft form and final and effective versions are yet to be published.

In addition, the Measures for Cybersecurity Review, which took effect on February 15, 2022, requires, among others, prior cybersecurity review for online platform operators holding over one million users' personal information before any public listing in a foreign country. The Measures on Security Assessment of Cross-border Data Transfer, effective on September 1, 2022, specify that data controllers and/or critical information infrastructure operators will be subject to security assessment. There remain uncertainties as to whether such measures are applicable to our business. See also "We are subject to stringent privacy and cybersecurity laws, information security policies and contractual obligations related to data privacy and security, and we may be exposed to risks related to our management of the medical data of subjects enrolled in our clinical trials and other personal or sensitive information."

On February 24, 2023, the CSRC and other PRC governmental authorities jointly issued the Provisions on Strengthening Confidentiality and Archives Administration of Overseas Securities Offering and Listing by Domestic Companies (the "Confidentiality Provisions"), which will come into effect on March 31, 2023. According to the Confidentiality Provisions, PRC domestic companies that directly or indirectly conduct overseas offerings and listings shall strictly abide by the laws and regulations on confidentiality when providing or publicly disclosing, whether directly or through their overseas listed entities, materials to securities services providers. In the event such materials contain state secrets or working secrets of government agencies, PRC domestic companies shall first obtain approval from authorities, and file with the secrecy administrative department at the same level with the approving authority; in the event that such materials, if divulged, will jeopardize national security or public interest, PRC domestic companies shall comply with procedures stipulated by national regulations. PRC domestic companies shall also provide a written statement of the specific sensitive information provided when providing materials to securities service providers, and such written statements shall be retained for inspection. As the Confidentiality Provisions were recently promulgated and are yet to take effect, their interpretation and implementation remain substantially uncertain.

If (i) we mistakenly conclude that certain regulatory filings, permissions and approvals are not required or (ii) applicable laws, regulations, or interpretations change and (iii) we are required to obtain such filings, permissions or approvals in the future, we may be unable to obtain them in a timely manner, or at all, and such filings, permissions or approvals may be denied or rescinded even if obtained. We may face adverse actions or sanctions by the CSRC or other PRC regulatory agencies if we are unable to comply with such requirements, which may result in fines and penalties, restrictions on our operations, having to delist from a stock exchange outside of China, the halting of securities offerings to foreign investors and other actions that could materially and adversely affect our operations and the interest of our investors and cause a significant depreciation in the price of our ordinary shares and ADSs.

Certain PRC regulations may make it more difficult for us to pursue growth through acquisitions. Any failure or perceived failure by us to comply with PRC anti-monopoly laws and regulations may result in governmental investigations or enforcement actions, litigation or claims against us and could have an adverse effect on our business, financial condition and results of operations.

We may pursue potential strategic acquisitions that are complementary to our business and operations. In doing so, we will be subject to a variety of PRC anti-monopoly laws. The Regulations on Mergers and Acquisitions of Domestic Enterprises by Foreign Investors, or the M&A Rules, adopted by six PRC regulatory agencies in 2006 and amended in 2009, established additional procedures and requirements that could make merger and acquisition activities by foreign investors more time-consuming and complex. For example, the M&A Rules require that the MOFCOM be notified in advance of any change-of-control transaction in which a foreign investor takes control of a PRC domestic enterprise if (i) any important industry is concerned, (ii) such transaction involves factors that have or may have impact on the national economic security or (iii) such transaction will lead to a change in control of a domestic enterprise which holds a famous trademark or PRC time-honored brand. The approval from the MOFCOM must be obtained in circumstances where overseas companies established or controlled by PRC enterprises or residents acquire affiliated domestic companies. Mergers, acquisitions or contractual arrangements that allow one market player to take control of or to exert decisive impact on another market player must also be notified in advance to the SAMR when the threshold under the Provisions on Thresholds for Prior Notification of Concentrations of Undertakings, or the Prior Notification Rules, issued by the State Council in 2008 and amended in 2018, is triggered. PRC national security review rules, which became effective in September 2011, require a strict review of (a) mergers and acquisitions by foreign investors that raise "national defense and security" concerns and (b) mergers and acquisitions through which foreign investors may acquire de facto control over domestic enterprises that raise "national security" concerns. The rules also prohibit any activities attempting to bypass a security review, including by structuring the transaction through a proxy or contractual control arrangement.

Further, the Measures for the Security Review of Foreign Investments promulgated by the NDRC and MOFCOM, which became effective from January 2021, require that a security review by relevant governmental authorities must be conducted for foreign investments that affect or may affect national security in accordance with the provisions thereunder.

The PRC anti-monopoly enforcement agencies have in recent years strengthened enforcement under the PRC Anti-Monopoly Law. In March 2018, the SAMR was formed as a new governmental agency to take over, among other things, the anti-monopoly enforcement functions from the relevant departments under the MOFCOM, the NDRC and SAMR. Since its inception, the SAMR has continued to strengthen anti-monopoly enforcement. In November 2021, the State Council inaugurated the National Anti-Monopoly Bureau, which aims to further implement fair competition policies and strengthen anti-monopoly supervision in the PRC, particularly to strengthen oversight and law enforcement in areas involving innovation, science and technology, information security and people's livelihoods.

Complying with the requirements of these regulations when pursuing acquisitive transactions could be time-consuming, and any required approval processes, including obtaining approval or clearance from the MOFCOM, may delay or inhibit our ability to complete such transactions, which could affect our ability to expand our business or maintain our market share. Due to the enhanced enforcement of the Anti-Monopoly Law, we may receive greater scrutiny and attention from regulators and more frequent and rigid investigations or review by regulators, which may increase our compliance costs and subject us to heightened risks and challenges. In addition, there are significant uncertainties on the evolving legislative activities and varied local implementation practices of anti-monopoly and competition laws and regulations in China. The amended Anti-Monopoly Law, published in October 2021 in draft form for public comment, became effective in August 2022. It imposes a higher regulatory requirement to complete an acquisitive transaction. Any failure or perceived failure by us to comply with the anti-monopoly laws and regulations may result in governmental investigations or enforcement actions, lawsuits or claims against us and could have an adverse effect on our business, financial condition and results of operations. See also "Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs—We may engage in strategic transactions, including acquisitions, investments, joint ventures or divestitures that may have an adverse effect on our business. If we engage in a strategic transaction, there is no assurance that the transaction will be consummated."

Restrictions on currency exchange may limit our ability to receive and use our revenue effectively.

Substantially all of our revenue is denominated in renminbi, which currently is not a freely convertible currency. A portion of our revenue may be converted into other currencies to meet our foreign currency obligations, including, among others, payments of dividends declared, if any, in respect of our ordinary shares or ADSs. Under China's existing foreign exchange regulations, our subsidiaries and joint ventures are able to pay dividends in foreign currencies or convert renminbi into other currencies for use in operations without prior approval from the PRC State Administration of Foreign Exchange, or the SAFE, by complying with certain procedural requirements. However, we cannot assure you that the PRC government will not take future measures to restrict access to foreign currencies for current account transactions.

Our PRC subsidiaries' and joint ventures' ability to obtain foreign exchange is subject to significant foreign exchange controls and, in the case of amounts under the capital account, requires the approval of and/or registration with PRC government authorities, including the SAFE. In particular, if we finance our PRC subsidiaries or joint ventures by means of foreign debt from us or other foreign lenders, the amount is not allowed to exceed either the cross-border financing risk weighted balance calculated based on a formula by the PBOC or the difference between the amount of total investment and the amount of the registered capital. Further, such loans must be filed with and registered with the SAFE or their local branches and the National Development and Reform Commission (if applicable). If we finance our PRC subsidiaries or joint ventures by means of additional capital contributions, the amount of these capital contributions must first be filed with the relevant government approval authority. These limitations could affect the ability of our PRC subsidiaries and joint ventures to obtain foreign exchange through debt or equity financing.

Our business benefits from certain PRC government tax incentives. Any changes to, or our PRC subsidiaries/joint ventures failing to continuously meet the criteria for these incentives could have a material adverse effect on our operating results by significantly increasing our tax expenses.

Certain of our PRC subsidiaries and a joint venture have been granted High and New Technology Enterprise, or HNTE, status by the relevant PRC authorities. This status allows the relevant enterprise to enjoy a reduced Enterprise Income Tax, or EIT, rate at 15% on its taxable profits. For the duration of its HNTE grant, the relevant PRC enterprise must continue to meet the relevant HNTE criteria or else the 25% standard EIT rate will be applied from the beginning of the calendar year when the enterprise fails to meet the relevant criteria. If the rules for such incentives are amended, it would be uncertain whether any criteria as amended can be met, in which case the higher EIT rate may apply resulting in increased tax burden which will impact our business, financial condition, results of operations and growth prospects.

We may be treated as a resident enterprise for PRC Tax purposes under China's Enterprise Income Tax Law and Implementation Rules, or the EIT Law, and our global income may therefore be subject to PRC income tax.

China's EIT Law defines the term "de facto management bodies" as "bodies that substantially carry out comprehensive management and control on the business operation, employees, accounts and assets of enterprises." Under the EIT Law, an enterprise incorporated outside of China whose "de facto management bodies" are located in China is considered a "resident enterprise" and will be subject to a uniform 25% EIT rate on its global income. On April 22, 2009, China's State Administration of Taxation, or the SAT, in the Notice Regarding the Determination of Chinese-Controlled Offshore-Incorporated Enterprises as PRC Tax Resident Enterprises on the Basis of De Facto Management Bodies, or Circular 82, further specified certain criteria for the determination of what constitutes "de facto management bodies." If all of these criteria are met, the relevant foreign enterprise may be regarded to have its "de facto management bodies" located in China and therefore be considered a resident enterprise in China. These criteria include: (i) the enterprise's day-to-day operational management is primarily exercised in China; decisions relating to the enterprise's financial and human resource matters are made or subject to approval by organizations or personnel in China; (ii) the enterprise's primary assets, accounting books and records, company seals, and board and shareholders' meeting minutes are located or maintained in China; and (iii) 50% or more of voting board members or senior executives of the enterprise habitually reside in China. Although Circular 82 only applies to foreign enterprises that are majority-owned and controlled by PRC enterprises, not those owned and controlled by foreign enterprises or individuals, the determining criteria set forth in Circular 82 may be adopted by the PRC tax authorities as the test for determining whether the enterprises are PRC tax residents, regardless of whether they are majority-owned and controlled by PRC enterprises.

Except for our PRC subsidiaries and joint ventures incorporated in China, we believe that none of our entities incorporated outside of China is a PRC resident enterprise for PRC tax purposes. However, the tax resident status of an enterprise is subject to determination by the PRC tax authorities, and uncertainties remain with respect to the interpretation of the term "de facto management body."

If we are treated as a PRC tax resident, dividends distributed by us to our non-PRC shareholders and ADS holders or any gains realized by non-PRC shareholders and ADS holders from the transfer of our shares or ADSs may be subject to PRC tax.

Under the EIT Law, dividends payable by a PRC enterprise to its foreign investor who is (i) a non-PRC resident enterprise with no office or premises established in China, or (ii) a non-PRC resident enterprise with an office or premises established in China but whose income (i.e. dividends received) has no de facto relationship with said office or premises, as well as gains on transfers of shares of a PRC enterprise by such a foreign investor will generally be subject to a 10% withholding tax, unless such non-PRC resident enterprise's jurisdiction of tax residency has an applicable tax treaty with the PRC that provides for an exemption or a reduced rate of withholding tax.

If the PRC tax authorities determine that we should be considered a PRC resident enterprise for EIT purposes, any dividends payable by us to our non-PRC resident enterprise shareholders or ADS holders, as well as gains realized by such investors from the transfer of our shares or ADSs may be subject to a 10% withholding tax. Furthermore, if we are considered a PRC resident enterprise for EIT purposes, it is unclear whether our non-PRC individual shareholders (including our ADS holders) would be subject to any PRC tax on dividends or gains obtained by such non-PRC individual shareholders. If any PRC tax were to apply to dividends or gains realized by non-PRC individuals, it would generally apply at a rate of up to 20% (which in the case of dividends may be withheld at source). The foregoing rates may be reduced by an applicable tax treaty, but it is unclear if a non-PRC resident shareholder or ADS holder would be able to obtain in practice the benefits of any tax treaties between their country of tax residence and the PRC in the event that we are treated as a PRC resident enterprise. If dividends payable to our non-PRC resident shareholders, or gains from the transfer of our shares or ADSs by such shareholders are subject to PRC tax, the value of your investment in our shares or ADSs may decline significantly.

There is uncertainty regarding the PRC withholding tax rate that will be applied to distributions from our PRC subsidiaries and joint ventures to their respective Hong Kong immediate holding companies, which could have a negative impact on our business.

The EIT Law provides that a withholding tax at the rate of 10% is applicable to dividends payable by a PRC resident enterprise to investors who are "non-resident enterprises" (i.e., that do not have an establishment or place of business in the PRC or that have such establishment or place of business but the relevant dividend is not effectively connected with the establishment or place of business). However, pursuant to Article 10.2(1), or the Article, of the Arrangement between the Mainland of China and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income, or the Arrangement, withholding tax at a reduced rate of 5% may be applicable to dividends payable by PRC resident enterprises to beneficial owners of the dividends that are Hong Kong tax residents if certain requirements are met. There is uncertainty regarding whether the PRC tax authorities will consider us to be eligible to the reduced tax rate. If the Article is deemed not to apply to dividends payable by our PRC subsidiaries and joint ventures to their respective Hong Kong immediate holding companies that are ultimately owned by us, the withholding tax rate applicable to us will be the statutory rate of 10% instead of 5% which may potentially impact our business, financial condition, results of operations and growth prospects.

Any failure to comply with PRC regulations regarding our employee equity incentive plans may subject the PRC plan participants or us to fines and other legal or administrative sanctions, which could adversely affect our business, financial condition and results of operations.

In February 2012, the SAFE promulgated the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Stock Incentive Plans of Overseas Publicly Listed Companies. Based on this regulation, PRC residents who are granted shares or share options by a company listed on an overseas stock market under its employee share option or share incentive plan are required to register with the SAFE or its local counterparts by following certain procedures. We and our employees who are PRC residents and individual beneficial owners who have been granted shares or share options have been subject to these rules due to our listing on the AIM market, Nasdaq and SEHK. We have registered the option schemes and the share incentive plan and will continue to assist our employees to register their share options or shares. However, any failure of our PRC individual beneficial owners and holders of share options or shares to comply with the SAFE registration requirements in the future may subject them to fines and legal sanctions and may, in rare instances, limit the ability of our PRC subsidiaries to distribute dividends to us.

In addition, the SAT has issued circulars concerning employee share options or restricted shares. Under these circulars, employees working in the PRC who exercise share options, or whose restricted shares vest, will be subject to PRC individual income tax. The PRC subsidiaries of an overseas listed company have obligations to file documents related to employee share options or restricted shares with relevant tax authorities and to withhold individual income tax of those employees related to their share options or restricted shares. Although the PRC subsidiaries currently withhold individual income tax from the PRC employees in connection with their exercise of share options, if they fail to report and pay the tax withheld according to relevant laws, rules and regulations, the PRC subsidiaries may face sanctions imposed by the tax authorities or other PRC government authorities.

We may be involved in litigation, legal disputes, claims or administrative proceedings which could be costly and time-consuming to resolve.

We may become subject, from time to time, to legal proceedings and claims that arise in the ordinary course of business or pursuant to governmental or regulatory enforcement activity. Any litigation or proceeding to which we become a party might result in substantial costs and divert management's attention and resources. Furthermore, any litigation, legal disputes, claims or administrative proceedings which are initially not of material importance may escalate and become important to us due to a variety of factors, such as changes in the facts and circumstances of the cases, the likelihood of loss, the monetary amount at stake and the parties involved. Our insurance might not cover claims brought against us, provide sufficient payments to financially cover all of the costs to resolve such claims or continue to be available on terms acceptable to us.

The political relationships between China and other countries may affect our business operations.

We conduct our business primarily through our subsidiaries and joint ventures in China, but we also have clinical operations in the United States and other foreign jurisdictions. As a result, China's political relationships with the United States and other jurisdictions may affect our business operations. There can be no assurance that our clinical trial participants or customers will not alter their perception of us or their preferences as a result of adverse changes to the state of political relationships between China and the relevant foreign jurisdictions. Any tensions and political concerns between China and the relevant foreign jurisdictions may adversely affect our business, financial condition, results of operations, cash flows and prospects.

Risks Relating to Intellectual Property

If we, our joint ventures or our collaboration partners are unable to protect our or their products and drug candidates through intellectual property rights, our competitors may compete directly against us or them.

Our success depends, in part, on our, our joint venture partners' and our collaboration partners' ability to protect our and our joint ventures' and our collaboration partners' products and drug candidates from competition by establishing, maintaining and enforcing our or their intellectual property rights. We, our joint ventures and our collaboration partners seek to protect the products and technology that we and they consider commercially important by filing PRC and international patent applications, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. As of December 31, 2022, we had 232 issued patents, including 18 Chinese patents, 22 U.S. patents and 12 European patents, 295 patent applications pending in major market jurisdictions, and 7 pending Patent Cooperation Treaty, or PCT, patent applications relating to the drug candidates of our Oncology/Immunology operations. For more details, see Item 4.B. "Business Overview—Patents and Other Intellectual Property." Patents may become invalid and patent applications may not be granted for a number of reasons, including known or unknown prior art, deficiencies in the patent application or the lack of originality of the technology. In addition, the PRC and the United States have adopted the "first-to-file" system under which whoever first files an invention patent application will be awarded the patent. Under the first-to-file system, third parties may be granted a patent relating to a technology which we invented. Furthermore, the terms of patents are finite. The patents we hold and patents to be issued from our currently pending patent applications generally have a twenty-year protection period starting from the date of application.

We, our joint ventures and/or our collaboration partners may become involved in patent litigation against third parties to enforce our or their patent rights, to invalidate patents held by such third parties, or to defend against such claims. A court may refuse to stop the other party from using the technology at issue on the grounds that our or our joint ventures' patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we or our joint ventures infringe their intellectual property or that a patent we, our joint ventures or our collaboration partners have asserted against them is invalid or unenforceable. In patent litigation, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us or our intellectual property to assert such challenges to our intellectual property rights.

The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information or made a misleading statement during prosecution. It is possible that prior art of which we, our joint ventures or our collaboration partners and the patent examiner were unaware during prosecution exists, which could render our or their patents invalid. Moreover, it is also possible that prior art may exist that we, our joint ventures or our collaboration partners are aware of but do not believe is relevant to our or their current or future patents, but that could nevertheless be determined to render our patents invalid. The cost to us or our joint ventures of any patent litigation or similar proceeding could be substantial, and it may consume significant management time. We and our joint ventures do not maintain insurance to cover intellectual property infringement.

An adverse result in any litigation proceeding could put one or more of our or our joint ventures' patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our or our joint ventures' products or our drug candidates, we could lose at least part, and perhaps all, of the patent protection covering such product or drug candidate. Competing drugs may also be sold in other countries in which our or our joint ventures' patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our or our joint ventures' infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a materially adverse effect on our business.

Intellectual property and confidentiality legal regimes in China may not afford protection to the same extent as in the United States or other countries. Implementation and enforcement of PRC intellectual property laws may be deficient and ineffective. Policing unauthorized use of proprietary technology is difficult and expensive, and we or our joint ventures may need to resort to litigation to enforce or defend patents issued to us or them or to determine the enforceability, scope and validity of our proprietary rights or those of others. The experience and capabilities of PRC courts in handling intellectual property litigation varies, and outcomes are unpredictable. Further, such litigation may require a significant expenditure of cash and may divert management's attention from our or our joint ventures' operations, which could harm our business, financial condition and results of operations. An adverse determination in any such litigation could materially impair our or our joint ventures' intellectual property rights and may harm our business, prospects and reputation.

Developments in patent law could have a negative impact on our business.

From time to time, authorities in the United States, China and other government authorities may change the standards of patentability, and any such changes could have a negative impact on our business. For example, in the United States, the Leahy-Smith America Invents Act, or the America Invents Act, which was signed into law in 2011, includes a number of significant changes to U.S. patent law. These changes include a transition from a "first-to-invent" system to a "first-to-file" system, changes to the way issued patents are challenged, and changes to the way patent applications are disputed during the examination process. As a result of these changes, patent law in the United States may favor larger and more established companies that have greater resources to devote to patent application filing and prosecution. The U.S. Patent and Trademark Office, or USPTO, has developed regulations and procedures to govern the full implementation of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and, in particular, the first-to-file provisions became effective on March 16, 2013. Substantive changes to patent law associated with the America Invents Act, including continually developing case law, may affect our ability to obtain patents, and if obtained, to enforce or defend them. Accordingly, it is not clear what, if any, impact the America Invents Act will have on the cost of prosecuting our or our joint ventures' patent applications and our or their ability to obtain patents based on our or our joint ventures' discoveries and to enforce or defend any patents that may issue from our or their patent applications, all of which could have a material adverse effect on our business.

If we are unable to maintain the confidentiality of our and our joint ventures' trade secrets, the business and competitive position of ourselves and our joint ventures may be harmed.

In addition to the protection afforded by patents and the PRC's State Secret certification, we and our joint ventures rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our and our joint ventures' proprietary technology and processes, in part, by entering into confidentiality agreements with our and their collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our and their consultants and employees. We and our joint ventures may not be able to prevent the unauthorized disclosure or use of our or their technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we and our joint ventures may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third-party illegally obtained and is using our or our joint ventures' trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts in China and other jurisdictions outside the United States are sometimes less prepared or willing to protect trade secrets.

Our and our joint ventures' trade secrets could otherwise become known or be independently discovered by our or their competitors. For example, competitors could purchase our drugs and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our or our joint ventures' trade secrets were to be lawfully obtained or independently developed by a competitor, we and our joint ventures would have no right to prevent them, or others to whom they communicate it, from using that technology or information to compete against us or our joint ventures. If our or our joint ventures' trade secrets are unable to adequately protect our business against competitors' drugs, our competitive position could be adversely affected, as could our business.

We and our joint ventures are dependent on trademark and other intellectual property rights licensed from others. If we lose our licenses for any of our products, we or our joint ventures may not be able to continue developing such products or may be required to change the way we market such products.

We and our joint ventures are parties to licenses that give us or them rights to third-party intellectual property that are necessary or useful for our or our joint ventures' businesses. In particular, the "Hutchison", "Chi-Med", "Hutchison China MediTech" and "HUTCHMED" brands, among others, have been licensed to us by Hutchison Whampoa Enterprises Limited, an affiliate of our largest shareholder, Hutchison Healthcare Holdings Limited. Hutchison Whampoa Enterprises Limited grants us a royalty-free, worldwide license to such brands. For more details, please see "Item 7. Major Shareholders and Related Party Transactions—Related Party Transactions—Relationship with CK Hutchison—Intellectual property licensed by the CK Hutchison group." Under the terms of our brand license agreement, Hutchison Whampoa Enterprises Limited has the right to terminate the license if, among other things, we commit a material breach of the agreement, or within any twelve-month period the aggregate direct or indirect shareholding in our company held by CK Hutchison is reduced to less than 35%, 30% or 20%. Furthermore, the trademarks of Elunate and Orpathys are licensed to us in China by our collaboration partner Eli Lilly and AstraZeneca, respectively.

In some cases, our licensors have retained the right to prosecute and defend intellectual property rights licensed to us or our joint ventures. We depend in part on the ability of our licensors to obtain, maintain and enforce intellectual property protection for such licensed intellectual property. Such licensors may not successfully maintain their intellectual property, may determine not to pursue litigation against other companies that are infringing on such intellectual property, or may pursue litigation less aggressively than we or our joint ventures would. Without protection for the intellectual property we or our joint ventures license, other companies might be able to offer substantially identical products or branding, which could adversely affect our competitive business position and harm our business prospects.

If our or our joint ventures' products or drug candidates infringe the intellectual property rights of third parties, we and they may incur substantial liabilities, and we and they may be unable to sell these products.

Our commercial success depends significantly on our and our joint ventures' ability to operate without infringing the patents and other proprietary rights of third parties. In the PRC, invention patent applications are generally maintained in confidence until their publication 18 months from the filing date. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and invention patent applications are filed. Even after reasonable investigation, we may not know with certainty whether any third-party may have filed a patent application without our knowledge while we or our joint ventures are still developing or producing that product. While the success of pending patent applications and applicability of any of them to our or our joint ventures' programs are uncertain, if asserted against us or them, we could incur substantial costs and we or they may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- redesign products or processes to avoid infringement; and
- stop producing products using the patents held by others, which could cause us or them to lose the use of one or more of our or their products.

To date, we and our joint ventures have not received any material claims of infringement by any third parties. If a third-party claims that we or our joint ventures infringe its proprietary rights, any of the following may occur:

- we or our joint ventures may have to defend litigation or administrative proceedings that may be costly whether we or they win or lose, and which could result in a substantial diversion of management resources;
- we or our joint ventures may become liable for substantial damages for past infringement if a court decides that our technology infringes a third-party's intellectual property rights;
- a court may prohibit us or our joint ventures from producing and selling our or their product(s) without a license from the holder of the intellectual property rights, which may not be available on commercially acceptable terms, if at all; and

- we or our joint ventures may have to reformulate product(s) so that it does not infringe the intellectual property rights of others, which may not be possible or could be very expensive and time consuming.

Any costs incurred in connection with such events or the inability to sell our or our joint ventures' products may have a material adverse effect on our business and results of operations.

We, our joint ventures and our collaboration partners may not be able to effectively enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our or our joint venture's products or drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our, our joint ventures' or our collaboration partners' ability to protect and enforce our or their intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, may not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us or our joint ventures to stop the infringement of our or their patents or the misappropriation of our or their other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our or our joint ventures' inventions throughout the world. Competitors may use our or our joint ventures' technologies in jurisdictions where we or they have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we or our joint ventures have patent protection, if our, our joint ventures' or our collaboration partners' ability to enforce our or their patents to stop infringing activities is inadequate. These drugs may compete with our drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our or our joint ventures' patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our or their efforts and resources from other aspects of our and their businesses. While we intend to protect our intellectual property rights in the major markets for our drug candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our drug candidates. Furthermore, some of our collaborators are responsible for enforcing our intellectual property rights, for example, AstraZeneca is responsible for enforcing our intellectual property rights with respect to savolitinib on our behalf, we may be unable to ensure that such rights are enforced or maintained in all jurisdictions. Accordingly, our efforts to protect the intellectual property rights of our drug candidates in such countries may be inadequate.

We and our joint ventures may be subject to damages resulting from claims that we or they, or our or their employees, have wrongfully used or disclosed alleged trade secrets of competitors or are in breach of non-competition or non-solicitation agreements with competitors.

We and our joint ventures could in the future be subject to claims that we or they, or our or their employees, have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our and our joint ventures' employees and consultants do not improperly use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us or our joint ventures, we or our joint ventures may in the future be subject to claims that we or they caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we, our joint ventures, or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against these claims. Even if we and our joint ventures are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our or our joint ventures' defenses to these claims fail, in addition to requiring us and them to pay monetary damages, a court could prohibit us or our joint ventures from using technologies or features that are essential to our or their products or our drug candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business, and may prevent us from successfully commercializing our drug candidates. In addition, we or our joint ventures may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our or our joint ventures' ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have an adverse effect on our business, results of operations and financial condition.

Patent terms may be inadequate to protect the competitive position of our drug candidates for an adequate amount of time, and the absence of patent linkage, patent term extension and data and market exclusivity for NMPA-approved pharmaceutical products could increase the risk of early generic competition for our drug candidates in China.

In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984, generally referred to as the Hatch-Waxman Amendments, and similar legislation in the E.U. and certain other countries, provides the opportunity for limited patent term extension. The Hatch-Waxman Amendments permit a patent-term extension of up to five years to reflect patent term lost during certain portions of product development and the FDA regulatory review process. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of drug approval; only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. Depending upon the timing, duration and specifics of any FDA marketing approval process for any drug candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we fail to obtain patent term extensions or if the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and thus our revenue could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and pre-clinical data and launch their product earlier than might otherwise be expected, and our competitive position, business, financial condition, results of operations and prospects could be materially adversely affected.

The Hatch-Waxman Amendments also include a process for patent linkage, pursuant to which the FDA will stay approval of certain follow-on applications during the pendency of litigation between the follow-on applicant and the patent holder or licensee, generally for a period of 30 months. Moreover, the Hatch-Waxman Amendments provide for statutory exclusivities that can prevent submission or approval of certain follow-on marketing applications. For example, federal law provides a five-year period of exclusivity within the United States to the first applicant to obtain approval of a new chemical entity and three years of exclusivity protecting certain innovations to previously approved active ingredients where the applicant was required to conduct new clinical investigations to obtain approval for the modification. Similarly, the U.S. Orphan Drug Act provides seven years of market exclusivity for certain drugs to treat rare diseases, where the FDA designates the drug candidate as an orphan drug and the drug is approved for the designated orphan indication. See "Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates—Although we have obtained orphan drug designation for surufatinib for the treatment of pancreatic NETs in the United States, we may not be able to obtain or maintain the benefits associated with orphan drug status, including market exclusivity."

Chinese regulators have set forth a framework for integrating patent linkage and data exclusivity into the China regulatory regime, as well as for establishing a pilot program for patent term extension. To be implemented, this framework will require adoption of regulations. On October 17, 2020, the Standing Committee of the National People's Congress published the Patent Law of PRC (Amended in 2020), which came into effect on June 1, 2021, or the Amended Patent Law. The Amended Patent Law provides that, among other things, the owner of the patent for an innovative new drug that has been granted the marketing authorization in China is entitled to request the Patent Administration Department under the State Council to grant a patent term extension of up to five years, in order to compensate the time required for the regulatory approval for the commercialization of such innovative new drug, provided that the patent term of such innovative new drug shall not exceed a total of 14 years. Furthermore, the PRC government entered into the Economic and Trade Agreement Between the Government of the People's Republic of China and the Government of the United States of America with the U.S. government in January 2020 which provides that the owner of the patent for an innovative new drug that has been granted the marketing authorization in China is entitled to request a patent term extension of up to five years, provided that the patent term of such innovative new drug shall not exceed a total of 14 years from the date of marketing approval in China. If we are unable to obtain patent term extension, or the term of any such extension is less than that we request, our competitors or other third parties may obtain approval of competing products following our patent expiration. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Risks Relating to Our ADSs

The PCAOB had historically been unable to inspect our auditor in relation to their audit work performed for our financial statements and the inability of the PCAOB to conduct inspections of our auditor in the past has deprived our investors with the benefits of such inspections.

Our auditor, the independent registered public accounting firm that issues the audit report included elsewhere in this annual report, as an auditor of companies that are traded publicly in the United States and a firm registered with the PCAOB, is subject to laws in the United States pursuant to which the PCAOB conducts regular inspections to assess its compliance with the applicable professional standards. The auditor is located in mainland China, a jurisdiction where the PCAOB was historically unable to conduct inspections and investigations completely before 2022. As a result, we and investors in the ADSs were deprived of the benefits of such PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China in the past has made it more difficult to evaluate the effectiveness of our independent registered public accounting firm's audit procedures or quality control procedures as compared to auditors outside of China that are subject to the PCAOB inspections. On December 15, 2022, the PCAOB issued a report that vacated its December 16, 2021 determination and removed mainland China and Hong Kong from the list of jurisdictions where it is unable to inspect or investigate completely registered public accounting firms. However, if the PCAOB determines in the future that it no longer has full access to inspect and investigate completely accounting firms in mainland China and Hong Kong, and we use an accounting firm headquartered in one of these jurisdictions to issue an audit report on our financial statements filed with the Securities and Exchange Commission, we and investors in our ADSs would be deprived of the benefits of such PCAOB inspections again, which could cause investors and potential investors in the ADSs to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

Our ADSs may be prohibited from trading in the United States under the HFCAA in the future if the PCAOB is unable to inspect or investigate completely auditors located in China. The delisting of the ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment.

Pursuant to the HFCAA, if the SEC determines that we have filed audit reports issued by a registered public accounting firm that has not been subject to inspections by the PCAOB for two consecutive years, the SEC will prohibit our shares or ADSs from being traded on a national securities exchange or in the over-the-counter trading market in the United States.

On December 16, 2021, the PCAOB issued a report to notify the SEC of its determination that the PCAOB was unable to inspect or investigate completely registered public accounting firms headquartered in mainland China and Hong Kong and our auditor was subject to that determination. In March 2022, the SEC conclusively listed us as a Commission-Identified Issuer under the HFCAA following the filing of our annual report on Form 20-F for the fiscal year ended December 31, 2021. On December 15, 2022, the PCAOB removed mainland China and Hong Kong from the list of jurisdictions where it is unable to inspect or investigate completely registered public accounting firms. For this reason, we do not expect to be identified as a Commission-Identified Issuer under the HFCAA after we file this annual report on Form 20-F for the fiscal year ended December 31, 2022.

Each year, the PCAOB will determine whether it can inspect and investigate completely audit firms in mainland China and Hong Kong, among other jurisdictions. If the PCAOB determines in the future that it no longer has full access to inspect and investigate completely accounting firms in mainland China and Hong Kong and we use an accounting firm headquartered in one of these jurisdictions to issue an audit report on our financial statements filed with the Securities and Exchange Commission, we would be identified as a Commission-Identified Issuer following the filing of the annual report on Form 20-F for the relevant fiscal year. In accordance with the HFCAA, our securities would be prohibited from being traded on a national securities exchange or in the over-the-counter trading market in the United States if we are identified as a Commission-Identified Issuer for two consecutive years in the future. Although our ordinary shares have been listed on the SEHK and AIM and the ADSs and ordinary shares are fully fungible, we cannot assure your that an active trading market for our ordinary shares on the Hong Kong Stock Exchange or AIM of the London Stock Exchange will be sustained or that the ADSs can be converted and traded with sufficient market recognition and liquidity, if our shares and ADSs are prohibited from trading in the United States. A prohibition of being able to trade in the United States would substantially impair your ability to sell or purchase our ADSs when you wish to do so, and the risk and uncertainty associated with delisting would have a negative impact on the price of our ADSs. Also, such a prohibition would significantly affect our ability to raise capital on terms acceptable to us, or at all, which would have a material adverse impact on our business, financial condition, and prospects.

The listings of our shares in multiple venues may adversely affect the liquidity and value of them.

Our ADSs continue to be listed on Nasdaq, and our shares continue to be admitted to trading on the AIM. Our shares were listed on the SEHK in June 2021. The listing of the shares on the AIM and the SEHK, and the ADSs on Nasdaq, may reduce the liquidity of these securities in one or each of these markets and may adversely affect the development of an active trading market for the shares in each of these markets. The price of the shares could also be adversely affected by trading on Nasdaq. Similarly, the price of the ADSs could also be adversely affected by trading on the AIM and the SEHK. We may also seek further listings on other stock exchanges such as the Shanghai Stock Exchange, which could further affect the liquidity and value of the shares and the ADSs. Furthermore, the shares trade on the SEHK largely in electronic book-entry form. However, the ADSs are backed by physical ordinary share certificates, and the depositary for our ADS program is unable to accept book-entry interests into its custody in order to issue ADSs. As a result, if a holder of the shares wishes to deposit the shares into the ADS program and hold ADSs for trading on Nasdaq or vice versa, the issuance and cancellation process may be longer than if the depositary could accept such book-entry interests.

Our largest shareholder owns a significant percentage of our ordinary shares, which may limit the ability of other shareholders to influence corporate matters.

As of February 15, 2023, Hutchison Healthcare Holdings Limited owned approximately 38.5% of our ordinary shares. Accordingly, Hutchison Healthcare Holdings Limited can influence the outcome of any corporate transaction or other matter submitted to shareholders for approval and the interests of Hutchison Healthcare Holdings Limited may differ from the interests of our other shareholders. Under our Articles of Association, certain matters, such as amendments to our amended and restated Memorandum and Articles of Association, require the approval of not less than three-fourths of votes cast by such shareholders as, being entitled so to do, vote in person (or, in the case of such shareholders as are corporations, by their respective duly authorized representative) or by proxy. Therefore, Hutchison Healthcare Holdings Limited's approval will be required to achieve any such threshold. In addition, Hutchison Healthcare Holdings Limited has and will continue to have a significant influence over the management and the strategic direction of our company.

Substantial future sales or perceived potential sales of our ADSs, ordinary shares or other equity or equity-linked securities in the public market could cause the price of our ADSs to decline significantly.

Sales of our ADSs, ordinary shares or other equity or equity-linked securities in the public market, or the perception that these sales could occur, could cause the market price of our ADSs to decline significantly. All of our ordinary shares represented by ADSs are freely transferable by persons other than our affiliates without restriction or additional registration under the Securities Act of 1933, or the Securities Act. The ordinary shares held by our affiliates are also available for sale, subject to volume and other restrictions as applicable under Rules 144 and 701 under the Securities Act, under sales plans adopted pursuant to Rule 10b5-1 or otherwise.

We have filed with the SEC registration statements on Form F-3, commonly referred to as a "shelf registration," that permit us to sell any number of ADSs in a registered offering at our discretion. We have completed registered offerings raising aggregate gross proceeds of approximately $537.9 million under such shelf registration statements. Furthermore, our largest shareholder has completed registered secondary offerings raising aggregate gross proceeds of approximately $310.4 million for it as a selling shareholder under a shelf registration statement. In addition, we completed our initial public offering in Hong Kong and global offering of our ordinary shares in 2021, raising aggregate gross proceeds of approximately $614.9 million, including $80.2 million through the fulfillment of the over-allotment. We may decide to conduct future offerings from time to time, and such sales could cause the price of our ADSs to decline significantly.

In connection with the issuance of ordinary shares in private placements in 2020 and 2021, we agreed to provide three shareholders Form F-3 registration rights. Registration of the ordinary shares held by such shareholders may result in these shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. Sales of these shares, or the perception that such sales could occur, could cause the price of our ADSs to decline. In addition, any changes in the investment strategies or philosophies of our major shareholders may lead to the sale of our ADSs and other securities, which could cause the price of our ADSs to decline.

We may be at a risk of securities litigation.

Historically, securities litigation, particularly class action lawsuits brought in the United States, have often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant share price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our business, the price of our ADSs could decline.

The trading market for our ADSs will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may not be able to maintain continuous research coverage by industry or financial analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

As a foreign private issuer, we are not subject to certain U.S. securities law disclosure requirements that apply to a domestic U.S. issuer, which may limit the information publicly available to our shareholders.

As a foreign private issuer we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act and therefore there may be less publicly available information about us than if we were a U.S. domestic issuer. For example, we are not required to file quarterly reports on Form 10-Q. We are also not subject to the proxy rules in the United States, and we are not required to follow the related disclosure requirements with respect to our annual general meetings, including disclosing a compensation discussion and analysis. Our disclosure with respect to our annual general meetings will be governed by the AIM Rules for Companies, or the AIM Rules, listing rules in Hong Kong and Cayman Islands requirements. In addition, our officers, directors and principal shareholders are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and the rules thereunder. Therefore, our shareholders may not know on a timely basis when our officers, directors and principal shareholders purchase or sell our ordinary shares or ADSs.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with corporate governance listing standards.

As a foreign private issuer, we are permitted to take advantage of certain provisions in the Nasdaq listing rules that allow us to follow Cayman Islands law for certain governance matters. Certain corporate governance practices in the Cayman Islands may differ significantly from corporate governance listing standards as, except for general fiduciary duties and duties of care, Cayman Islands law has no corporate governance regime which prescribes specific corporate governance standards. We intend to continue to follow Cayman Islands corporate governance practices in lieu of the corporate governance requirements of the Nasdaq Global Select Market in respect of the following: (i) the majority independent director requirement under Section 5605(b)(1) of the Nasdaq listing rules, (ii) the requirement under Section 5605(d) of the Nasdaq listing rules that a remuneration committee comprised solely of independent directors governed by a remuneration committee charter oversee executive compensation and (iii) the requirement under Section 5605(e) of the Nasdaq listing rules that director nominees be selected or recommended for selection by either a majority of the independent directors or a nominations committee comprised solely of independent directors. Cayman Islands law does not impose a requirement that our board of directors consist of a majority of independent directors, nor does Cayman Islands law impose specific requirements on the establishment of a remuneration committee or nominating committee or nominating process. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. We have voluntarily complied with the Corporate Governance Code contained in Appendix 14 of the Rules Governing the Listing of Securities on SEHK. See Item 6.C. "Board Practice—Hong Kong Corporate Governance Code" for more details.

We may in the future lose our foreign private issuer status under U.S. securities laws, which could result in significant additional costs and expenses.

We are a foreign private issuer as defined in the Securities Act, and therefore, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act. The determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter, and, accordingly, the next determination will be made with respect to us on June 30, 2023. We would lose our foreign private issuer status if, for example, more than 50% of our ordinary shares are directly or indirectly held by residents of the United States on June 30, 2023 and we fail to meet additional requirements necessary to maintain our foreign private issuer status. If we lose our foreign private issuer status on this date, we will be required to file with the SEC periodic reports and registration statements on U.S. domestic issuer forms beginning on January 1, 2024, which are more detailed and extensive than the forms available to a foreign private issuer. We will also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors and principal shareholders will become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the Exchange Act. In addition, we will lose our ability to rely upon exemptions from certain corporate governance requirements under the Nasdaq listing rules. As a U.S.-listed public company, should we lose our foreign private issuer status, we will incur significant additional legal, accounting and other expenses that we would not incur as a foreign private issuer.

Fluctuations in the value of the renminbi may have a material adverse effect on your investment.

The value of the renminbi against the U.S. dollar and other currencies fluctuates and is affected by, among other things, changes in China's and international political and economic conditions and the PRC government's fiscal and currency policies. Since 1994, the conversion of renminbi into foreign currencies, including U.S. dollars, has been based on rates set by the PBOC, which are set daily based on the previous business day's inter-bank foreign exchange market rates and current exchange rates on the world financial markets. It is expected that China may further reform its exchange rate system in the future.

Significant revaluation of the renminbi may have a material adverse effect on your investment. For example, to the extent that we need to convert U.S. dollars into renminbi for our operations, appreciation of the renminbi against the U.S. dollar would have an adverse effect on the renminbi amount we would receive from the conversion. Conversely, if we decide to convert our renminbi into U.S. dollars, appreciation of the U.S. dollar against the renminbi would have a negative effect on the U.S. dollar amount available to us. Appreciation or depreciation in the value of the renminbi relative to the U.S. dollar would affect our financial results reported in U.S. dollar terms regardless of any underlying change in our business or results of operations. In addition, our operating transactions and assets and liabilities in the PRC are mainly denominated in renminbi. Such amounts are translated into U.S. dollars for purpose of preparing our consolidated financial statements, with translation adjustments reflected in accumulated other comprehensive income/(loss) in shareholders' equity. We recorded a foreign currency translation gain of $9.5 million, a foreign currency translation gain of $3.0 million and a foreign currency translation loss of $8.5 million for the years ended December 31, 2020, 2021 and 2022, respectively.

Very limited hedging options are available in China to reduce our exposure to exchange rate fluctuations. To date, we have not entered into any hedging transactions in an effort to reduce our exposure to foreign currency exchange risk. While we may decide to enter into hedging transactions in the future, the availability and effectiveness of these hedges may be limited and we may not be able to adequately hedge our exposure or at all. In addition, our currency exchange losses may be magnified by PRC exchange control regulations that restrict our ability to convert renminbi into foreign currency.

We do not currently intend to pay dividends on our securities, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of the ADSs.

We have never declared or paid any dividends on our ordinary shares. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your ADSs at least in the near term, and the success of an investment in ADSs will depend upon any future appreciation in its value. Consequently, investors may need to sell all or part of their holdings of ADSs after price appreciation, which may never occur, to realize any future gains on their investment. There is no guarantee that the ADSs will appreciate in value or even maintain the price at which our shareholders have purchased the ADSs.

The trading prices for our ADSs may be volatile which could result in substantial losses to you.

The market price of our ADSs has been volatile. From March 17, 2016 to January 31, 2023, the closing sale price of our ADSs ranged from a high of $43.94 to a low of $7.39 per ADS.

The market price for our ADSs is likely to be highly volatile and subject to wide fluctuations in response to factors, including the following:

- announcements of competitive developments;
- regulatory developments affecting us, our customers or our competitors;
- announcements regarding litigation or administrative proceedings involving us;
- actual or anticipated fluctuations in our period-to-period operating results;
- changes in financial estimates by securities research analysts;
- additions or departures of our executive officers;
- release or expiry of lock-up or other transfer restrictions on our outstanding ordinary shares or ADSs; and
- sales or perceived sales of additional ordinary shares or ADSs.

In addition, the securities markets have from time to time experienced significant price and volume fluctuations that are not related to the operating performance of particular companies. Prolonged global capital markets volatility may affect overall investor sentiment towards our ADSs, which would also negatively affect the trading prices for our ADSs.

The triple listing of our ordinary shares and the ADSs may adversely affect the liquidity and value of the ADSs.

Our ordinary shares are listed on the AIM market and on the SEHK. The triple listing of our ordinary shares and the ADSs may dilute the liquidity of these securities in one or more of these markets and may adversely affect the development of an active trading market for the ADSs in the United States or shares in Hong Kong and the United Kingdom. The price of the ADSs could also be adversely affected by trading in our ordinary shares on the AIM market and the SEHK.

Fluctuations in the exchange rate between the U.S. dollar, Hong Kong dollar and the pound sterling may increase the risk of holding the ADSs.

Our share price is quoted on the SEHK and AIM market in Hong Kong dollar and pence sterling, respectively, while the ADSs trade on Nasdaq in U.S. dollars. Fluctuations in the exchange rate between the U.S. dollar, Hong Kong dollar and the pound sterling may result in temporary differences between the value of the ADSs and the value of our ordinary shares, which may result in heavy trading by investors seeking to exploit such differences. In addition, as a result of fluctuations in the exchange rate between the U.S. dollar, Hong Kong dollar and the pound sterling, the U.S. dollar equivalent of the proceeds that a holder of the ADSs would receive upon the sale in Hong Kong of any ordinary shares or in the United Kingdom of any ordinary shares withdrawn from the depositary and the dollar equivalent of any cash dividends paid in Hong Kong dollar or pound sterling on our shares represented by the ADSs could also decline.

Securities traded on the AIM market or on the SEHK may carry or be perceived to carry a higher risk than shares traded on other exchanges and may impact the value of your investment.

Our ordinary shares are currently traded on the AIM market and on the SEHK. Investment in equities traded on AIM and the SEHK may be perceived by some to carry a higher risk than an investment in equities quoted on exchanges, such as the New York Stock Exchange or the Nasdaq. You should be aware that the value of our ordinary shares may be influenced by many factors, some of which may be specific to us and some of which may affect AIM-listed or Hong Kong-listed companies generally, including the depth and liquidity of the market, our performance, a large or small volume of trading in our ordinary shares, legislative changes and general economic, political or regulatory conditions, and that the prices may be volatile and subject to extensive fluctuations. Therefore, the market price of our ordinary shares underlying the ADSs may not reflect the underlying value of our company.

The depositary for our ADSs gives us a discretionary proxy to vote our ordinary shares underlying your ADSs if you do not vote at shareholders' meetings, except in limited circumstances, which could adversely affect your interests.

Under the deposit agreement for the ADSs, the depositary gives us a discretionary proxy to vote our ordinary shares underlying your ADSs at shareholders' meetings if you do not vote, unless:

- we do not wish a discretionary proxy to be given;
- we are aware or should reasonably be aware that there is substantial opposition as to a matter to be voted on at the meeting; or
- a matter to be voted on at the meeting would materially and adversely affect the rights of shareholders.

The effect of this discretionary proxy is that you cannot prevent our ordinary shares underlying your ADSs from being voted, absent the situations described above, and it may make it more difficult for shareholders to influence the management of our company. Holders of our ordinary shares are not subject to this discretionary proxy.

Holders of ADSs have fewer rights than shareholders and must act through the depositary to exercise their rights.

Holders of our ADSs do not have the same rights as our shareholders and may only exercise the voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement. Under our amended and restated Memorandum and Articles of Association, an annual general meeting shall be called by notice with not less than 21 clear days, and all other general meetings (including an extraordinary general meeting) shall be called by notice with not less than 14 clear days. When a general meeting is convened, you may not receive sufficient notice of a shareholders' meeting to permit you to withdraw the ordinary shares underlying your ADSs to allow you to vote with respect to any specific matter. If we ask for your instructions, we will give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date and the depositary will send a notice to you about the upcoming vote and will arrange to deliver our voting materials to you. The depositary and its agents, however, may not be able to send voting instructions to you or carry out your voting instructions in a timely manner. We will make all reasonable efforts to cause the depositary to extend voting rights to you in a timely manner, but we cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote the ordinary shares underlying your ADSs. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, you may not be able to exercise your right to vote and you may lack recourse if your ADSs are not voted as you request. In addition, in your capacity as an ADS holder, you will not be able to call a shareholders' meeting.

You may not receive distributions on our ADSs or any value for them if such distribution is illegal or if any required government approval cannot be obtained in order to make such distribution available to you.

Although we do not have any present plan to pay any dividends, the depositary of our ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on ordinary shares or other deposited securities underlying our ADSs, after deducting its fees and expenses and any applicable taxes and governmental charges. You will receive these distributions in proportion to the number of ordinary shares your ADSs represent. However, the depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities whose offering would require registration under the Securities Act but is not so properly registered or distributed under an applicable exemption from registration. The depositary may also determine that it is not reasonably practicable to distribute certain property. In these cases, the depositary may determine not to distribute such property. We have no obligation to register under the U.S. securities laws any offering of ADSs, ordinary shares, rights or other securities received through such distributions. We also have no obligation to take any other action to permit the distribution of ADSs, ordinary shares, rights or anything else to holders of ADSs. This means that you may not receive distributions we make on our ordinary shares or any value for them if it is illegal or impractical for us to make them available to you. These restrictions may cause a material decline in the value of our ADSs.

Your right to participate in any future rights offerings may be limited, which may cause dilution to your holdings.

We may from time to time distribute rights to our shareholders, including rights to acquire our securities. However, we cannot make rights available to you in the United States unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. Also, under the deposit agreement, the depositary bank will not make rights available to you unless either both the rights and any related securities are registered under the Securities Act, or the distribution of them to ADS holders is exempted from registration under the Securities Act. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. If the depositary does not distribute the rights, it may, under the deposit agreement, either sell them, if possible, or allow them to lapse. Accordingly, you may be unable to participate in our rights offerings and may experience dilution in your holdings.

If we are a passive foreign investment company for any taxable year, U.S. investors could be subject to adverse U.S. federal income tax consequences.

The rules governing passive foreign investment companies, or PFICs, can have adverse U.S. federal income tax consequences for U.S. investors of non-U.S. corporations. The PFIC status of a non-U.S. corporation for any taxable year depends upon the composition of its income and assets, the value of its assets and the classification of items of its income and assets as active or passive under the PFIC rules, as discussed further in Item 10.E. “Taxation—U.S. Taxation—Material U.S. Federal Income Tax Considerations with Respect to Ordinary Shares and ADSs.” Based on the composition of our income and assets and the estimated average value of our assets (including goodwill), we believe that we were not a PFIC for our taxable year ended December 31, 2022. However, our PFIC status is a factual determination that is made on an annual basis and depends on particular facts and circumstances (such as the value of our assets, including goodwill and other intangible assets). We hold a substantial amount of cash and financial investments and while this continues to be the case, our PFIC status depends primarily on the average value of our goodwill. The value of our goodwill may be determined, in large part, by reference to our market capitalization, which has been, and may continue to be, volatile. Therefore, if our market capitalization declines we may become a PFIC. In addition, there is uncertainty as to how to apply the PFIC rules for purposes of classifying certain of our income and assets as active or passive. In light of the foregoing, no assurance can be provided that we are not, or will not be, a PFIC for any taxable year.

If we are or become a PFIC, U.S. investors in our ordinary shares and ADSs generally will be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferential tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U.S. federal income tax laws and regulations. We do not expect to provide the information regarding our income that would be necessary in order for a U.S. investor to make a qualified electing fund, or QEF, election if we are a PFIC for any taxable year. U.S. investors in our ordinary shares or ADSs should consult their tax advisors regarding all aspects of the application of the PFIC rules to the ordinary shares and ADSs.

Under certain attribution rules, certain of our non-U.S. subsidiaries are expected to be treated as “controlled foreign corporations” for U.S. federal income tax purposes, and, as a result, there could be adverse U.S. federal income tax consequences to U.S. investors that own (directly or indirectly) our ordinary shares or ADSs and are treated as “Ten Percent Shareholders.”

Certain “Ten Percent Shareholders” (as defined below) in a non-U.S. corporation that is a “controlled foreign corporation” (a “CFC”) for U.S. federal income tax purposes generally are required to include in income for U.S. federal income tax purposes their pro rata share of the CFC’s “Subpart F income,” investment of earnings in U.S. property, and “global intangible low-taxed income,” even if the CFC has made no distributions to its shareholders. A non-U.S. corporation generally will be a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own, directly, indirectly or constructively (through attribution), more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A “Ten Percent Shareholder” is a United States person (as defined by the U.S. Internal Revenue Code of 1986, as amended) that owns directly or indirectly, or is considered to own constructively, 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation or 10% or more of the total value of the stock of such corporation. We are not expected to be a CFC. However, under certain “downward attribution” rules, certain of our non-U.S. subsidiaries are expected to be treated as CFCs by virtue of being constructively owned by our U.S. subsidiaries. As a non-U.S. company, we do not intend to take these U.S. tax rules into consideration in structuring its operations, nor do we intend to provide information to Ten Percent Shareholders that may be required in order for those shareholders to properly report their U.S. taxable income with respect to our operations. U.S. investors that are or may become Ten Percent Shareholders who directly or indirectly own our ordinary shares or ADSs should consult their tax advisors with respect to the application of the CFC rules to them.

We may be treated as a resident enterprise for U.K. corporate tax purposes, and our global income may therefore be subject to U.K. corporation tax.

U.K. resident companies are taxable in the United Kingdom on their worldwide profits. A company incorporated outside of the United Kingdom would be regarded as a resident if its central management and control resides in the United Kingdom. The place of central management and control generally means the place where the high-level strategic decisions of a company are made.

We are an investment holding company incorporated in the Cayman Islands and are admitted to trading on the AIM market of the London Stock Exchange or the AIM market. Our central management and control resides in Hong Kong, and therefore we believe that we are not a U.K. resident for corporate tax purposes. However, the tax resident status of a non-resident entity could be challenged by the U.K. tax authorities.

If the U.K. tax authorities determine that we are a U.K. tax resident, our profits will be subject to U.K. Corporation Tax rate at 19%, subject to the potential availability of certain exemptions related to dividend income and capital gains. This may have a material adverse effect on our financial condition and results of operations.

You may have difficulty enforcing judgments obtained against us.

We are a company incorporated under the laws of the Cayman Islands, and substantially all of our assets are located outside the United States. Substantially all of our current operations are conducted in the PRC. In addition, most of our directors and officers are nationals and residents of countries other than the United States. A substantial portion of the assets of these persons are located outside the United States. As a result, it may be difficult for you to effect service of process within the United States upon these persons. It may also be difficult for you to enforce in U.S. courts judgments obtained in U.S. courts based on the civil liability provisions of the U.S. federal securities laws against us and our officers and directors, all of whom are not residents in the United States and whose assets are located outside the United States. In addition, there is uncertainty as to whether the courts of the Cayman Islands or the PRC would recognize or enforce judgments of U.S. courts against us or such persons predicated upon the civil liability provisions of the securities laws of the United States or any state.

You may be subject to limitations on transfers of your ADSs.

Your ADSs are transferable on the books of the depositary. However, the depositary may close its transfer books at any time or from time to time when it deems expedient in connection with the performance of its duties. In addition, the depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason.

It may be difficult for overseas regulators to conduct investigations or collect evidence within China.

Shareholder claims or regulatory investigation that are common in the United States generally are difficult to pursue as a matter of law or practicality in China. For example, in China, there are significant legal and other obstacles to providing information needed for regulatory investigations or litigation initiated outside China. Although the authorities in China may establish a regulatory cooperation mechanism with the securities regulatory authorities of another country or region to implement cross-border supervision and administration, such cooperation with the securities regulatory authorities in the Unities States may not be efficient in the absence of mutual and practical cooperation mechanisms. Furthermore, according to Article 177 of the PRC Securities Law, or Article 177, which became effective in March 2020, no overseas securities regulator is allowed to directly conduct investigations or evidence collection activities within the territory of the PRC. While detailed interpretations of or implementation rules under Article 177 have yet to be promulgated, the inability for an overseas securities regulator to directly conduct investigations or evidence collection activities within China may further increase difficulties you may face in protecting your interests.

We are a Cayman Islands company. As judicial precedent regarding the rights of shareholders under Cayman Islands law is different from U.S. law, English law or Hong Kong law, shareholders may have different shareholder rights than they would have under U.S. law, English law or Hong Kong law and may face difficulties in protecting your interests.

We are an exempted company with limited liability incorporated in the Cayman Islands. Our corporate affairs are governed by our Articles of Association (as may be further amended from time to time), the Companies Act (As Revised) of the Cayman Islands and the common law of the Cayman Islands. The rights of shareholders to take action against the directors, actions by minority shareholders and the fiduciary responsibilities of our directors are to a large extent governed by the common law of the Cayman Islands. This common law is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, which has persuasive, but not binding, authority on a court in the Cayman Islands. The laws of the Cayman Islands relating to the protection of the interests of minority shareholders differ in some aspects from those in the United States, the United Kingdom and Hong Kong. Such differences mean that the remedies available to our minority shareholders may be different from those they would have under the laws of United States, the United Kingdom, Hong Kong or other jurisdictions. In addition, some states in the United States, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law than the Cayman Islands.

In addition, as a Cayman Islands exempted company, our shareholders have no general rights under Cayman Islands law to inspect corporate records and accounts or to obtain copies of lists of shareholders of these companies with the exception that the shareholders may request a copy of the Articles of Association. Our directors have discretion under our Articles of Association to determine whether or not, and under what conditions, our corporate records may be inspected by our shareholders, but are not obliged to make them available to our shareholders. This may make it more difficult for you to obtain the information needed to establish any facts necessary for a shareholder motion or to solicit proxies from other shareholders in connection with a proxy contest. As a Cayman Islands company, we may not have standing to initiate a derivative action in U.S. federal courts, English courts or Hong Kong courts. As a result, you may be limited in your ability to protect your interests if you are harmed in a manner that would otherwise enable you to sue in U.S. federal courts, English courts or Hong Kong courts. In addition, shareholders of Cayman Islands companies may not have standing to initiate a shareholder derivative action in U.S. federal courts, English courts or Hong Kong courts.

Most of our directors and executive officers reside outside of the United States and a substantial portion of their assets are located outside of the United States. As a result, it may be difficult or impossible for you to bring an action against us or against these individuals in the United States in the event that you believe that your rights have been infringed under the securities laws of the United States or otherwise. In addition, some of our operating subsidiaries are incorporated in China. To the extent our directors and executive officers reside in China or their assets are located in China, it may not be possible for investors to effect service of process upon us or our management inside China. Even if you are successful in bringing an action, the laws of the Cayman Islands and China may render you unable to enforce a judgment against our assets or the assets of our directors and officers. There is no statutory recognition in the Cayman Islands of judgments obtained in the United States, Hong Kong or China, although the courts of the Cayman Islands will generally recognize and enforce a non-penal judgment of a foreign court of competent jurisdiction without retrial on the merits subject to certain conditions.

As a result of all of the above, public shareholders may have more difficulty in protecting their interests in the face of actions taken by management, members of the board of directors or controlling shareholders than they would as public shareholders of an English company, a U.S. company or a Hong Kong company.

We cannot assure you that our ordinary shares will remain listed on the AIM or the SEHK or our ADSs will remain listed on Nasdaq.

Although it is currently intended that our ordinary shares and ADSs will remain listed on the AIM, the SEHK and Nasdaq, as applicable, there is no guarantee of the continued listing of our securities on any of these exchanges. We may decide at some point in the future to delist voluntarily (subject to the applicable regulatory requirements) from one or more of these exchanges, or we may be delisted involuntarily if, among other factors, we do not continue to satisfy the listing requirements of the applicable exchange or comply with applicable law. For example, we could be delisted from the Nasdaq if the PCAOB continues to be unable to inspect our independent registered public accounting firm for three consecutive years. The AIM Rules for companies provide that a voluntary cancellation of admission to AIM is conditional upon the consent of not less than 75% of votes cast by its shareholders at a general meeting unless the London Stock Exchange otherwise agrees. Circumstances where the London Stock Exchange might otherwise agree that shareholder consent at a general meeting is not required would include the situation where the AIM securities are already admitted to trading on an “AIM Designated Market” (which includes Nasdaq) to enable shareholders to trade their AIM securities in the future. The SEHK rules allow an issuer whose primary listing is on SEHK and which has an alternative listing on another stock exchange to withdraw its listing with the prior approval of shareholders by ordinary resolution obtained at a duly convened meeting of the shareholders and the satisfaction of other requirements. SEHK may also cancel the listing of any securities that have been suspended from trading for a continuous period of 18 months. We cannot predict the effect a delisting of our shares on the SEHK or AIM market or our ADSs on Nasdaq would have on the market price of our shares and/or ADSs. We may also seek further listings on other stock exchanges such as the Shanghai Stock Exchange. However, there is no assurance that we would proceed with a listing and if we do proceed, that a listing would materialize.

The characteristics of the Hong Kong, U.S. and U.K. capital markets are different.

The SEHK, Nasdaq and the AIM have different trading hours, trading characteristics (including trading volume and liquidity), trading and listing rules, market regulations, and investor bases (including different levels of retail and institutional participation). As a result of these differences, the trading prices of the shares and the ADSs might not be the same, even allowing for currency differences. Circumstances peculiar to the U.S. capital markets could materially and adversely affect the price of the shares. Because of the different characteristics of the Hong Kong, U.S. and U.K. equity markets, the historical market prices of our securities may not be indicative of the performance of the shares.

We are subject to Hong Kong, Nasdaq and AIM listing and regulatory requirements concurrently.

As we are listed on the SEHK, the Nasdaq and the AIM, we are required to comply with the listing rules (where applicable) and other regulatory regimes of each stock exchange, unless otherwise agreed by the relevant regulators. We may also seek further listings on other stock exchanges such as the Shanghai Stock Exchange. Accordingly, we may incur additional costs and resources in complying with the requirements of each stock exchange.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company.

HUTCHMED (China) Limited (formerly known as Hutchison China MediTech Limited) was incorporated in the Cayman Islands on December 18, 2000 as an exempted company with limited liability under the Companies Act (As Revised) of the Cayman Islands. Our company was founded by a wholly owned subsidiary of CK Hutchison, a multinational conglomerate with operations in over 50 countries. CK Hutchison is the ultimate parent company of our largest shareholder Hutchison Healthcare Holdings Limited.

We launched our novel drug research and development operations in 2002 with the establishment of our subsidiary HUTCHMED Limited, which is focused on discovering, developing and marketing drugs for the treatment of cancer and immunological diseases. A dozen of our in-house discovered drug candidates have entered clinical trials around the world and three have so far been approved for sale. Since 2001, we have also developed drug marketing and distribution platforms in China, which primarily focus on prescription drug and consumer health products through several joint ventures and subsidiary companies and are included in our Other Ventures.

We listed our ordinary shares on the AIM market in 2006, ADSs on the Nasdaq Global Select Market in 2016 and our ordinary shares on the SEHK in 2021.

On March 4, 2021 we announced the consolidation of the two corporate identities that we have used since our inception. Hutchison China MediTech, or Chi-Med, which had been used as our group identity, while Hutchison MediPharma had been the identity of our novel drug research and development operations under which our oncology products had been developed and marketed. The brand HUTCHMED immediately replaced Chi-Med as our abbreviated name, and we changed our group company name at our Annual General Meeting in April 2021 from Hutchison China MediTech Limited to HUTCHMED (China) Limited.

On September 28, 2021, we disposed of our entire investment in Hutchison Baiyunshan, our non-core and non-consolidated over-the-counter drug joint venture business, to GL Mountrose Investment Two Limited, a company controlled and managed by GL Capital Group. GL Capital Group is an investment firm that focuses on buyout and growth opportunities in China's healthcare industry. As our focus is the discovery and development of novel therapies in oncology and immunology, the sale of our interest in Hutchison Baiyunshan allows us to focus resources on our primary aim of accelerating investment in our Oncology/Immunology assets. We are also considering divesting other non-core businesses in our Other Ventures segment, including Shanghai Hutchison Pharmaceuticals.

Our principal executive offices are located at 48th Floor, Cheung Kong Center, 2 Queen's Road Central, Hong Kong. Our telephone number at that address is +852 2121 8200. The address of our registered office in the Cayman Islands is P.O. Box 309, Ugland House, Grand Cayman, KY1-1104, Cayman Islands.

See Item 5.B. "Liquidity and Capital Resources" for details on our capital expenditures for the years ended December 31, 2020, 2021 and 2022.

We are subject to the informational requirements of the Exchange Act and are required to file reports and other information with the SEC. The SEC maintains a website at *www.sec.gov* that contains reports, proxy and information statements, and other information regarding registrants that make electronic filings with the SEC using its EDGAR system. We also make available on our website's investor relations page, free of charge, our annual report and the text of our reports on Form 6-K, including any amendments to these reports, as well as certain other SEC filings, as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. The address for our investor relations page is *www.hutch-med.com/shareholder-information.* The information contained on our website is not incorporated by reference in this annual report.

B. Business Overview.

Overview

We are a global commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies and immunotherapies for the treatment of patients with cancer and immunological diseases. Our company started in China in 2000 and has since developed fully integrated capabilities and expanded oncology and immunology drug development operations globally. Our operational achievements and capabilities to date include:

Broad pipeline of differentiated targeted therapies and immunotherapies built for the global market. We have a pipeline of differentiated drug candidates covering both novel and validated targets, including MET, VEGFR, FGFR, CSF-1R, PI3Kδ, Syk, EZH2, IDH, ERK, BTK, CD47 and EGFR. The aim of our research is to develop drugs with high selectivity and superior safety profiles, a key benefit of which is that our drug candidates have the potential to be effectively paired with other oncology and immunology therapies at effective dosages with fewer side effects.

Commercially launching products while continuing to discover new assets. In China, three of our internally developed drugs, Elunate (fruquintinib), Sulanda (surufatinib) and Orpathys (savolitinib) are commercially available to patients. All three drugs are in late-stage development outside of China, with the most advanced being fruquintinib for which a rolling NDA submission to the United States FDA is being submitted. To accelerate the availability of our innovative medicines for patients globally, we seek partnerships to commercialize our drugs outside of China, such as our partnership with AstraZeneca on savolitinib, and our recently agreed partnership with Takeda on fruquintinib. In addition, we have eleven additional drug candidates that have entered clinical development and several pre-clinical drug candidates.

Comprehensive global in-house discovery and development capabilities. We have a comprehensive drug discovery and development operation covering chemistry, biology, pharmacology, toxicology, chemistry and manufacturing controls for clinical and commercial supply, clinical and regulatory and other functions. It is led by a team of approximately 960 scientists, who have created one of the broadest global clinical pipelines among our peer oncology and immunology focused biotechnology companies. Currently, we are conducting approximately 40 different clinical studies in oncology patients globally, including over 15 Phase III registration and Phase II registration-intent studies underway.

Long-standing drug marketing and distribution experience to support the realization of in-house oncology innovations in China. We have built large-scale and profitable drug marketing and distribution capabilities through our Other Ventures operations, which primarily manufacture, market and distribute prescription drugs in China. Our more than 20 years of track record and deep institutional knowledge of the drug marketing and distribution process are being leveraged to bring our in-house oncology innovations to patients. We have built and continue to expand our in-house oncology drug sales team to over 870 persons at end of 2022 to support the commercialization of Elunate, Sulanda and our other innovative drugs, if approved, throughout mainland China, Hong Kong and Macau. Our oncology drug sales team covers over 3,000 hospitals and over 33,000 oncology physicians in China, a network that we estimate represents over 90% of oncology drug sales in China.

Our Strategies

Our vision is to be a global leader in the discovery, development and commercialization of targeted therapies and immunotherapies for the treatment of patients with cancer and immunological diseases. Key elements of our strategy are to:

Realize the global potential of our oncology drug candidates

Our first wave of innovation - namely, fruquintinib (partnered in China with Eli Lilly and to be partnered outside of China with Takeda), savolitinib (partnered globally with AstraZeneca) and surufatinib (unpartnered) - are either commercialized, under review for marketing authorization or in registrational studies in multiple jurisdictions. In tandem with our ongoing progression of such drugs, we will continue to invest in the future with our deep pipeline of unpartnered next wave of oncology assets for which we own all rights globally and have significant flexibility in driving their development. We intend to accelerate our global drug development by leveraging our advanced clinical trial data from China, selectively conducting early-stage and proof-of-concept clinical trials in other jurisdictions so that the programs progress globally, then form partnerships to complete late-stage development and/or commercial launch outside China.

Continue designing and creating molecules to develop into medicines with specific and differentiated characteristics for the benefit of patients

We believe our world-class drug discovery engine is our key competitive advantage. We strive to create differentiated novel oncology and immunology treatments with global potential. Our drug discovery team has utilized our expertise in advanced medicinal chemistry to develop next-generation TKI that have both high selectivity and superior pharmacokinetic properties. Equally importantly, we will continue to design chemical and biologic drug candidates with profiles that allow them to be used in innovative combinations with other selective inhibitors, chemotherapy agents and immunotherapies. Such combination therapies enable treatment of cancer via multiple pathways and modalities simultaneously, which has the potential to significantly improve treatment outcomes.

We plan to continue to build out our global pipeline of self-discovered drug candidates by advancing a rich pipeline of early-stage drug candidates, which include small molecule drugs targeting new pathways and biologics addressing novel targets designed for use in combination with our small molecules, as well as potentially a broad range of third-party therapies.

Build and scale our marketing and commercialization capabilities globally

We plan to leverage our long-standing drug marketing and distribution know-how and infrastructure to support our innovative oncology product launches, focusing in particular on the Chinese market. We have a more than 20-year track record of marketing and selling products in China. We aim to steadily grow our in-house oncology drug sales team in mainland China, Hong Kong and Macau from over 870 at the end of 2022. Outside of China, we look to form collaborations with leading biopharmaceutical companies and/or contract sales organizations to fully realize the value of our assets. We will also continue to scale our manufacturing capacity to support the sales of our approved drugs, including through the expansion beyond our existing Suzhou production facility after the completion of our new plant in Shanghai, which will provide a five-fold increase in our existing production capacity.

Identify China business development opportunities to complement our internal research and development activities

We plan to explore opportunities to in-license complementary late-stage drug candidates in China to supplement our in-house research and development capabilities, with a focus on drug candidates with the potential to both complement our existing drug pipeline including through having synergistic effects and augment our oncology commercial portfolio, such as Tazverik from Ipsen. In addition, we expect to progress some of our drug candidates by pursuing business development opportunities with other biopharmaceutical companies in China such as our collaborations to evaluate combining fruquintinib with anti-PD-1 antibodies for the treatment of various solid tumor cancers. We will also continue to work with our partners, AstraZeneca, Eli Lilly and Takeda (subject to closing of our recent agreement), to optimize the potential of our drug candidates savolitinib (globally with AstraZeneca) and fruquintinib (outside China with Takeda and in China with Eli Lilly).

Capitalize on regulatory reforms currently underway in China aimed at addressing existing unmet medical needs and improving the health of its people

We believe the Chinese oncology market, which comprises approximately a quarter of the global oncology patient population, represents a substantial and fast-growing market opportunity. Over the past decade, the PRC government has endeavored to foster an innovative biopharmaceutical ecosystem, and in the last few years, the pace of reforms has accelerated with a clear focus on providing Chinese patients access to world-class oncology therapies through expanded insurance reimbursement and reduced time for clinical trials and drug approvals. As a result, the oncology drug market in China is growing rapidly. Having invested in drug innovation in China for over 20 years, beginning at a time when almost no other domestic companies were involved in innovative oncology research, we believe we are well positioned to capture this market opportunity.

Oncology Commercial Operations

Savolitinib

In late June 2021, savolitinib became the first-in-class selective MET inhibitor to be approved in China and was launched as Orpathys. Our partner, AstraZeneca, then launched Orpathys in mid-July 2021, less than three weeks after its conditional approval by the NMPA for patients with MET exon 14 skipping alteration NSCLC. More than a third of the world’s lung cancer patients are in China. Among those with NSCLC globally, approximately 2-3% have tumors with MET exon 14 skipping alterations.

In 2021 and 2022, Orpathys was sold as a self-pay drug. AstraZeneca introduced a patient access program in late 2021 which subsidizes use of Orpathys, through progressive disease. In-market sales for Orpathys grew by 159% in 2022 to $41.2 million (2021: $15.9m) resulting in our consolidation of $22.3 million (2021: $11.3m) in revenues from manufacturing fees and royalties in 2022. Following negotiations with the China NHSA in January 2023, starting on March 1, 2023, Orpathys will be included in the updated NRDL, broadening patient access to this medicine.

Market understanding of the need for MET testing has improved significantly, with Orpathys’s brand share more than doubling since the end of 2021 in the rapidly growing targeted therapy area. In the National Health Commission’s Treatment Guidelines for Primary Lung Cancer 2022 and the China Medical Association Oncology Committee Lung Cancer Group’s China Medical Association Guideline for Clinical Diagnosis and Treatment of Lung Cancer, Orpathys was identified as the only targeted therapy recommended for MET exon 14 patients, while similar guideline from CSCO also recommended Orpathys as the standard of care for such patients.

Fruquintinib

Fruquintinib is approved for the treatment of third-line metastatic CRC for which there is an approximate incidence of 83,000 new patients per year in China and was launched as Elunate. We estimate that in 2022, approximately 32,000 (2021: approximately 22,000) new patients were treated with Elunate in China resulting in in-market sales of $93.5 million, up 32% versus 2021 ($71.0 million). Following negotiations with the China NHSA, Elunate continues to be included in the NRDL for a new two-year term starting in January 2022. For this renewal, we agreed to a discount of 5% relative to the 2021 NRDL price. In January 2022, Elunate was approved in the Macau Special Administrative Region, our first drug to be approved in the territory and the first based on NMPA approval, following the latest update to the Macau provisions on new drug importation which allow drugs approved in one or more specified jurisdictions to be authorized for use in Macau.

We are collaborating with Eli Lilly on the development and commercialization in China. Under the terms of our agreement with Eli Lilly, we manage all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in China. We recognize as revenues approximately 70-80% of Elunate in-market sales from manufacturing fees, service fees and royalties paid to us by Eli Lilly. In 2022, we recognized $69.9 million in revenue for Elunate, equal to 74.8% of in-market sales.

In January 2023, we entered into an agreement with a subsidiary of Takeda whereby it will receive an exclusive worldwide license to develop, manufacture and commercialize fruquintinib in all indications and territories outside of China. In China, it is marketed and will continue to be marketed by us in partnership with Eli Lilly. The deal is subject to customary closing conditions, including completion of antitrust regulatory reviews. Following these clearances, Takeda will become solely responsible for the development and commercialization of fruquintinib in all the included territories.

Surufatinib

Surufatinib launched as Sulanda in 2021 for the treatment of all advanced NETs for which there is an approximate incidence of 34,000 new patients per year in China.

In 2021, Sulanda was sold as a self-pay drug. We used means-tested early access and patient access programs to help patients afford Sulanda. Despite these access programs, duration of treatment was often affected by the economic constraints of patients. Following negotiations with the China NHSA, Sulanda was included in the NRDL starting in January 2022 at a 52% discount on our main 50mg dosage form, relative to the 2021 self-pay price. Under the NRDL, actual out-of-pocket costs for patients in 2022 represented approximately 15-20% of the 2021 self-pay price.

As a result of inclusion in the NRDL and our continued marketing activities, patient access to Sulanda, as well as duration of treatment, have been expanding with total sales in 2022 increasing by 178% to $32.3 million (2021: $11.6 million). In 2022, approximately 12,000 new patients were treated with Sulanda, representing approximately 2.5 times the approximately 4,800 new patients in 2021.

In April 2022, surufatinib was approved in the Macau Special Administrative Region.

Tazemetostat

In May 2022, tazemetostat was approved by the Health Commission and Medical Products Administration of Hainan Province to be used in the Hainan Boao Lecheng International Medical Tourism Pilot Zone (Hainan Pilot Zone), under the Clinically Urgently Needed Imported Drugs scheme, for the treatment of certain patients with epithelioid sarcoma and follicular lymphoma consistent with the label as approved by the FDA. Launched in 2013 and located in China, the Hainan Pilot Zone is a destination for international medical tourism and global hub for scientific innovation, welcoming 83,900 medical tourists in 2020, according to official data.

Following inclusion in the 2022 CSCO guidelines for epithelioid carcinoma, three patients began treatment in 2022, with the first patient having remained on medication for over six months. In December 2022, a market authorization application was submitted in Hong Kong.

Clinical Drug Development Summary

We are the Marketing Authorization Holder in China of three internally discovered and developed innovative oncology medicines, savolitnib, fruquintinib and surufatinib, which are marketed as Orpathys, Elunate and Sulanda, respectively. Besides the three marketed drugs, we have additional drug candidates in earlier stage clinical development. Several of our oncology drug candidates are in development outside China including savolitinib, for which we are in a global partnership with AstraZeneca, fruquintinib, for which we have agreed to license non-China rights to Takeda.

The following table summarizes the status of our clinical drug portfolio's development as of the date of the filing of this annual report:

Table of Contents

Program	Investigational treatment	Disease	Target patient	Study name	Country/region	Dose finding / safety run-in	Proof of concept	Registration
Fruquintinib VEGFR-1, -2, -3	**Fruquintinib**	CRC	Refractory	FRESCO-2	Global			
	Fruquintinib	CRC, BC			US			
	Fruquintinib + tislelizumab (PD-1)	MSS -CRC^			Korea/China			
	Fruquintinib + tislelizumab (PD-1)	Solid tumors^			Korea/China			
	Fruquintinib	CRC	≥3L; chemotherapy refractory	FRESCO	China			
	Fruquintinib + paclitaxel	GC	2L	FRUTIGA	China			
	Fruquintinib + sintilimab (PD-1)	EMC			China			
	Fruquintinib + sintilimab (PD-1)	RCC			China			
	Fruquintinib + sintilimab (PD-1)	CRC			China			
	Fruquintinib + sintilimab (PD-1)	GI, NSCLC, Cervical			China			
	Fruquintinib + tislelizumab (PD-1)	CRC^			China			
	Note: ^ The Phase II study in China and Korea for GC, CRC or NSCLC is led by BeiGene.							
Savolitinib MET	**Savolitinib** + osimertinib (EFGR)	NSCLC	EGFRm/MET+ osimertinib-refractory	SAVANNAH	Global	*		
	Savolitinib + osimertinib (EFGR)	NSCLC	EGFRm/MET+ osimertinib-refractory	SAFFRON	Global			
	Savolitinib + durvalumab (PD-L1)	Papillary RCC	MET+	SAMETA	Global			
	Savolitinib	NSCLC	MET exon 14 skipping alteration		China			
	Savolitinib	NSCLC	MET exon 14 skipping alteration		China	(Confirmatory)		
	Savolitinib + osimertinib (EFGR)	NSCLC	Treatment-naïve, MET+ /EGFRm	SANOVO	China			
	Savolitinib + osimertinib (EFGR)	NSCLC	2L, MET+ /EGFR TKI-refractory	SACHI	China			
	Savolitinib	GC	2L, MET+		China			
	Savolitinib + durvalumab (PD-L1)	NSCLC	MET driven; EGFR wild type	SOUND	China			
	Note: HUTCHMED is investigating savolitinib in a global collaboration with AstraZeneca. AstraZeneca leads development outside of China.							
Surufatinib VEGFR-1, -2, -3, FGFR1, CSF-1R	**Surufatinib**	NET			Japan	(Bridging)		
	Surufatinib	Pancreatic NET	All	SANET-p	China			
	Surufatinib	Non-Pancreatic NET	All	SANET-ep	China			
	Surufatinib + toripalimab (PD-1)	NEC		SURTORI-01	China			
	Surufatinib + toripalimab (PD-1)	SCLC			China			
	Surufatinib + toripalimab (PD-1)	BTC, Solid tumors			China			
Amdizalisib (HMPL-689) PI3Kδ	**Amdizalisib**	FL	Relapsed/refractory		China			
	Amdizalisib	MZL	Relapsed/refractory		China			
Sovleplenib (HMPL-523) SYK	**Sovleplenib**	HL/NHL			US/EU			
	Sovleplenib	ITP	Relapsed/refractory	ESLIM-01	China			
	Sovleplenib	wAIHA	All		China			
Tazemetostat EZH2	**Tazemetostat**	ES, FL			China			
	Tazemetostat	FL	Relapsed/refractory	SYMPHONY-1	China			
	Tazemetostat	FL	3L		China	(Bridging)		
	Tazemetostat + amdizalisib	Lymphoma	Relapsed/refractory		China			
	Note: Tazemetostat developed by Epizyme. Approved in the US for ES and FL as a monotherapy. HUTCHMED rights are for Greater China – bridging study being planned.							
HMPL-453 FGFR1, 2, 3	**HMPL-453**	IHCC			China			
	HMPL-453 + multiple combos	Solid tumors			China			
HMPL-306 IDH 1/2	**HMPL-306**	Solid tumors	Relapsed/refractory		US/EU			
	HMPL-306	AITL, AML, MDS, MPN	Relapsed/refractory		US/EU			
	HMPL-306	AML, CMML, MDS, MPN	Relapsed/ refractory		China			
HMPL-295 ERK, MAPK pathway	**HMPL-295**	Solid tumors			China			
HMPL-760 BTK	**HMPL-760**	NHL	Relapsed/refractory		China			
HMPL-653 CSF-1R	**HMPL-653**	Solid tumors, TGCT			China			
HMPL-A83 CD47	**HMPL-A83**	Malignant Neoplasms	Advanced		China			

Global China

* Phase II registration-intent study subject to regulatory discussion;

Note: AITL = Angioimmunoblastic T-cell lymphoma; AML = Acute myeloid leukemia; BC = Breast cancer; BTC = Biliary tract cancer; CD-47 = Cluster of differentiation 47; CMML = Chronic myelomonocytic leukemia; CRC = Colorectal cancer; ERK = Extracellular signal-regulated kinase; ES = Epithelioid sarcoma; EZH2 = Enhancer of zeste homolog 2; FL = follicular lymphoma; GC= gastric cancer; GI= gastrointestinal; HL = Hodgkin's lymphoma; IHCC = Intrahepatic cholangiocarcinoma; ITP = Immune thrombocytopenia purpura; NDA = New Drug Application; NEC = Neuroendocrine carcinoma; MAA = Marketing Authorization Application; MAPK pathway = RAS-RAF-MEK-ERK signaling cascade; MDS = myelodysplastic syndrome; MDS = Myelodysplastic syndromes; MET = mesenchymal epithelial transition receptor; MZL = marginal zone lymphoma; NSCLC = non-small cell lung cancer; EGFRm = epidermal growth factor receptor mutation; RCC = renal cell carcinoma; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; FGFR 1 = fibroblast growth factor receptor 1; CSF-1R = colony stimulating factor-1 receptor; NET = neuroendocrine tumors; TN = triple negative; EMC = endometrial cancer; PI3Kδ = Phosphatidylinositol-3-Kinase delta; NHL = Non-Hodgkin's Lymphoma; PTCL = peripheral T-cell lymphoma; Syk = spleen tyrosine kinase; SCLC = Small cell lung cancer; IDH 1/2 = isocitrate dehydrogenase 1/2; BTK = Bruton's tyrosine kinase; TGCT = Tenosynovial giant cell tumor; wAIHA = warm autoimmune hemolytic anemia.

Savolitinib – selective MET inhibitor in late-stage clinical development as a monotherapy and in combination therapies in global partnership with AstraZeneca

Savolitinib is a potent and selective small molecule inhibitor of the MET receptor tyrosine kinase, an enzyme which has been shown to function abnormally in many types of solid tumors. We designed savolitinib through chemical structure modification to specifically address kidney toxicity, the primary issue that halted development of several other selective MET inhibitors. In clinical trials to date in over 1,500 patients globally, savolitinib has shown promising signs of clinical efficacy in patients with multiple types of MET gene alterations in lung cancer, kidney cancer and gastric cancer with an acceptable safety profile.

In June 2021, the NMPA approved savolitinib for marketing for the treatment of NSCLC with MET exon 14 skipping alterations, making savolitinib the first-in-class selective MET inhibitor in China. This approval follows a priority review designation by the NMPA and is the first regulatory approval globally for this oral, potent and selective MET TKI. The approval by the NMPA was based on positive results from a Phase II trial conducted in China in patients with NSCLC with this mutation, including patients with the more aggressive pulmonary sarcomatoid carcinoma subtype. Savolitinib demonstrated effective anti-tumor activity based on an independent review of objective response rate ("ORR") and disease control rate ("DCR"). The approval is conditional upon successful completion of an ongoing confirmatory study in this patient population. The results reviewed by the NMPA when it approved savolitinib were also published in *The Lancet Respiratory Medicine*.

We are currently testing savolitinib in global partnership with AstraZeneca, both as a monotherapy and in combination with immunotherapy and targeted therapy. Most notably, MET-aberration is a major mechanism for acquired resistance to both first-generation EGFR TKIs as well as third-generation EGFR TKIs like Tagrisso. Savolitinib has been studied extensively in these patients in the TATTON and SAVANNAH studies. Final results from the TATTON study were presented at World Conference on Lung Cancers ("WCLC"), in January 2021, and preliminary results from SAVANNAH were presented at WCLC in August 2022. Findings based on SAVANNAH and the TATTON studies supported the initiation of the SAFFRON global Phase III study in patients with EGFR-mutated, MET-driven, locally advanced or metastatic NSCLC whose disease progressed on first- or second-line treatment with Targrisso as the most recent therapy, with no prior chemotherapy in the metastatic setting allowed. China-based Phase III studies SACHI and SANOVO were also initiated. Savolitinib was granted fast track designation by the FDA for the combination treatment with Tagrisso of NSCLC patients harboring MET overexpression and/or amplification following progression on Targrisso.

Proof-of-concept studies of savolitinib in kidney cancer (as a monotherapy as well as in combination with a PD-L1 inhibitor) and gastric cancer (as a monotherapy as well as in combinations with chemotherapy) have demonstrated positive results, with subsequent clinical development ongoing or in planning. For example, we initiated a global Phase III pivotal trial (SAMETA) in October 2021 for savolitinib in combination with Imfinzi, AstraZeneca's anti-PD-L1 antibody durvalumab, in MET positive patients with papillary renal cell carcinoma or PRCC, a form of kidney cancer. Savolitinib opportunities are also continuing to be explored in multiple other MET-driven tumor settings via investigator-initiated studies.

Fruquintinib—selective VEGFR 1, 2 and 3 inhibitor with the best selectivity for its targets in global NDA submission and commercially launched as Elunate in China in CRC in November 2018

Fruquintinib is a highly selective and potent oral inhibitor of vascular endothelial growth factor or VEGF receptors, known as VEGFR 1, 2 and 3. We believe that fruquintinib has the potential to become a selective small molecule VEGFR 1, 2 and 3 inhibitor for many types of solid tumors that has the highest selectivity, and we are currently studying fruquintinib in CRC, gastric cancer, endometrial cancer, kidney and other solid tumor types. Fruquintinib was designed to improve kinase selectivity to minimize off-target toxicities, improve tolerability and provide more consistent target coverage. The tolerability in patients to date, along with fruquintinib's low potential for drug-drug interaction based on pre-clinical assessment, suggests that it may be highly suitable for combinations with other anti-cancer therapies.

Building on the data collected from our successful Phase III trial in China, known as the FRESCO study, which supported fruquintinib's approval in China, we initiated FRESCO-2, a large randomized controlled study of fruquintinib in the United States, Europe, Japan and Australia. The FDA granted fast track designation for the development of fruquintinib for the treatment of patients with mCRC in June 2020, enabling us to submit sections of the NDA on a rolling basis. Based on the successful results of the FRESCO-2 study, we initiated the filing of a rolling submission of an NDA to the FDA for fruquintinib for the treatment of mCRC.

Aside from its first approved indication of late-line CRC in China that is being applied for globally, we are conducting studies of fruquintinib in combination with other drugs in various indications. For example, we plan to submit a supplemental NDA in China for the treatment of gastric cancer in combination with paclitaxel following the results of the FRUTIGA Phase III study, and we have several ongoing registration-intent studies of fruquintinib combined with chemotherapy (FRUTIGA study in gastric cancer) or checkpoint inhibitors (Tyvyt combo, in endometrial cancer and RCC) in China.

Fruquintinib is being commercialized and developed in partnership with Eli Lilly in China, where we are responsible for development, manufacturing, on-the-ground medical detailing, promotion and local and regional marketing activities. In January 2023, we entered into an agreement whereby Takeda will receive an exclusive worldwide license to develop, manufacture and commercialize fruquintinib in all indications and territories outside of China. The Takeda partnership is subject to customary closing conditions, including completion of antitrust regulatory reviews. Following these clearances, Takeda will become solely responsible for the development and commercialization of fruquintinib in all the included territories.

Surufatinib—unique angio-immuno kinase inhibitor commercially launched as Sulanda in China in advanced NETs; first VEGFR/FGFR/CSF-1R inhibitor for all advanced NETs

Surufatinib is a novel, oral angio-immuno kinase, small molecule inhibitor that selectively inhibits the tyrosine kinase activity associated with VEGFR and FGFR, which both inhibit angiogenesis, and colony stimulating factor-1 receptor, or CSF-1R, which regulates tumor-associated macrophages, promoting the body's immune response against tumor cells. Its unique dual mechanism of action may be very suitable for possible combinations with other immunotherapies. We believe surufatinib is potentially the first VEGFR/FGFR/CSF-1R inhibitor for all advanced NETs.

Surufatinib was approved by the NMPA in December 2020 for the treatment of non-pancreatic NETs and is now being marketed by us in China under the brand name Sulanda. This NMPA approval of surufatinib was based on results from the SANET-ep study, a Phase III trial in patients with advanced non-pancreatic NETs conducted in China. The positive results of this trial were highlighted in an oral presentation at the 2019 ESMO Congress and published in *The Lancet Oncology* in September 2020. In June 2021, surufatinib was approved by the NMPA for the treatment of advanced pancreatic NETs. This NMPA approval of surufatinib was based on results from the SANET-p study, a Phase III trial in patients with advanced pancreatic NETs conducted in China. The positive results of this trial were highlighted in an oral presentation at the 2020 ESMO Congress and published in *The Lancet Oncology* in September 2020. In 2022, we presented a pooled analysis of safety data from the SANET-p and SANET-ep studies at the 2022 ASCO annual meeting.

Outside of China, we are conducting a bridging study to support registration of surufatinib for advanced NET in Japan. This Japan trial was initiated in September 2021 and the results are expected in the first half of 2023. In the United States and Europe, we submitted an NDA to the FDA and MAA to the EMA for surufatinib monotherapy for the treatment of NETs. After receiving a Complete Response Letter from the FDA and negative feedback from EMA reviewers, we withdrew our NDA and MAA.

We have various additional clinical trials of surufatinib ongoing in combination with checkpoint inhibitors.

We own all rights to surufatinib globally.

Sovleplenib (HMPL-523)—potentially the first selective Syk inhibitor for hematological cancer

Sovleplenib is a novel, highly selective, oral, small molecule inhibitor targeting the spleen tyrosine kinase, or Syk, for the treatment of hematological cancers and certain chronic immune diseases. Syk is a major component in B-cell receptor signaling and is an established therapeutic target in multiple subtypes of B-cell lymphomas. Because B-cell malignancies are heterogeneous and patients commonly experience relapse despite current therapies, there is a need for new therapies.

We have various clinical trials of sovleplenib ongoing. Based on the encouraging data from Phase Ib study of sovleplenib in adult patients with immune thrombocytopenia, we commenced a Phase III study in the same indication and the final patient enrolled in the study received their first dose in December 2022. In January 2022, sovleplenib received the Breakthrough Therapy Designation in China for treatment of primary immune thrombocytopenia. The NMPA grants Breakthrough Therapy Designation to new drugs that treat life-threatening diseases or serious conditions for which there are no effective treatment options, and where clinical evidence demonstrates significant advantages over existing therapies. In September 2022, we also initiated a randomized, double-blind, placebo-controlled Phase II/III study to evaluate the efficacy, safety, tolerability, and pharmacokinetics of sovleplenib in the treatment of warm AIHA.

We own all rights to sovleplenib globally.

Amdizalisib (HMPL-689)—novel, highly selective PI3Kδ inhibitor with potential in hematological cancer

Amdizalisib is a novel, highly selective and potent small molecule inhibitor targeting the isoform PI3Kδ. In pre-clinical pharmacokinetic studies, amdizalisib's pharmacokinetic properties have been found to be favorable with good oral absorption, moderate tissue distribution and low clearance. Amdizalisib is also expected to have low risk of drug accumulation and drug-drug interaction and is highly potent, particularly at the whole blood level. Amdizalisib received Breakthrough Therapy Designation from the CDE of the NMPA in China for the treatment of refractory follicular lymphoma in September 2021.

We have multiple ongoing clinical studies of amdizalisib for various subtypes of lymphomas. In April 2021, we commenced a registration-intent, single-arm, open-label Phase II trial in China in approximately 100 patients with relapsed/refractory follicular lymphoma and approximately 80 patients with relapsed/refractory marginal zone lymphoma, two subtypes of non-Hodgkin's lymphoma. The trial is being conducted in over 35 sites in China, has fully enrolled the follicular lymphoma cohort and is expected to complete enrollment for the marginal zone lymphoma cohort around mid-year.

We own all rights to amdizalisib globally.

Tazemetostat

In August 2021, we entered into a strategic collaboration with Epizyme, Inc. (a subsidiary of Ipsen Pharma SAS), to research, develop, manufacture and commercialize tazemetostat (Tazverik) in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Tazemetostat is an inhibitor of EZH2 developed by Ipsen that is approved by the FDA for the treatment of certain epithelioid sarcoma and follicular lymphoma patients. It received accelerated approval from the FDA based on ORR and DOR in January and June 2020 for epithelioid sarcoma and follicular lymphoma, respectively.

We are developing and plan to seek approval for tazemetostat in various hematological and solid tumors, in Greater China, through a bridging study and other studies including in combination with amdizalisib. We are participating in Ipsen's SYMPHONY-1 (EZH-302) study, leading it in Greater China. We have initiated a Phase II study of tazemetostat with amdizalisib in 2023. We will generally be responsible for funding all clinical trials of tazemetostat in Greater China, including the portion of global trials conducted there. We are responsible for the research, manufacturing and commercialization of tazemetostat in Greater China.

HMPL-306—potentially the first dual inhibitor of IDH1 and IDH2 with applications in hematological malignancies and solid tumors

HMPL-306 is a novel small molecule dual-inhibitor of isocitrate dehydrogenase 1 and 2, or IDH 1 and 2, enzymes. IDH1 and IDH2 mutations have been implicated as drivers of certain hematological malignancies and solid tumors, particularly among acute myeloid leukemia patients. A Phase I trial in China was initiated in July 2020, in patients of relapsed or refractory hematological malignancies with an IDH1 and/or IDH2 mutation. We plan to initiate the dose expansion portion of this Phase I study in early 2023.

We own all rights to HMPL-306 globally.

HMPL-760—an investigational, highly selective, third-generation oral inhibitor of BTK with improved potency versus first generation BTK inhibitors against both wild type & C481S mutant enzymes

HMPL-760 is an investigational, non-covalent, third-generation BTK inhibitor. It is a highly potent, selective, and reversible inhibitor with long target engagement against BTK, including wild-type and C481S-mutated BTK. In January 2022, we initiated a Phase I trial in China in patients with previously treated chronic lymphocytic leukemia/small lymphocytic lymphoma or other types of non-Hodgkin lymphoma, including patients treated with a prior regimen containing a BTK inhibitor, whose disease carries either wild-type BTK or acquired resistance to first generation BTK inhibitors due to additional mutations to BTK. The initial dose escalation stage to determine the maximum tolerated dose and/or the RP2D is to be followed by a dose expansion phase where patients will receive HMPL-760 to further evaluate the safety, tolerability, and clinical activity at the RP2D.

We own all rights to HMPL-760 globally.

HMPL-453—highly selective FGFR 1/2/3 inhibitor with potential in solid tumors

HMPL-453 is a novel, selective, oral inhibitor targeting FGFR 1/2/3. Aberrant FGFR signaling is associated with tumor growth, promotion of angiogenesis, as well as resistance to anti-tumor therapies. A Phase II study is ongoing in patients with advanced intrahepatic cholangiocarcinoma, or IHCC, with FGFR2 fusion that had failed at least one line of systemic therapy. We have recently agreed a registration enabling study design for HMPL-453 for IHCC with the CDE. IHCC is a cancer that develops within the bile ducts, the second most common primary hepatic malignancy after hepatocellular carcinoma. Approximately 10-15% of IHCC patients have tumors that harbor FGFR2 fusion. We also initiated a Phase I/II study of HMPL-453 in combination with chemotherapies or toripalimab for advanced solid tumors in China in January 2022.

We own all rights to HMPL-453 globally.

HMPL-295 – an investigative and highly selective small molecule inhibitor of ERK in the MAPK pathway with the potential to address intrinsic or acquired resistance from upstream mechanisms such as RAS-RAF-MEK

HMPL-295 is a novel ERK inhibitor. ERK is a downstream component of the RAS-RAF-MEK-ERK signaling cascade (MAPK pathway). This is our first of multiple candidates in discovery targeting the MAPK pathway. A China Phase I study of HMPL-295 as a monotherapy was initiated in July 2021.

We own all rights to HMPL-295 globally.

HMPL-653—CSF-1R inhibitor

HMPL-653 is a novel, highly selective, and potent CSF-1R inhibitor designed to target CSF-1R driven tumors as a monotherapy or in combination with other drugs. We initiated a China Phase I study in January 2022.

We own all rights to HMPL-653 globally.

HMPL-A83, IgG4-type humanized anti-CD47 monoclonal antibody

HMPL-A83 is an investigational IgG4-type humanized anti-CD47 monoclonal antibody that exhibits high affinity for CD47. HMPL-A83 blocks CD47 binding to Signal regulatory protein (SIRP) α and disrupts the "do not eat me" signal that cancer cells use to shield themselves from the immune system.

We own all rights to HMPL-A83 globally.

Discovery Research & Pre-clinical Development

We have built a drug discovery engine based in China, which has already produced a pipeline of around 20 differentiated clinical and late pre-clinical stage drug candidates covering both novel and validated targets of which three are now marketed. We strive to create differentiated novel oncology and immunology treatments with global potential. These include furthering both small molecule and biologic therapies which address aberrant genetic drivers and cancer cell metabolism; modulate tumor immune microenvironment; and target immune cell checkpoints. We design drug candidates with profiles that enable them to be used in innovative combinations with other therapies, such as chemotherapy, immunotherapy and other targeted therapies in order to attack disease simultaneously through multiple modalities and pathways. We believe that this approach can significantly improve treatment outcomes for patients.

Beyond these clinical and pre-clinical stage candidates, we continue to conduct research into discovering new types of drug candidates, including among others, small molecules addressing cancer-related apoptosis, cell signaling, epigenetics and protein translation; biologic drug candidates including bispecific antibodies; and novel technologies including antibody-drug conjugates and heterobifunctional small molecules.

Manufacturing

We use contract manufacturing organizations in China to produce our clinical and commercial API supplies. For manufacturing drug products, we currently use a combination of contract manufacturers and our internal manufacturing facility. We have a drug product facility in Suzhou which manufactures both clinical and commercial supplies for some of our products. We are building a new drug product facility in Pudong, Shanghai, which will increase our novel drug product manufacturing capacity by over five times. The construction and qualification of the Shanghai facility is expected to be completed in mid-2023 and technology transfer will start for some projects into the facility in late 2023. We expect to manufacture clinical supplies from the new facility starting in 2023 and commercial supplies around 2025 after the necessary regulatory filings and approvals.

We completed technology transfer for the API and drug product of amdizalisib and sovleplenib into the selected commercial manufacturing facilities in preparation for potential NDA filings. Process validation for these products (both API and drug product) is expected to complete in 2023. We also completed the NDA enabling work related to manufacturing for the global launch of fruquintinib at the commercial manufacturing sites. Process validation for API of this product has been completed, and process validation for drug product will be completed in the second half of 2023 in time for potential approval and launch.

Other Ventures

In addition to our Oncology/Immunology operations, our Other Ventures include large-scale drug marketing and distribution platforms covering about 290 cities and towns in China with approximately 2,900 manufacturing and commercial personnel as of December 31, 2022. Built over the past 20 years, it primarily focuses on prescription drug and consumer health products mainly through: (i) Shanghai Hutchison Pharmaceuticals, a non-consolidated joint venture with a commercial team of about 2,300 staff managing the medical detailing and marketing of a range of own-brand prescription drug products and (ii) Hutchison Sinopharm, a consolidated joint venture focused on providing commercial services for our own marketed drugs, as well as marketing third-party prescription drug products. Hutchison Baiyunshan, a former non-consolidated joint venture focused on the manufacturing, marketing and distribution of primarily own-brand OTC drugs, was also a part of our Other Ventures' operations before its disposal in September 2021.

Net income attributable to our company from our Other Ventures totaled $72.8 million, $142.9 million and $54.6 million for the years ended December 31, 2020, 2021 and 2022, respectively, and are remitted to our group through dividend payments primarily from our non-consolidated joint venture mentioned above. In 2022, dividends of an aggregate amount of $43.7 million were distributed from Shanghai Hutchison Pharmaceuticals to our group, with aggregate dividends received by our group since inception of over $280 million.

Our Clinical Pipeline

The following is a summary of the clinical pipeline for our drug candidates, many of which are being investigated against multiple indications.

1. Savolitinib (HMPL-504), MET Inhibitor

Savolitinib is a potent and selective inhibitor of MET, an enzyme which has been shown to function abnormally in many types of solid tumors. We designed savolitinib to address human metabolite-related renal toxicity, the primary issue that halted development of several other selective MET inhibitors. In clinical studies to date, savolitinib has shown promising signs of clinical efficacy in patients with MET gene alterations in NSCLC, PRCC, CRC and gastric cancer with an acceptable safety profile. In global partnership with AstraZeneca, savolitinib has been studied in over 1,500 patients to date, both as a monotherapy and in combinations. For more information regarding our partnership with AstraZeneca, see "—Overview of Our Collaborations—AstraZeneca."

Mechanism of Action

MET is a signaling pathway that has specific roles in normal mammalian growth and development. However, the MET pathway has also been shown to function abnormally in a range of different cancers, primarily through MET gene amplification, overexpression and gene mutations. The aberrant activation of MET has been demonstrated to be highly correlated in many cancer indications, including kidney, lung, gastric, colorectal, esophageal and brain cancer. It plays a major role in cancer pathogenesis (i.e., the development of the cancer), including tumor growth, survival, invasion, metastasis, the suppression of cell death as well as tumor angiogenesis.

MET also plays a role in drug resistance in many tumor types. For instance, MET gene aberrations has been found in NSCLC and CRC following anti-EGFR treatment, leading to drug resistance. Furthermore, MET dysregulation is considered to play a role in the immunosuppression and pathogenesis of kidney cancer.

Savolitinib Research Background

First generation selective MET inhibitors previously discovered by multinational pharmaceutical companies had positive pre-clinical data that supported their high MET selectivity and pharmacokinetic and toxicity profiles, but did not progress very far due to kidney toxicity. The issue appeared to be that certain metabolites of earlier compounds had dramatically reduced solubility and appeared to crystalize in the kidney, resulting in obstructive toxicity. With this understanding, we designed our compound, savolitinib (also known as AZD6094 and HMPL-504, formerly known as volitinib), differently while preserving high MET inhibition properties across multiple types of MET aberrations. Savolitinib has not shown any renal toxicity to date and does not appear to carry the same metabolite problems as the earlier selective MET compounds based on studies in over 1,500 patients conducted by AstraZeneca in global partnership with the company.

Savolitinib Pre-clinical Evidence

In pre-clinical trials, savolitinib demonstrated strong in vitro activity against MET, affecting its downstream signaling targets and thus blocking the related cellular functions effectively, including proliferation, migration, invasion, scattering and the secretion of VEGF that plays a pivotal role in tumor angiogenesis.

One of our key areas of focus in our pre-clinical trials is to achieve superior selectivity on a number of kinases. A commonly used quantitative measure of selectivity is through comparing enzyme IC_{50}, which represents the concentration of a drug that is required for 50% inhibition of the target kinase in vitro and the plasma concentration required for obtaining 50% of a maximum effect in vivo. High selectivity is achieved with a very low IC_{50} for the target cells, and a very high IC_{50} for the healthy cells (approximately 100 times higher than for the target cells). IC_{50} is measured in nM (nano-mole, a microscopic unit of measurement for the number of small molecules required to deliver the desired inhibitory effect).

In the MET enzymatic assay, savolitinib showed potent activity with IC_{50} of 5 nM. In a kinase selectivity screening with 274 kinases, savolitinib had potent activity against the MET Y1268T mutant (comparable to the wild-type), weaker activity against other MET mutants and almost no activity against all other kinases. Savolitinib was found to be approximately 1,000 times more potent to MET than the next non-MET kinase. Similarly, in cell-based assays measuring activity against MET phosphorylation, savolitinib demonstrated potent activity in both ligand-independent (gene amplified) and ligand-dependent (overexpressed) cells with IC_{50} at low nanomolar levels. In target related tumor cell function assays, savolitinib showed high potency with IC_{50} of less than 10 nM. Furthermore, savolitinib demonstrated cytotoxicity only on tumor cells that were MET gene amplified or MET overexpressed. In other cells, inhibition measurements demonstrated that IC_{50} amounts were over 30,000 nM, which is thousands of times higher than the IC_{50} on MET tumor cells.

The data above suggest that (i) savolitinib has potent activity against tumor cell lines with MET gene amplification in the absence of hepatocyte growth factor, or HGF, indicating that there is HGF-independent MET activation in these cells; (ii) savolitinib has potent activity in tumor cell lines with MET overexpressed, but only in the presence of HGF, indicating HGF-dependent MET activation; and (iii) savolitinib has no activity in tumor cell lines with low MET overexpression/gene amplification, suggesting that savolitinib has strong kinase selectivity.

Savolitinib Clinical Development

As discussed below, we have tested, and are currently testing, savolitinib in partnership with AstraZeneca in multiple indications, both as a monotherapy and in combination with other targeted therapies.

Non-small Cell Lung Cancer

The table below shows a summary of clinical trials for savolitinib in NSCLC patients.

Clinical Trials of Savolitinib in NSCLC

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Savolitinib monotherapy	MET exon 14 skipping alterations	China	II Registration	Approved and launched in 2021. Final OS analysis at ELCC 2022	NCT02897479
Savolitinib monotherapy	MET exon 14 skipping alterations	China	III Confirmatory	Ongoing since 2021	NCT04923945
Savolitinib + Imfinzi	SOUND: MET-driven, EGFR wild type	China	II	Ongoing since 2022	NCT05374603
Savolitinib + Tagrisso	SAVANNAH: 2L/3L EGFRm+; Tagrisso refractory; MET+	Global	II Registration-intent	Ongoing. Data that supported Phase IIIs at WCLC 2022	NCT03778229
Savolitinib + Tagrisso	SAFFRON:2L/3L EGFRm+; Tagrisso refractory; MET+	Global	III	Ongoing since 2022	NCT05261399
Savolitinib + Tagrisso	SACHI: 2L EGFR TKI refractory NSCLC; MET+	China	III	Ongoing since 2021	NCT05015608
Savolitinib + Tagrisso	SANOVO: Naïve patients with EGFRm & MET+	China	III	Ongoing since 2021	NCT05009836

Notes: Global = more than two countries; 2L = second line; 3L = third line; and refractory = resistant to prior treatment.

Savolitinib Monotherapy

More than one third of the world's lung cancer patients are in China and, among those with NSCLC, approximately 2-3% have tumors with MET exon 14 skipping alterations.

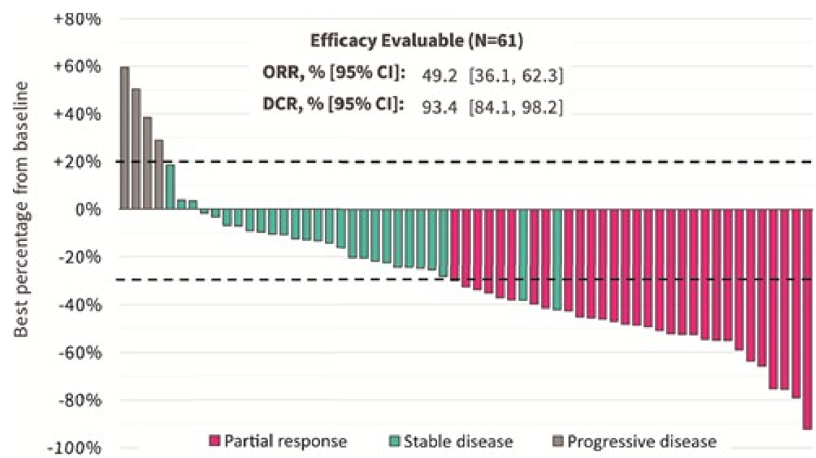
Phase II study of savolitinib monotherapy in NSCLC patients with MET exon 14 alteration (NCT02897479).

We have completed a 70-patient Phase II registration-enabling study in China of savolitinib as a monotherapy for MET exon 14 skipping NSCLC patients who have progressed following prior systemic therapy, or unable to receive chemotherapy.

At the ASCO annual meeting in June 2020, we presented interim data on 70 treated patients, of which 61 patients were efficacy evaluable at the data cut-off date of March 31, 2020. The overall data were encouraging, with efficacy in line with other selective MET inhibitors, despite the inclusion of patients with a more aggressive subtype (36% with pulmonary sarcomatoid carcinoma) and with tolerable safety. Efficacy measurements included the objective response rate, or ORR, (the percentage of patients in the study who show either partial response (tumor measurement reduction of greater than 30%) or complete response), disease control rate, median progression-free survival or PFS and median OS.

At subsequent data cut-off date of August 3, 2020, in the 61 evaluable patients, ORR was 49.2% and disease control rate was 93.4%. Median duration of response was 8.3 months (95% confidence interval: 5.3-16.6). Results from this study were published in *The Lancet Respiratory Medicine* and formed the basis for an NDA filing, which was approved by the NMPA in June 2021. Final OS and subgroup analysis was presented for this trial at European Lung Cancer Congress 2022 and published in the journal JTO Clinical and Research Reports. The updated results further confirmed the favorable benefit of savolitinib in these patients and in each subgroup and the acceptable safety profile. At final data cut off-date of June 28, 2021. In the full analysis set of 70 patients, median PFS was 6.9 months (95% confidence interval: 4.6-8.3). Median OS was 12.5 months (95% confidence interval: 10.5-21.4). A 95% confidence interval means that there is a 95% chance that the results will be within the stated range. CTC grade 3 or above TEAEs, with greater than 5% incidence related to savolitinib treatment were peripheral edema (9%), increased aspartate aminotransferase (13%) and increased alanine aminotransferase (10%). Clinical data demonstrated an acceptable safety profile with an adverse events-related discontinuations rate of 14.3%.

Phase II Study of Savolitinib Monotherapy Showing Effect in MET Exon 14 Alteration NSCLC Patients



Notes: N = number of patients; ORR = objective response rate; DCR = disease control rate; and CI = confidence interval.

Source: Lu S, Fang J et al. Once-daily savolitinib in Chinese patients with pulmonary sarcomatoid carcinomas and other non-small-cell lung cancers harboring MET exon 14 skipping alterations: a multicenter, single-arm, open-label, phase 2 study. Lancet Respir Med. 2021;9(10):1154-1164. doi:10.1016/S2213-2600(21)00084-9

Savolitinib in Combination with Tagrisso

In 2015, AstraZeneca received FDA approval for Tagrisso, its drug for the treatment of T790M+ EGFRm+, TKI-resistant NSCLC. A drug with this type of activity is known as a third-generation EGFR inhibitor. In 2018, Tagrisso’s label was expanded to include previously untreated patients with EGFRm+ NSCLC. In December 2020, Tagrisso’s label was further expanded to include adjuvant therapy after tumor resection in EGFRm+ NSCLC patients. Tagrisso has been established as a new standard of care in the treatment of EGFRm+ NSCLC and has now been approved in over 80 countries. Understanding the mechanism of acquired resistance following Tagrisso treatment is a key clinical question to inform the next treatment choice. A portion of EGFRm+ TKI-resistant patients and a portion of T790M+ EGFRm+ TKI-resistant patients progress because of MET aberrations. Savolitinib was granted fast track designation by the FDA for the combination treatment with Tagrisso of NSCLC patients harboring MET overexpression and/or amplification following progression on Targrisso.

As discussed in more detail below, we and AstraZeneca are studying savolitinib in combination with Tagrisso as a treatment choice for patients who have developed a resistance to TKI (primarily Tagrisso). The acceptance and uptake of Tagrisso indicates that the market potential for savolitinib in Tagrisso-resistant, NSCLC could be material.

In January 2023, the U.S. FDA designated as a Fast Track development program the investigation of savolitinib for use in combination with Tagrisso for the treatment of patients with locally advanced or metastatic NSCLC whose tumors have MET overexpression and/or amplification, as detected by an FDA-approved test, and who have had disease progression during or following prior Tagrisso.

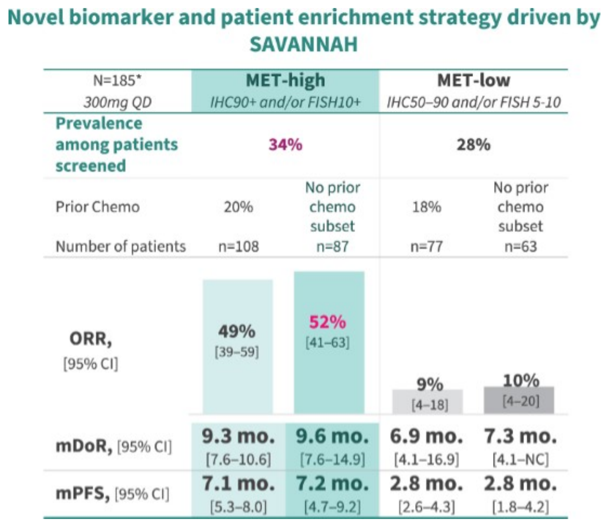
SAVANNAH study: Phase II study of savolitinib in combination with Tagrisso in NSCLC Tagrisso-refractory EGFRm+ patients (NCT03778229).

Based on the encouraging results of the multiple TATTON studies, we and AstraZeneca have initiated this global Phase II study in patients whose disease have progressed following Tagrisso due to MET amplification or overexpression, which has three dose cohorts of savolitinib combined with Tagrisso. In addition to continuing Tagrisso treatment, patients received savolitinib 300mg QD, 300mg BID, or 600mg QD. The study reopened for enrollment to further reinforce the strength of data, initially presented at WCLC 2022. Recruitment is expected to be completed in the second half of 2023. We continue to evaluate the possibility of using the SAVANNAH study as the basis for U.S. accelerated approval.

The results presented at the WCLC 2022 were based on an analysis of 193 efficacy evaluable patients who received savolitinib 300mg once daily plus Tagrisso 80mg once daily at data cut-off date of August 27, 2021. Qualifying MET aberrations were FISH5+ or IHC50+. Importantly, additional analysis using a higher cut-off level of MET aberration were presented. The higher cut-off levels for MET aberration are FISH10+ and/or IHC90+. The prevalence of this higher cut-off levels of MET aberration was 34% of patients centrally tested for enrollment in this study versus 62% at the lower, qualifying cut-off level.

Results showed a trend toward improved response rates with increasing level of MET aberration. Across all patients in this analysis, ORR was 32% (95% CI: 26-39%), median DoR was 8.3 months (95% CI: 6.9-9.7 months), and median PFS was 5.3 months (95% CI: 4.2-5.8 months). These results are consistent with the TATTON and ORCHARD global studies. Among the 108 SAVANNAH patients who met the criteria for higher cut-off levels of MET aberration, ORR was 49% (95% CI: 39-59%), median DoR was 9.3 months (95% CI: 7.6-10.6 months), and median PFS was 7.1 months (95% CI: 5.3-8.0 months).

Importantly, among the 87 patients who did not receive prior chemotherapy, ORR was 52% (95% CI: 41-63%), median DoR was 9.6 months (95% CI: 7.6-14.9 months), and median PFS was 7.2 months (95% CI: 4.7-9.2 months). The safety profile of savolitinib plus Tagrisso was consistent with the known profiles of the combination and each treatment alone.



Novel biomarker and patient enrichment strategy driven by SAVANNAH

N=185* 300mg QD	MET-high IHC90+ and/or FISH10+		MET-low IHC50–90 and/or FISH 5-10	
Prevalence among patients screened	34%		28%	
Prior Chemo	20%	No prior chemo subset	18%	No prior chemo subset
Number of patients	n=108	n=87	n=77	n=63
ORR, [95% CI]	49% [39–59]	52% [41–63]	9% [4–18]	10% [4–20]
mDoR, [95% CI]	9.3 mo. [7.6–10.6]	9.6 mo. [7.6–14.9]	6.9 mo. [4.1–16.9]	7.3 mo. [4.1–NC]
mPFS, [95% CI]	7.1 mo. [5.3–8.0]	7.2 mo. [4.7–9.2]	2.8 mo. [2.6–4.3]	2.8 mo. [1.8–4.2]

* Evaluable for efficacy defined as dosed patients with measurable disease at baseline who had ≥2 on-treatment RECIST scans.
Excludes eight patients with invalid or missing test results for IHC90+ and/or FISH10+ status, these patients were excluded from the subgroup analyses based on MET levels.
Source: Ahn MJ, De Marinis F et al. EP08.02-140 MET Biomarker-based Preliminary Efficacy Analysis in SAVANNAH: savolitinib+osimertinib in EGFRm NSCLC Post-Osimertinib. .J Thorac Oncol. 2022 Sep;17(9):S469-S470.

WCLC 2022 Abstract # EP08.02-140.

SAFFRON study: Phase III study of savolitinib in combination with Tagrisso in NSCLC Tagrisso-refractory EGFRm+ patients (NCT05261399)

Findings based on SAVANNAH and the TATTON studies supported the initiation of the SAFFRON global Phase III study in patients with EGFR-mutated, MET-driven, locally advanced or metastatic NSCLC whose disease progressed on first- or second-line treatment with Tagrisso as the most recent therapy, with no prior chemotherapy in the metastatic setting allowed. Patients are prospectively selected for the higher level of MET aberration of FISH10+ and/or IHC90+. The SAFFRON study will evaluate the efficacy and safety of savolitinib in combination with Tagrisso compared to pemetrexed plus platinum doublet-chemotherapy, the current standard-of-care treatment in this setting. The primary endpoint of the study is PFS. Enrollment of SAVANNAH is being prioritized until it is fully enrolled.

SACHI study: Phase III study of combination with Targrisso in 2L EGFR TKI refractory, MET amplified NSCLC patients (NCT05015608).

We have initiated SACHI, a China Phase III study of savolitinib in combination with Tagrisso. The Phase III trial is a multi-center, open-label, randomized, controlled study in patients with locally advanced or metastatic EGFR mutation-positive NSCLC with MET amplification after disease progression on EGFR inhibitor therapy. The study will evaluate the efficacy and safety of savolitinib in combination with Tagrisso, compared to platinum-based doublet-chemotherapy (pemetrexed plus cisplatin or carboplatin), the standard of care treatment option in this setting. The primary endpoint of the study is median PFS as assessed by investigators. Other endpoints include median PFS assessed by an independent review committee, median overall survival, ORR, duration of response, disease control rate, time to response, and safety. The first patient was dosed in November 2021. We expect to complete the enrollment of this trial in 2024.

SANOVO study: Phase III study of combination with Targrisso in naïve NSCLC patients with EGFR mutant and MET positive (NCT05009836).

We have initiated SANOVO, a China Phase III study of savolitinib in combination with Targrisso as a first-line treatment in certain NSCLC patients whose tumors harbor EGFR mutations and overexpress MET. The Phase III trial is a blinded, randomized, controlled study in previously untreated patients with locally advanced or metastatic NSCLC with activating EGFR mutations and MET overexpression. The study will evaluate Targrisso in combination with savolitinib comparing to Targrisso alone, a standard of care treatment option for these patients. The primary endpoint of the study is median progression free survival as assessed by investigators. Other endpoints include median progression-free survival assessed by an independent review committee, median overall survival, ORR, duration of response, disease control rate, time to response and safety. The first patient was dosed in September 2021. We expect to complete the enrollment of this trial in 2024.

Savolitinib in Combination with Imfinzi

Imfinzi is a human monoclonal antibody developed by AstraZeneca that binds to the PD-L1 protein and blocks the interaction of PD-L1 with PD-1 and CD80 proteins, countering the tumor's immune-evading tactics and releasing the inhibition of immune responses.

SOUND study: Phase II study of combination with Imfinzi in EGFR/ALK/ROS1 wild-type, locally advanced or metastatic NSCLC patients with MET aberrations (NCT05374603).

The SOUND Phase II trial is an open-label, interventional, multicenter, exploratory Phase II study to evaluate savolitinib combined with Imfinzi in EGFR/ALK/ROS1 wild-type, locally advanced or metastatic NSCLC patients with MET aberrations. The primary endpoint is PFS.

Kidney Cancer

The table below shows a summary of the clinical trial for savolitinib in kidney cancer patients.

Clinical Trial of Savolitinib in Kidney Cancer

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Savolitinib + Imfinzi	SAMETA: MET-driven, unresectable and locally advanced or metastatic PRCC	Global	III	Ongoing since 2021	NCT05043090

Notes: PRCC = papillary renal cell carcinoma; Global = more than two countries; and MET = mesenchymal epithelial transition receptor.

PRCC is a subtype of kidney cancer, representing about 15% of patients, with no treatments approved for patients with tumors that harbor MET-driven alterations. MET is a key genetic driver in papillary RCC, and emerging evidence suggests that combining immunotherapies with a MET inhibitor could enhance anti-tumor activity. Immune checkpoints such as PD-L1 are sometimes used by cancer cells to avoid being attacked by the immune system. As such, drugs that target these checkpoints are being developed or marketed as cancer treatments. Imfinzi is an anti-PD-L1 antibody owned by AstraZeneca. Anti-PD-L1 antibodies have been associated with clinical benefits in metastatic RCC, and MET dysregulation has been considered to play an important role in PRCC pathogenesis (including in our savolitinib Phase I and Phase II monotherapy studies) and is a mechanism of resistance against kinase inhibitors in clear cell RCC. Moreover, it is believed that the MET signaling pathway has a complex interplay with the immune system, including correlation with PD-L1 expression, immune suppression through angiogenesis and many other facets of the immune system.

During an Australian Phase I study, our investigators noted positive outcomes among PRCC patients with a strong correlation to MET gene amplification status. Out of a total of eight PRCC patients in our Australia Phase I study who were treated with various doses of savolitinib, three achieved confirmed partial responses. A further three of these eight PRCC patients achieved stable disease, which means patients without partial response but with a tumor measurement increase of less than 20%. This aggregate ORR of 38% was very encouraging for PRCC, which has no effective approved treatments. These responses were also durable as demonstrated by a patient who has been on the therapy for over 30 months and had tumor measurement reduction of greater than 85%. Importantly, the level of tumor response among these PRCC patients correlated closely with the level of MET gene amplification. The patients with consistent MET gene amplification across the whole tumor responded most to savolitinib, and with those patients with the highest level of MET gene amplification responding most to the treatment. We have conducted multiple global studies of savolitinib in PRCC patients, including the SAVOIR monotherapy and CALYPSO combination therapy global Phase II trials, that both demonstrated highly encouraging results. These results led to the initiation of a global Phase III, the SAMETA study, in 2021.

The CALYPSO study is an investigator-initiated open-label Phase II study of savolitinib in combination with Imfinzi. The study evaluated the safety and efficacy of the savolitinib and Imfinzi combination in PRCC patients at sites in the U.K. and Spain. Interim results of the PRCC cohort of the CALYPSO study were presented at the 2021 ASCO annual meeting and showed encouraging efficacy across all patients, both MET+ and MET-. In the 41 patients who were selected regardless of PD-L1 or MET status, ORR was 29% (12/41), while median PFS was 4.9 months (95% confidence interval: 2.5-10.0 months). Median OS was 14.1 months (95% confidence interval: 7.3-30.7 months). For the 14 patients whose tumors are MET-driven, ORR was 57% (8/14), median PFS was 10.5 months (95% confidence interval: 2.9-15.7), and median OS was 27.4 months (95% confidence interval: 7.3-NR). Tolerability was consistent with established single agent safety profiles. In the analysis previously presented at ASCO's Genitourinary Cancers Symposium in 2020, there were 13 treatment related CTC grade 3 or above TEAEs that occurred in more than three patients, with edema (10%), nausea (5%) and transaminitis (5%) being most frequent.

SAMETA study: Phase III in combination with Imfinzi PD-L1 inhibitor in MET-driven, unresectable and locally advanced or metastatic PRCC (NCT05043090)

The Phase III trial is an open-label, randomized, controlled study in treatment-naïve patients with MET-driven, unresectable and locally advanced or metastatic PRCC, to evaluate the efficacy and safety of savolitinib in combination with Imfinzi compared to single agent Imfinzi or single agent Sutent, an oral multi-kinase inhibitor considered as the standard of care treatment option in PRCC. The primary endpoint of the study is median PFS. Other endpoints include median OS, ORR, duration of response, 6-months and 12-months DCR, time to second progression, safety, pharmacokinetics and quality of life. The first patient was dosed in October 2021.

Gastric Cancer

The table below shows a summary of clinical trial for savolitinib in gastric cancer patients.

Clinical Trial of Savolitinib in Gastric Cancer

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Savolitinib monotherapy	2L+ gastric cancer with MET amplification. Two-stage, single-arm study	China	II registration intent	Ongoing since 2021; Consult CDE on registration-intent in H1 2023	NCT04923932

MET-driven gastric cancer has a very poor prognosis. Multiple Phase II studies have been conducted in Asia to study savolitinib in MET-driven gastric cancer, which account for approximately 5% of all gastric cancer patients, demonstrated promising efficacy, including VIKTORY, which reported a 50% ORR with savolitinib monotherapy in gastric cancer patients whose tumors harbor MET amplification.

The VIKTORY study is a biomarker-based, Phase II umbrella trial in gastric cancer conducted by the Samsung Medical Center in South Korea. Patients were allocated to one of 12 biomarker-driven arms, based on a master screening protocol with tissue-based molecular analyses. Patients that tested positive for MET amplification or overexpression were treated with either savolitinib monotherapy or a combination of savolitinib and Taxotere. A total of 715 gastric cancer patients were successfully sequenced and MET amplification was observed in 3.5% of these patients (25/715). Of the 10 associated clinical trials under the VIKTORY umbrella, the highest ORR was observed in the MET amplification arm in patients treated with savolitinib monotherapy, which reported an ORR of 50% (10/20, 95% confidence interval: 28.0-71.9) and met pre-specified 6-week PFS rates. While the savolitinib and Taxotere combination was well tolerated, the VIKTORY study investigators decided to stop enrollment in the two combination cohorts in order to direct patients to the savolitinib monotherapy arm of the VIKTORY study as discussed above. The VIKTORY study investigators concluded that encouraging clinical efficacy of savolitinib in MET-amplified gastric cancer warrants further study.

Phase II study of savolitinib with potential for registration intent in 2L+ gastric cancer with MET amplification (NCT04923932)

This Phase II registration-intent study is a two-stage and single-arm study to evaluate the efficacy, safety and pharmacokinetics of savolitinib in locally advanced or metastatic GC or GEJ patients whose disease progressed after at least one line of standard therapy. The primary endpoint is ORR as assessed by an independent review committee. Other endpoints include 12-week and 6-month progression-free survival rates, median progression-free survival, duration of response, disease control rate, median overall survival, safety, pharmacokinetics and quality of life. The first patient was dosed in July 2021. Subject to the results of the first stage of this study, we will discuss with the CDE of NMPA the appropriate approach and necessary criteria for registration.

Overview of Orpathys Commercial Launch

Sold under the brand name Orpathys, savolitinib was granted conditional approval in China by the NMPA and launched in July 2021 by our partner, AstraZeneca. Orpathys is for the treatment of patients with non-small cell lung cancer with MET exon 14 skipping alterations who have progressed following prior systemic therapy or are unable to receive chemotherapy. This approval follows a priority review designation by the NMPA.

The revenues we generate from Orpathys are comprised of royalty revenue and revenue from the product sales of Orpathys which we source from a third-party manufacturer and sell to AstraZeneca at cost. In 2021, we generated $11.3 million in total revenue from Orpathys, of which $4.8 million was royalty revenue and $6.5 million was revenue from sales of goods to AstraZeneca. In 2022, we generated $22.3 million in total revenue from Orpathys, of which $12.4 million was royalty revenue and $9.9 million was revenue from sales of goods to AstraZeneca.

Following negotiations with the China NHSA in January 2023, starting on March 1, 2023, Orpathys will be included in the updated NRDL, broadening patient access to this medicine.

Partnership with AstraZeneca

In December 2011, we entered into a global licensing, co-development, and commercialization agreement for savolitinib with AstraZeneca. As noted above, given the complexity of many of the signal transduction pathways and resistance mechanisms in oncology, the industry is increasingly studying combinations of targeted therapies (TKI, monoclonal antibodies and immunotherapies) and chemotherapy as potentially the best approach to treating this complex and constantly mutating disease. Based on savolitinib's clinical progress as a highly selective MET inhibitor in a number of cancers, in August 2016, December 2020 and November 2021, we and AstraZeneca amended our global licensing, co-development, and commercialization agreement for savolitinib. We believe that AstraZeneca's portfolio of proprietary targeted therapies is well suited to be used in combinations with savolitinib, and we are studying combinations with Tagrisso (EGFRm+, T790M+) and Imfinzi (PD-L1). These combinations of multiple global first-in-class compounds are difficult to replicate, and we believe represent a significant opportunity for us and AstraZeneca. For more information regarding our partnership with AstraZeneca, see "—Overview of Our Collaborations—AstraZeneca."

2. Fruquintinib (HMPL-013), VEGFR 1, 2 and 3 Inhibitor

Fruquintinib is a novel, selective, oral inhibitor of VEGFR 1/2/3 kinases that was designed to improve kinase selectivity with the destination of minimizing off-target toxicity and thereby improve efficacy and tolerability. Fruquintinib has been studied in clinical trials with about 5,000 patients to date, both as a monotherapy and in combination with other agents.

Aside from its first approved indication of third-line CRC in China, several studies of fruquintinib combined with various checkpoint inhibitors (including Tyvyt and tislelizumab) are underway, some of which presented encouraging data in 2021. Registration-intent studies combined with chemotherapy (FRUTIGA study in gastric cancer) or checkpoint inhibitors (Tyvyt combo, in endometrial cancer and RCC) are completing or ongoing in China.

We are partnered with Eli Lilly in China and have agreed to partner with Takeda outside of China.

Mechanism of Action

During the development of cancer, tumors at an advanced stage can secrete large amounts of VEGF, a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumor in order to provide greater blood flow, oxygen, and nutrients to fuel the rapid growth of the tumor. Since essentially all solid tumors require angiogenesis to progress beyond a few millimeters in diameter, VEGFR drugs have demonstrated benefits in a wide variety of tumor types. VEGF and other ligands can bind to three VEGF receptors, VEGFR 1, 2 and 3, each of which has been shown to play a role in angiogenesis. Therefore, inhibition of the VEGF/VEGFR signaling pathway can act to stop the growth of the vasculature around the tumor and thereby starve the tumor of the nutrients and oxygen it needs to grow rapidly.

This therapeutic strategy has been well validated with several first-generation VEGF inhibitors having been approved globally since 2005 and 2006. These include both small molecule multi-kinase inhibitor drugs such as Nexavar and Sutent as well as monoclonal antibodies such as Avastin. The success of these drugs validated VEGFR inhibition as a new class of therapy for the treatment of cancer.

Fruquintinib Pre-clinical Evidence

Pre-clinical trials have demonstrated that fruquintinib is a highly selective VEGFR 1, 2 and 3 inhibitor with high potency and low cell toxicity at the enzymatic and cellular levels. In a kinase selectivity screening, fruquintinib was found to be approximately 250 times more selective to VEGFR 3 than to the next non-VEGFR kinase.

As a result of off-target side effects, existing VEGFR inhibitors are often unable to be dosed high enough to completely inhibit VEGFR, the intended target. In addition, the complex off-target toxicities resulting from inhibition of multiple signaling pathways are often difficult to manage in clinical practice. Combining such drugs with chemotherapy can lead to severe toxicities that can cause more harm than benefit to patients. To date, the first generation VEGFR TKI have been rarely used in combination with other therapies, thereby limiting their potential. Because of the potency and selectivity of fruquintinib, we believe that it has the potential to be safely combined with other oncology drugs, which could significantly expand its clinical potential.

Fruquintinib Clinical Trials

Fruquintinib Monotherapy - Colorectal Cancer

The table below shows a summary of the clinical trials for fruquintinib in CRC patients. We have two additional trials in progress for fruquintinib in CRC in combination with a checkpoint inhibitor as discussed in more detail below under "— Fruquintinib Combinations with Checkpoint Inhibitors."

Current Clinical Trials of Fruquintinib in CRC

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Fruquintinib monotherapy	FRESCO: ≥3L CRC; chemotherapy refractory	China	III	Approved and launched in 2018	NCT02314819
Fruquintinib monotherapy (1)	FRESCO-2: mCRC	U.S./Europe/ Japan/Australia	III	U.S., EU, Japan filings to complete in 2023; Results at ESMO 2022.	NCT04322539
Fruquintinib monotherapy	CRC, TN & HR+/HER2- breast cancer	U.S.	I/Ib	CRC data at ASCO GI 2022. Close to completion	NCT03251378

Notes: (1) The FDA granted fast track designation for the development of fruquintinib for the treatment of patients with mCRC in June 2020.

CRC = colorectal cancer; ≥3L= third line or above; refractory = resistant to prior treatment; TN = triple-negative; HR+ = hormone receptor-positive; and HER2 = human epidermal growth factor receptor 2.

FRESCO study; Phase III study of fruquintinib monotherapy in third-line CRC (NCT02314819)

In 2014, we initiated the FRESCO study, which is a randomized, double-blind, placebo-controlled, multi-center, Phase III pivotal trial in China in patients with locally advanced or mCRC who had failed at least two prior systemic antineoplastic therapies, including fluoropyrimidine, Eloxatin and Camptosar. At the time, no drug was approved in third-line CRC in China with best supportive care being the general standard of care. This study followed a Phase II proof-of-concept trial in third-line CRC that met its primary endpoint of PFS in 2014.

Enrollment was completed in May 2016, and 519 patients were screened. The intent-to-treat population of 416 patients was randomized at a 2:1 ratio to receive either: 5 mg of fruquintinib orally once daily, on a three-weeks-on/one-week-off cycle, plus best supportive care (278 patients) or placebo plus best supportive care (138 patients). Randomization was stratified for prior anti-VEGF therapy and K-RAS gene status. The trial concluded in January 2017.

In June 2017, we presented the results of the FRESCO study in an oral presentation at the ASCO annual meeting. Results showed that FRESCO met all primary and secondary endpoints including significant improvements in OS and PFS with a manageable safety profile and lower off-target toxicities compared to other targeted therapies. The primary endpoint of median OS was 9.30 months (95% confidence interval: 8.18-10.45 months) in the fruquintinib group versus 6.57 months (95% confidence interval: 5.88-8.11 months) in the placebo group, with a hazard ratio of 0.65 (95% confidence interval: 0.51-0.83; two-sided $p<0.001$). The secondary endpoint of median PFS was 3.71 months (95% confidence interval: 3.65-4.63 months) in the fruquintinib group versus 1.84 months (95% confidence interval: 1.81-1.84 months) in the placebo group, with a hazard ratio of 0.26 (95% confidence interval: 0.21-0.34; two-sided $p<0.001$). Significant benefits were also seen in other secondary endpoints. The disease control rate in the fruquintinib group was 62% versus 12% for placebo ($p<0.001$), while the ORR based on confirmed responses was 5% versus 0% for placebo ($p=0.012$).

We have not performed a head-to-head clinical trial of fruquintinib versus Stivarga. While it is difficult to directly evaluate and compare clinical results across separate trials, data from the FRESCO study compare favorably to the data from the CONCUR study, a Phase III study of Stivarga monotherapy in CRC conducted in Asia, and the CORRECT study, a global Phase III study of Stivarga in CRC. In particular, in the Chinese patient subgroup of the CONCUR study, Stivarga had a disease control rate of 46% versus 7% in the placebo group. Median PFS was 2.0 months in the Stivarga group versus 1.7 months in the placebo group, and median OS was 8.4 months in the Stivarga group versus 6.2 months in the placebo group. In the CORRECT study, Stivarga had a disease control rate of 41% versus 15% in the placebo group. Median PFS was 1.9 months in the Stivarga group versus 1.7 months for the placebo group, and median OS was 6.4 months in the Stivarga group versus 5.0 months in the placebo group.

In terms of safety, results showed that fruquintinib had a manageable safety profile with lower off-target toxicities compared to Stivarga, the other VEGFR TKI approved for third-line CRC. Of particular interest was that the CTC grade 3 or above hepatotoxicity was similar for the fruquintinib group as compared to the placebo group, which was in contrast to Stivarga which was markedly higher and often difficult to manage in the Chinese patient population in the CONCUR study. Adverse events led to dose interruptions in 69% of patients in the Chinese patient subgroup of the CONCUR study, compared to 35% in the FRESCO study. The most frequently reported fruquintinib-related CTC grade 3 or above TEAEs included hypertension (21%), hand-foot skin reaction (11%), proteinuria (3%) and diarrhea (3%), all possibly associated with VEGFR inhibition. No other CTC grade 3 or above TEAEs exceeded 2% in the fruquintinib population, including hepatic function adverse events such as elevations in bilirubin (1%), alanine aminotransferase (<1%) or aspartate aminotransferase (<1%).

In terms of tolerability, dose interruptions or reductions occurred in only 35% and 24% of patients in the fruquintinib arm, respectively, and only 15% of patients discontinued treatment of fruquintinib due to adverse events versus 6% for placebo. The FRESCO study was published in the Journal of the American Medical Association in June 2018.

Subgroup analysis

In June 2018, a further subgroup analysis of data from the FRESCO Phase III study was presented at the ASCO annual meeting. This analysis explored possible effects of prior target therapy on the efficacy and safety of fruquintinib by analyzing the subgroups of patients with prior target therapy and those without prior target therapy.

Results showed that the benefits of fruquintinib were generally consistent across all subgroups. Among a total of 278 fruquintinib-treated patients, 111 had received prior target therapy while 55 of the 138 placebo-treated patients had received prior target therapy. In the prior target therapy subgroup, fruquintinib significantly prolonged OS and PFS. Median OS was 7.69 months for patients treated with fruquintinib versus 5.98 months for placebo (hazard ratio = 0.63; $p = 0.012$). Median PFS was 3.65 months for patients treated with fruquintinib versus 1.84 months for placebo (hazard ratio = 0.24; $p < 0.001$).

Among these 278 patients, the results showed that a subgroup of 84 patients who had received prior anti-VEGF treatment also benefited from fruquintinib. In this subgroup, the median OS was 7.20 months for fruquintinib versus 5.91 months for placebo (hazard ratio = 0.68; $p = 0.066$) and the median PFS was 3.48 months for fruquintinib versus 1.84 months for placebo (hazard ratio = 0.24; $p < 0.001$).

In the subgroup of 250 patients without prior targeted therapies, the median OS was 10.35 months for 167 patients treated with fruquintinib versus 6.93 months for 83 patients treated with placebo (hazard ratio = 0.63; $p = 0.003$), and the median PFS for patients treated with fruquintinib was 3.81 months versus 1.84 months for placebo (hazard ratio = 0.28; $p < 0.001$).

Additional data showed that there were no observed cumulative CTC grade 3 or above TEAEs in the subgroup of patients with prior target therapy. The CTC grade 3 or above TEAEs rates of fruquintinib were similar in the subgroups with prior target therapy (61.3%) and without prior target therapy (61.1%). This subgroup analysis is consistent with the previously reported results from the FRESCO study's intent-to-treat population.

The results of this analysis showed that fruquintinib had clinically meaningful benefits in third-line mCRC patients regardless of prior target therapy without observed cumulative toxicity.

Quality-adjusted survival analysis

At the 2018 ASCO Annual Meeting, an analysis was presented that aimed to compare the quality-adjusted survival between the two arms of the FRESCO study using quality-adjusted time without symptoms or toxicity, or Q-TWiST, methodology and to investigate the Q-TWiST benefit of fruquintinib treatment among subgroups. Q-TWiST is a tool to evaluate relative clinical benefit-risk from a patient's perspective and has been widely used in oncology treatment assessment. The survival time for each patient was divided into three portions: time with CTC grade 3 or above toxicity before progression, time without symptoms or CTC grade 3 or above toxicity, and time from progression or relapse until death or end of follow-up.

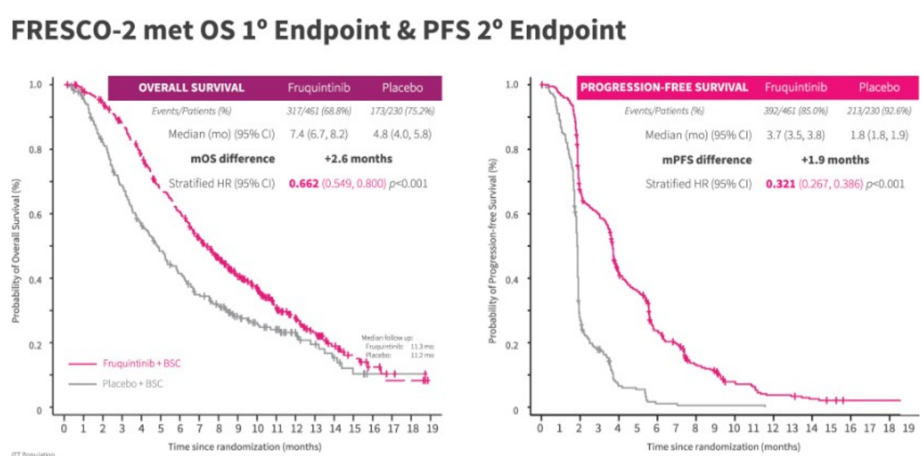
Patients treated with fruquintinib had longer Q-TWiST periods compared to patients treated with placebo. Q-TWiST benefits were observed regardless of prior lines of chemotherapy and prior anti-VEGF or anti-EGFR targeted therapy. The relative improvement of Q-TWiST with fruquintinib represents a clinically important quality-of-life benefit for mCRC patients.

Supported by data from the successful FRESCO study, we submitted an NDA for fruquintinib in June 2017. Fruquintinib was subsequently awarded priority review status by the NMPA in view of its clinical value in September 2017, and in September 2018, the NMPA approved fruquintinib for the treatment of patients with advanced CRC and was launched in November 2018. For more information regarding the Elunate product launch, see "—Overview of Elunate Commercial Launch."

FRESCO-2 study: Phase III study of fruquintinib monotherapy in mCRC (NCT04322539)

We initiated a global Phase III registration study, known as the FRESCO-2 study, in refractory metastatic CRC. The first patient was dosed in September 2020 in the United States and the enrollment was completed in December 2021, where 691 patients from over 150 sites in 14 countries were enrolled. In September 2022, we presented the results from FRESCO-2 study at the European Society for Medical Oncology Congress 2022. We plan to complete new drug application filings in the U.S., Europe and Japan in 2023.

The FRESCO-2 study demonstrated that treatment with fruquintinib resulted in a statistically significant and clinically meaningful increase in the primary OS endpoint and key secondary PFS endpoint compared to treatment with placebo. The positive OS and PFS were consistent across all subgroups. Specifically, the median OS was 7.4 months for the 461 patients treated with fruquintinib compared to 4.8 months for the 230 patients in the placebo group (hazard ratio 0.66; 95% confidence interval 0.55–0.80; p<0.001). Median PFS was 3.7 months for patients treated with fruquintinib compared to 1.8 months for patients in the placebo group (HR 0.32; 95% CI 0.27–0.39; p<0.001). The DCR was 55.5% in the fruquintinib group compared to 16.1% for patients in the placebo group. Median duration of follow-up was approximately 11 months for patients in both groups.



Notes: [1] ESMO 2022, LBA25. Dasari NA, et al. LBA25 - FRESCO-2: A global phase III multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer. 12 Sep 2022, Proffered Paper session 2: GI, lower digestive Session. Annals of Oncology (2022) 33 (suppl_7): S808-S869. 10.1016/annonc/annonc1089.

The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported fruquintinib studies. Grade 3 or above adverse events occurred in 62.7% of patients who received fruquintinib, compared to 50.4% of patients who received placebo. Grade 3 or above adverse events that occurred in more than 5% of patients who received fruquintinib were hypertension (13.6% vs. 0.9% in the placebo group), asthenia (7.7% vs. 3.9% in the placebo group) and hand-foot syndrome (6.4% vs. 0% in the placebo group).

Filing of a rolling submission of a NDA was initiated in December 2022, and expected to be completed in the first half of 2023. MAA filing to the EMA and NDA filing to the PMDA are expected to follow in 2023.

Phase I/Ib study of fruquintinib monotherapy in metastatic colorectal and breast cancers (NCT03251378)

We are conducting a multi-center, open-label, Phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetics of fruquintinib in U.S. patients, which has established the U.S. RP2D to be 5 mg, the same as that in China. This dose was used in the FRESCO-2 study described above.

Fruquintinib Monotherapy - Gastric Cancer

Advanced gastric cancer is a major medical need, particularly in Asian populations, with limited treatment options for patients who have failed first-line standard chemotherapy with 5-fluorouracil and platinum doublets. The table below shows a summary of the clinical study for fruquintinib in gastric cancer patients.

Clinical Trial of Fruquintinib in Gastric Cancer

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Fruquintinib + paclitaxel	FRUTIGA: 2L gastric cancer	China	III	Supplemental NDA to be filed in H1 2023	NCT03223376

Notes: 2L = second line.

FRUTIGA study: Phase III study of fruquintinib in combination with paclitaxel in gastric cancer (second-line) (NCT03223376)

This randomized, double-blind, Phase III study in China to evaluate fruquintinib combined with paclitaxel compared with paclitaxel monotherapy, for second-line treatment of advanced gastric cancer, enrolled 703 patients in July 2022. Its dual-primary endpoints are PFS and OS. The trial met the PFS endpoint at a statistically and clinically meaningful level. The OS endpoint was not statistically significant per the pre-specified statistical plan, although there was an improvement in median OS. Fruquintinib also demonstrated a statistically significant improvement in secondary endpoints including ORR, DCR and DoR. The safety profile of fruquintinib in FRUTIGA was consistent with previously reported studies. Full detailed results are subject to ongoing analysis and are expected to be disclosed at an upcoming scientific meeting. We plan to file a supplemental NDA with the NMPA in 2023.

Fruquintinib Combinations with Checkpoint Inhibitors

The table below shows a summary of clinical trials for fruquintinib in combination with checkpoint inhibitors.

Clinical Trials of Fruquintinib with Checkpoint Inhibitors

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Fruquintinib and Tyvyt (PD-1)	Endometrial cancer	China	II registration-intent	Ongoing since 2021; Ib data presented at CSCO 2021	NCT03903705
Fruquintinib and Tyvyt (PD-1)	RCC	China	III	Ongoing since 2022	NCT05522231
Fruquintinib and Tyvyt (PD-1)	RCC	China	Ib/II	Fully enrolled; 1L&2L data submission in 2023	NCT03903705
Fruquintinib and Tyvyt (PD-1)	CRC	China	II	Fully enrolled; Data at European Journal of Cancer 181 (2023) 26-37	NCT04179084
Fruquintinib and Tyvyt (PD-1)	Gastrointestinal tumors	China	Ib/II	Fully enrolled; data submission in 2023	NCT03903705
Fruquintinib and Tyvyt (PD-1)	NSCLC	China	Ib/II	Fully enrolled; data submission in 2023 if mature	NCT03903705
Fruquintinib and Tyvyt (PD-1)	Cervical cancer	China	Ib/II	Fully enrolled; data submission in 2023 if mature	NCT03903705
Fruquintinib and tislelizumab (PD-1)	MSS-CRC	U.S.	Ib/II	Ongoing since 2021; Fully enrolled; Submitting data to conference in H2 2023	NCT04577963
Fruquintinib and tislelizumab (PD-1)	CRC	Korea / China	Ib/II	Fully enrolled	NCT04716634

Notes: CRC = colorectal cancer; NSCLC = non-small cell lung cancer.

In November 2018, we entered into two collaboration agreements to evaluate the safety, tolerability and efficacy of fruquintinib in combination with checkpoint inhibitors. These include a global collaboration with Innovent to evaluate the combination of fruquintinib with Innovent's Tyvyt, a PD-1 monoclonal antibody approved in China, and a collaboration in China with Genor to evaluate the fruquintinib combination with geptanolimab, a PD-1 monoclonal antibody being developed by Genor. In May 2020, we entered into a collaboration agreement with BeiGene to evaluate the safety, tolerability and efficacy of combining two of our drug candidates, including fruquintinib, with BeiGene's anti-PD-1 antibody tislelizumab.

Tyvyt combination for advanced endometrial cancer registration-intent cohort (NCT03903705)

Platinum-based systemic chemotherapy is the standard first-line treatment for advanced endometrial cancer. However, patients who progress following first-line chemotherapy have limited treatment options, and the prognosis remains poor. As disclosed at CSCO 2021, as of the data cutoff date of August 31, 2021, 35 patients were enrolled (NCT03903705), including 7 treatment-naïve and 28 pretreated patients. Of them, 29 were efficacy evaluable, 4 were treatment-naïve and 25 were pretreated. All 4 treatment-naïve patients experienced confirmed tumor response, for ORR of 100% (95% CI: 39.8-100.0), and median PFS was not reached. Among the 25 pretreated patients, the confirmed ORR was 32.0% (95% CI: 14.9-53.5), DCR was 92.0% (95% CI: 74.0-99.0) and the median PFS was 6.9 months (95% CI: 4.1-NR). Among the 19 proficient mismatch repair (pMMR) patients in the pretreated cohort, the confirmed ORR was 36.8% (95% CI: 16.3-61.6), DCR was 94.7% (95% CI: 74.0-99.9), median PFS was 6.9 months (95% CI: 4.1-NR), and the median OS was not reached. Among the 35 enrolled patients, treatment-related adverse events of grade 3 or above that occurred in more than 10% of patients were hypertension (4 patients, 11.4%) and proteinuria (4 patients, 11.4%). 5 (14.3%) patients reported treatment-related serious adverse events. Following encouraging data in the advanced endometrial cancer cohort, it has been expanded into a single-arm registrational Phase II study of over 130 patients.

Tyvyt combination for advanced metastatic renal cell carcinoma (NCT05522231)

In first-line clear-cell renal cell carcinoma ("ccRCC"), clinical benefits have been demonstrated for the combination of antiangiogenic therapy and immunotherapy. However, there is limited evidence on the benefits of this combination in the second-line setting. Phase II data disclosed at CSCO 2021 showed encouraging anti-tumor efficacy and durability in these patients.

A Phase III trial of fruquintinib in combination with Tyvyt as second-line treatment for locally advanced or metastatic RCC was initiated in October 2022. The study is a randomized, open-label, active-controlled study to evaluate the efficacy and safety of fruquintinib in combination with Tyvyt versus axitinib or everolimus monotherapy for the second-line treatment of advanced RCC. The primary endpoint is PFS. Approximately 260 patients will be enrolled in the study.

Tyvyt combination for CRC (NCT04179084)

Encouraging preliminary data presented at ASCO 2021 for fruquintinib in combination with two PD-1 inhibitors, Tyvyt and geptanolimab, in advanced CRC showed a five-fold increase in ORR and a doubling of median PFS as compared to the FRESCO study for fruquintinib as a monotherapy.

In the Tyvyt combination study (NCT04179084), at the final analysis with data cut-off date of December 30, 2021, 44 patients were enrolled into the CRC cohort (43 efficacy evaluable), 22 (21 efficacy evaluable) of whom received the RP2D. ORR was 21% for all patients and 24% for those who received the RP2D. DCR was 88% for all patients and 100% for those who received the RP2D. Median PFS was 5.6 months for all patients, and 6.9 months for those who received the RP2D. Median OS was 14.3 months for all patients and 14.8 months for those who received PRZD.

In the geptanolimab combination study (NCT03977090), for the 15 patients in the CRC cohort ORR was 26.7% (including 1 patient with unconfirmed PR) and 33% in the group that received the RP2D. DCR for all evaluable patients was 80% and median PFS was 7.3 months (95% CI: 1.9-NR). Grade 3 treatment-related adverse events occurred in 47% of patients, and no incidences of grade 4 or 5 treatment-related adverse events were observed.

Tislelizumab combinations for CRC (NCT04577963 & NCT04716634)

A MSS-CRC cohort was added to an open-label, multi-center, non-randomized Phase Ib/II study in the U.S. to assess fruquintinib in combination with tislelizumab. The Phase II study in China and Korea for fruquintinib in combination with tislelizumab was initiated and is being led by BeiGene for the treatment of advanced or metastatic, unresectable CRC.

Fruquintinib Exploratory Development

In China, we support an investigator initiated trial program for fruquintinib, and there are about 30 of such trials ongoing in various solid tumor settings.

Overview of Elunate Commercial Launch

Fruquintinib capsules, sold under the brand name Elunate, were approved for marketing in China by the NMPA in September 2018 and commercially launched in late November 2018. We also received marketing approval for Elunate in Macau in February 2022. Elunate is for the treatment of patients with mCRC that have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-EGFR therapy (RAS wild type).

Starting on January 1, 2020, Elunate was included on China's NRDL at a 63% discount to its initial retail price for two years, paving the way to significantly broaden access for advanced CRC patients and rapidly build penetration in China over the coming years. The inclusion was renewed pursuant to which we agreed to a discount of 5% relative to the 2021 NRDL price, and Elunate will continue to be included in the NRDL starting January 2022 for another two years.

During 2022, we introduced Elunate through approximately 7,200 local, regional and national educational events involving approximately 215,000 healthcare professionals.

The revenues we generate from Elunate are comprised of royalty revenue, revenue from the sales of Elunate to Eli Lilly which we manufacture and sell at cost and, starting in October 2020, revenue from promotion and marketing services. In 2020, we generated $20.0 million in total revenue from Elunate, of which $4.9 million was royalty revenue, $11.3 million was revenue from sales of goods primarily to Eli Lilly and $3.8 million was revenue from promotion and marketing services to Eli Lilly. In 2021, we generated $53.5 million in total revenue from Elunate, of which $10.3 million was royalty revenue, $15.8 million was revenue from sales of goods primarily to Eli Lilly and $27.4 million was revenue from promotion and marketing services to Eli Lilly. In 2022, we generated $69.9 million in total revenue from Elunate, of which $13.9 million was royalty revenue, $14.7 million was revenue from sales of goods primarily to Eli Lilly and $41.3 million was revenue from promotion and marketing services to Eli Lilly.

Collaboration Partnerships

Eli Lilly

In October 2013, we entered into a license and collaboration agreement with Eli Lilly in order to accelerate and broaden our fruquintinib development program in China. As a result, we were able to quickly expand the clinical development of fruquintinib into indications with unmet medical needs in China including CRC and gastric cancer, as discussed above. In December 2018, we amended our license and collaboration agreement with Eli Lilly. This amendment gives us, among other things, all planning, execution and decision making responsibilities for life cycle indication development of fruquintinib in China. Support from Eli Lilly has also helped us to establish our own manufacturing (formulation) facility in Suzhou, China, which now produces clinical and commercial supplies of fruquintinib. In July 2020, we reached an agreement with Eli Lilly to take over development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in China starting on October 1, 2020. Under the terms of the new agreement, we will share gross profits linked to sales target performance. Subject to meeting pre-agreed sales targets, Eli Lilly will pay us an estimated total of 70% to 80% of Elunate in-market sales in the form of royalties, manufacturing costs and service payments.

For more information regarding our partnership with Eli Lilly, see "—Overview of Our Collaborations—Eli Lilly."

Takeda

In January 2023, we entered into an agreement with a subsidiary of Takeda whereby it will receive an exclusive worldwide license to develop, manufacture and commercialize fruquintinib in all indications and territories outside of mainland China, Hong Kong and Macau, where it is marketed and will continue to be marketed by us in partnership with Eli Lilly. Subject to the terms of the agreement, we will be eligible to receive up to $1.13 billion, including $400 million upfront on closing of the agreement, and up to $730 million in additional potential payments relating to regulatory, development and commercial sales milestones, as well as royalties on net sales. The deal is subject to customary closing conditions, including completion of antitrust regulatory reviews. Following these clearances, Takeda will become solely responsible for the development and commercialization of fruquintinib in all the included territories.

3. Surufatinib (HMPL-012), VEGFR 1, 2 and 3, FGFR1 and CSF-1R Inhibitor

Surufatinib is a novel, oral angio-immuno kinase inhibitor that selectively inhibits the tyrosine kinase activity associated with VEGFR and FGFR, both shown to be involved in tumor angiogenesis, and CSF-1R, which plays a key role in regulating tumor-associated macrophages, promoting the body's immune response against tumor cells. Surufatinib has been studied in clinical trials with around 1,200 patients to date, both as a monotherapy and in combinations, and is approved in China. We currently retain all rights to surufatinib worldwide.

Initial approvals for surufatinib in China are for the treatment of advanced NET patients. NETs present in the body's organ system with fragmented epidemiology. About 58% of NETs originate in the gastrointestinal tract and pancreas, 27% in the lung or bronchus, and a further 15% in other organs or unknown origins.

Surufatinib's ability to inhibit angiogenesis, block the accumulation of tumor associated macrophages and promote infiltration of effector T cells into tumors could help improve the anti-tumor activity of PD-1 antibodies. Several combination studies with PD-1 antibodies have shown promising data.

Mechanism of Action

Both VEGFR and FGFR signaling pathways can mediate tumor angiogenesis. CSF-1R plays an important role in the functions of macrophages. Recently, the roles in increasing tumor immune evasion of VEGFR, FGFR in regulation of T cells, tumor-associated macrophages and myeloid-derived suppressor cells have been demonstrated. Therefore, blockade of tumor angiogenesis and tumor immune evasion by simultaneously targeting VEGFR 1, 2 and 3, FGFR1 and CSF-1R kinases may represent a promising approach for oncology therapy.

Surufatinib Pre-clinical Evidence

Surufatinib inhibited VEGFR 1, 2, and 3, FGFR1 and CSF-1R kinases with IC_{50} in a range of 1 nM to 24 nM. It also strongly blocked VEGF-induced VEGFR2 phosphorylation in HEK293 cells and CSF-1R phosphorylation in RAW264.7 cells with an IC_{50} of 2 nM and 79 nM, respectively. Surufatinib also reduced VEGF- or FGF-stimulated human umbilical vein endothelial cell proliferation with an IC_{50} < 50 nM. In animal studies, a single oral dose of surufatinib inhibited VEGF-stimulated VEGFR2 phosphorylation in lung tissues of nude mice in an exposure-dependent manner. Furthermore, elevation of FGF23 levels in plasma 24 hours post dosing suggested suppression of FGFR signaling.

Surufatinib demonstrated potent tumor growth inhibition in multiple human xenograft models and decreased cluster of differentiation 31 expression remarkably, suggesting strong inhibition on angiogenesis through VEGFR and FGFR signaling. In a syngeneic murine colon cancer model, surufatinib demonstrated moderate tumor growth inhibition after single-agent treatment. Flow cytometry and immunohistochemistry analysis revealed an increase of certain T cells and a significant reduction in certain tumor-associated macrophages, including CSF-1R mutation positive tumor-associated macrophages in tumor tissue, indicating surufatinib has a strong effect on CSF-1R. Interestingly, a combination of surufatinib with a PD-L1 antibody resulted in enhanced anti-tumor effect. These results suggested that surufatinib has a strong effect in modulating angiogenesis and cancer immunity.

Surufatinib Clinical Trials

We currently have various clinical trials of surufatinib as a monotherapy and in combination with checkpoint inhibitors ongoing or expected to begin in the near term.

Surufatinib as a Monotherapy - Neuroendocrine Tumors

Neuroendocrine tumors begin in the specialized cells of the body's neuroendocrine system. Cells have traits of both hormone-producing endocrine cells and nerve cells. Neuroendocrine tumors are found throughout the body's organ system and have complex and fragmented epidemiology, about 58% of NETs originate in the gastrointestinal tract and pancreas, 27% in the lung or bronchus, and a further 15% in other organs or unknown origins. In China, there are an estimated approximately 34,000 new patients of advanced NETs per year.

NETs can be functional, releasing hormones and peptides that cause symptoms like diarrhea and flushing, or non-functional with no symptoms. Early-stage NETs, which are often functional, can be treated with somatostatin analogue subcutaneous injections, which are approved and reimbursed in China and alleviate symptoms and slow NET growth, but have limited tumor reduction efficacy.

Advanced NETs grow more quickly. In China, Sutent is approved in pancreatic NET while Afinitor, an mTOR inhibitor, is approved in non-functional NETs in the pancreas, lung and gastrointestinal tract. These approvals, however, cover only about half of advanced neuroendocrine tumor patients.

The table below shows a summary of clinical trials for surufatinib in neuroendocrine cancer patients.

Clinical Trials of Surufatinib in NETs

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Surufatinib monotherapy	SANET-ep: Non-pancreatic NET	China	III	Approved; Launched in 2021	NCT02588170
Surufatinib monotherapy	SANET-p: Pancreatic NET	China	III	Approved; Launched in 2021; Pooled analysis at ASCO 2022	NCT02589821
Surufatinib monotherapy(1)	NETs	U.S. & Europe	Ib/II Bridging	Completed	NCT02549937
Surufatinib monotherapy	NETs	Japan	Bridging	Ongoing since 2021	NCT05077384

Notes: (1) FDA granted surufatinib orphan drug designation for the treatment of pancreatic NETs in November 2019 and fast track designation for our pancreatic and non-pancreatic NET development programs in April 2020.

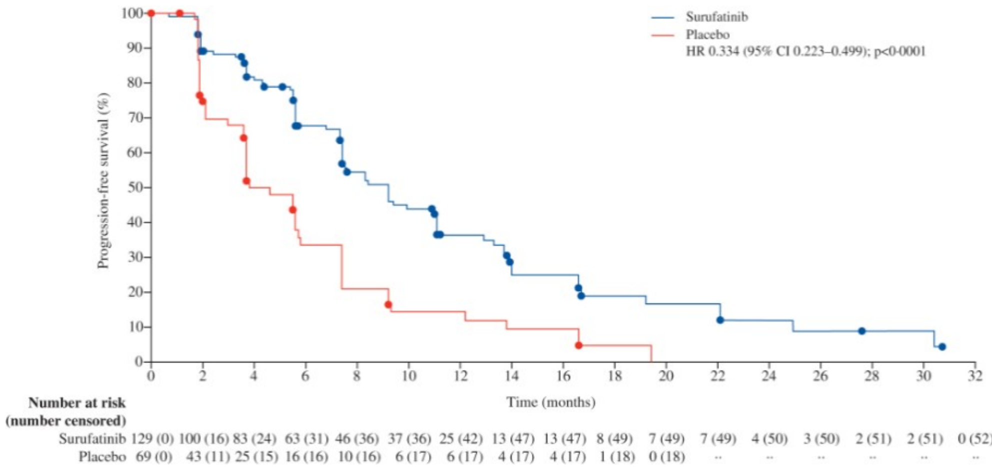
NET = neuroendocrine tumor.

SANET-ep study: Phase III study of surufatinib monotherapy in non-pancreatic NETs (NCT02588170)

In 2015, we initiated the SANET-ep study, which is a Phase III study in China in patients with grade 1 and 2 advanced non-pancreatic NETs. In this study, patients were randomized at a 2:1 ratio to receive either an oral dose of 300 mg of surufatinib or a placebo once daily on a 28-day treatment cycle. The primary endpoint was PFS, with secondary endpoints including ORR, disease control rate, time to response, duration of response, OS, safety and tolerability.

A 198-patient interim analysis was conducted on SANET-ep in mid-2019, leading the independent data monitoring committee, or IDMC, to determine that it had met the pre-defined primary endpoint of PFS and should be stopped early. The positive results of this trial were highlighted in an oral presentation at the 2019 European Society for Medical Oncology Congress, and subsequently published in *The Lancet Oncology* in September 2020. Median PFS per investigator assessment was 9.2 months for patients treated with surufatinib, as compared to 3.8 months for patients in the placebo group (HR 0.334; 95% CI: 0.223, 0.499; p<0.0001). Efficacy was also supported by a blinded independent image review committee assessment. Surufatinib was well-tolerated in this study and the safety profile was consistent with observations in prior clinical studies. CTC grade 3 or above TEAEs in this study with greater than 5% incidence were hypertension (36%), proteinuria (19%) and anemia (7%).

SANET-ep Clearly Succeeded in Meeting Primary Endpoint of PFS



Notes: P-value is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; CI = confidence interval; and HR = hazard ratio.

Source: Xu J, Shen L, Zhou Z, et al. Surufatinib in advanced extra-pancreatic neuroendocrine tumours (SANET-ep): a randomized, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(11):1500-1512. doi:10.1016/S1470-2045(20)30496-4.

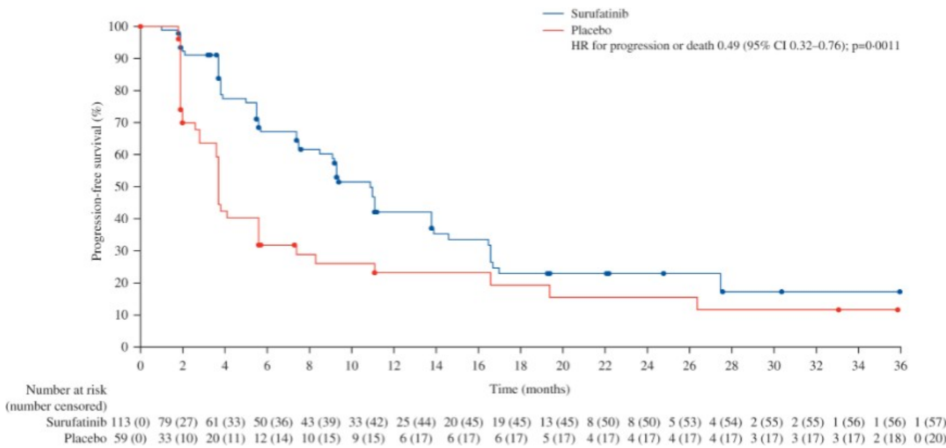
In late 2020, surufatinib was granted approval for drug registration by the NMPA for the treatment of non-pancreatic NET and launched in mid-January 2021 within three weeks of approval. We believe the benefits of surufatinib as a monotherapy to patients with non-pancreatic NETs in China could be significant as compared to the minimal treatment alternatives currently available to them.

SANET-p study: Phase III study of surufatinib monotherapy in pancreatic NETs (NCT02589821)

In 2016, we initiated the SANET-p study, which is a Phase III study in China in patients with low- or intermediate-grade, advanced pancreatic NETs. In this study, patients are randomized at a 2:1 ratio to receive either an oral dose of 300 mg of surufatinib or a placebo once daily on a 28-day treatment cycle. The primary endpoint is PFS, with secondary endpoints including ORR, disease control rate, time to response, duration of response, OS, safety and tolerability.

In early 2020, an interim analysis was conducted on SANET-p, leading the IDMC to recommend that the study stop early as the pre-defined primary endpoint of PFS had already been met. Investigator-assessed median PFS was 10.9 months for patients treated with surufatinib, as compared to 3.7 months for patients in the placebo group (HR 0.491; 95% CI: 0.319-0.755; p = 0.0011). ORRs were 19.2% for the efficacy evaluable patients in the surufatinib group versus 1.9% for the placebo group, with a DCR of 80.8% versus 66.0%, respectively. Most patients in the trial had Grade 2 disease with heavy tumor burden, including liver metastasis and multiple organ involvement. Efficacy was also supported by blinded independent image review committee assessment, with a median PFS of 13.9 months for surufatinib as compared to 4.6 months for placebo (HR 0.339; 95% CI 0.209-0.549; p<0.0001). The safety profile of surufatinib was manageable and consistent with observations in prior studies. Treatment was well tolerated for most patients, with discontinuation rates as a result of TEAEs of 10.6% in the surufatinib group as compared to 6.8% in the placebo group. CTC grade 3 or above TEAEs in this study with greater than 5% incidence were hypertension (38%), proteinuria (10%) and hypertriglyceridemia (7%).

SANET-p Clearly Succeeded in Meeting Primary Endpoint of PFS



Notes: P-value is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; CI = confidence interval; and HR = hazard ratio.

Source: Xu J, Shen L, Bai C, et al. Surufatinib in advanced pancreatic neuroendocrine tumours (SANET-p): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(11):1489-1499. doi:10.1016/S1470-2045(20)30493-9.

Surufatinib was granted approval for drug registration by the NMPA for the treatment of advanced pancreatic NET and launched in June 2021. We believe the benefits of surufatinib as a monotherapy to patients with pancreatic NETs in China could be significant as compared to the alternatives currently available to them. We believe that surufatinib is currently the only approved targeted therapy that can address and treat all subtypes of NETs.

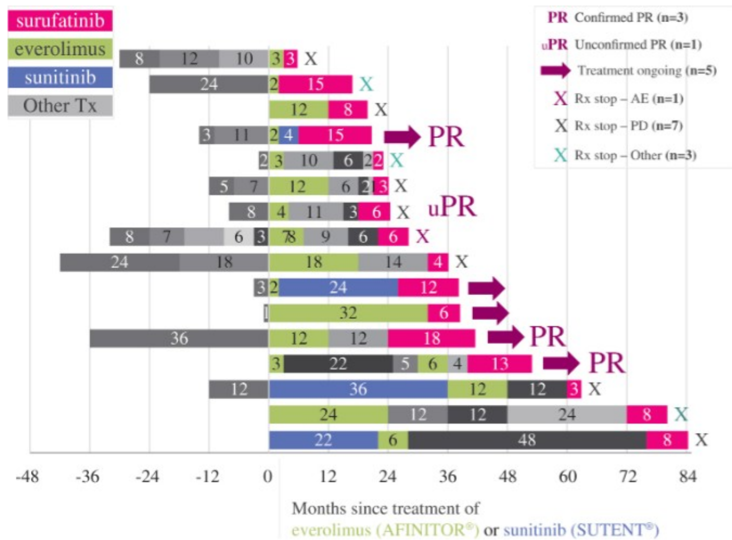
Global development of surufatinib in NET

Surufatinib received FDA Fast Track Designations in April 2020 for the treatment of pNETs and epNETs. Orphan Drug Designation for pNETs was granted in November 2019. In a May 2020 pre-NDA meeting, we reached an agreement with the FDA that the two positive Phase III studies of surufatinib in patients with pNETs and epNETs in China, along with the bridging trial in the U.S. could form the basis to support a U.S. NDA submission. The FDA accepted the filing of the NDA in June 2021. However, in April 2022, we received a Complete Response Letter from the FDA regarding the NDA for surufatinib for the treatment of pNETs and epNETs. Based on interactions with the FDA and EMA, a new multi-regional clinical trial would be required to move forward with this program in the U.S. and Europe. We will continue to explore conducting a multi-regional clinical trial with a partner that would support approval in U.S. and Europe. In addition, we initiated a registration-enabling bridging study in NET patients in Japan in September 2021.

Phase Ib/II bridging study of surufatinib monotherapy in heavily pretreated progressive NETs (NCT02549937)

We conducted a multi-center, open-label, Phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetics of surufatinib in U.S. patients, which has established the U.S. recommended Phase II dose, or RP2D, to be 300 mg, the same as that in China. At the 2021 ASCO annual meeting, preliminary data presented from the two NET cohorts in the ongoing U.S. Phase Ib trial for surufatinib demonstrated efficacy comparable to China data in heavily pretreated patients, including Afinitor and Sutent, with pancreatic or non-pancreatic NETs. The safety profile was also consistent with the larger pool of surufatinib safety data.

US Phase Ib: Encouraging Preliminary Efficacy in Afinitor and Sutent Refractory/Intolerant NET



Notes: Data cut-off as of April 21, 2020. PR = partial response; AE = adverse event; PD = progressive disease; Rx = treatment; Tx = treatment; and n = number of patients.

Source: Dasari, et al. Efficacy and safety of surufatinib in United States (US) patients (pts) with neuroendocrine tumors (NETs). Journal of Clinical Oncology 2020 38:15_suppl, 4610-4610.

Bridging study of surufatinib monotherapy in heavily pretreated progressive NETs (NCT05077384)

In September 2021, we initiated a Japan registration-enabling bridging study for surufatinib to support the registration of surufatinib in the treatment of patients with advanced NETs. This Japan study is a two-stage, open label study of surufatinib where approximately 34 patients are expected to be recruited. In part 1 of the study, the safety and tolerability of surufatinib 300mg once daily after 28 days of treatment will be assessed in patients with relapsed/refractory non-hematological malignancies; pharmacokinetics and anti-tumor activity of surufatinib are secondary endpoints. In Part 2 of the study, efficacy will be assessed in patients with locally advanced or metastatic NETs; the primary outcome measure is ORR. The secondary outcome measures include DCR, PFS, DoR, safety, and pharmacokinetics.

Based on dialogue with the Japanese PMDA, it was agreed that the Japanese NDA would include results from a 34-patient, registration-enabling bridging study in Japan to complement the existing data package. The trial was initiated in September 2021 and results are expected in the first half of 2023. We plan to engage with the PMDA when these results are available.

Surufatinib in Combination with Checkpoint Inhibitors

Surufatinib's ability to inhibit angiogenesis, block the accumulation of tumor associated macrophages and promote infiltration of effector T cells into tumors, could help improve the anti-tumor activity of PD-1 antibodies.

The table below shows a summary of clinical trials for surufatinib in combination with checkpoint inhibitors.

Clinical Trials of Surufatinib with Checkpoint Inhibitors

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Surufatinib and Tuoyi (PD-1)	SURTORI-01: 2L NEC	China	III	Ongoing since 2021	NCT05015621
Surufatinib and Tuoyi (PD-1)	Neuroendocrine neoplasms	China	II	Fully enrolled; Data presented at ASCO 2021 and ESMO IO 2021.	NCT04169672
Surufatinib and Tuoyi (PD-1)	BTC	China	II	Fully enrolled	NCT04169672
Surufatinib and Tuoyi (PD-1)	Small cell lung cancer	China	II	Ongoing since 2022	NCT05509699
Surufatinib and Tuoyi (PD-1)	Solid tumors	China	II	Fully enrolled	NCT04169672
Surufatinib and tislelizumab (PD-1)	Solid tumors	U.S./ Europe	Ib/II	Since 2021. Enrollment stopped	NCT04579757

Clinical Trials with Junshi's Tuoyi

In late 2018, we entered into a global collaboration with Junshi to evaluate the combination of surufatinib with Tuoyi. We completed a Phase I dose-finding study and presented the data at the AACR Conference in April 2020. The data showed that surufatinib plus Tuoyi were well tolerated with no unexpected safety signals observed. At the recommend Phase 2 dose, a DCR of 100% and ORR of 63.6% were reported for 11 efficacy evaluable patients, with 2 unconfirmed partial responses. Surufatinib plus Tuoyi showed encouraging antitumor activity in patients with advanced solid tumors. A Phase II China study combining surufatinib with Tuoyi enrolled patients in nine solid tumor indications, including NENs, BTC, gastric cancer, thyroid cancer, small cell lung cancer, soft tissue sarcoma, endometrial cancer, esophageal cancer and NSCLC. These have led to the initiation in September 2021 of the first Phase III trial combining surufatinib with a PD-1 antibody, the SURTORI-01 study in NEC and a Phase II study in SCLC in 2022.

NEC (subset of NENs) cohort — At the 2021 CSCO annual meeting, we presented data, with a cutoff date of July 30, 2021 for all 21 enrolled NEC patients that were efficacy evaluable. Average duration of treatment was 4.9 months (range 1-19) and median OS was 10.3 months (95% CI: 9.1-not reached). The median PFS was 4.14 months (95% CI: 1.5-5.5) and median DoR was 4.1 months (95% CI: 3.0-not reached). The confirmed ORR was 23.8% (95% CI: 8.2-47.2) and DCR was 71.4% (95% CI: 47.8-88.7). All patients experienced treatment-related adverse events, including 9 (42.9%) who experienced grade 3 or above treatment-related adverse events. 1 (4.8%) patient reported treatment-related serious adverse events. Hyperglycemia (3 patients, 14.3%), hypertension (2 patients, 9.5%) and hypertriglyceridemia (2 patients, 9.5%) were the most commonly (more than one patient) reported grade 3 or above treatment-related adverse events. No treatment-related adverse events led to treatment discontinuation or treatment-related deaths.

In September 2021, we initiated a Phase III study to evaluate the combination compared with FOLFIRI to treat patients with advanced NEC who have progression of disease or intolerable toxicity after previous first-line chemotherapy. It is a randomized, controlled, open-label, multi-center study where approximately 200 patients are expected to be enrolled. For the study group, all patients will receive study treatment in a 21-day cycle. The primary outcome measure is OS. We are the sponsor and responsible for the study's execution. We and Junshi Biosciences are jointly funding the study.

Clinical Trial with BeiGene's Tislelizumab

In May 2020, we entered into a global clinical collaboration agreement to evaluate the safety, tolerability and efficacy of combining surufatinib with BeiGene's anti-PD-1 antibody, tislelizumab. We de-prioritized and stopped recruitment into an open-label, Phase Ib/II study of surufatinib in combination with tislelizumab in the United States and Europe. The study was to evaluate the safety, tolerability, pharmacokinetics and efficacy in patients with multiple advanced solid tumors.

Surufatinib Exploratory Development

In China, we support an investigator initiated trial, or IIT, program for surufatinib, with about 50 IITs in various solid tumor settings being conducted for both combination and single agent regimens. These trials explore and answer important medical questions in addition to our own company-sponsored clinical trials.

Overview of Sulanda Commercial Launch

Surufatinib capsules, sold under the brand name Sulanda, were approved for marketing in China by the NMPA in December 2020 and June 2021 for the treatment of advanced non-pancreatic NETs and pancreatic NETs, respectively. In 2021, Sulanda was sold as a self-pay drug whereby patients paid for treatment out-of-pocket. We used means-test early access and patient access programs to help patients afford Sulanda. Following negotiations with the China National Healthcare Security Administration, Sulanda was included on China's NRDL at a 52% discount on our main 50mg dosage form, relative to the 2021 self-pay price, for two years starting on January 1, 2022.

During 2022, we introduced Sulanda through a campaign of approximately 4,900 local, regional and national educational events involving approximately 12,000 healthcare professionals. We have also confirmed a total of around 50 investigator-initiated studies in a broad range of exploratory solid tumor indications all of which are expected to gradually expand awareness of Sulanda in China. In 2022, approximately 12,000 new patients were treated with Sulanda, representing approximately 2.5 times the approximately 4,800 new patients in 2021.

4. Sovleplenib (HMPL-523), Syk Inhibitor

Sovleplenib is a novel, selective, oral inhibitor targeting Syk, for the treatment of hematological malignancies and immune diseases. Syk is a component in Fc receptor and B-cell receptor signaling pathway. In 2021, we initiated a Phase III study in China for primary ITP, for which it has received Breakthrough Therapy Designation, and presented data on both primary ITP and hematological malignancies at ASH 2021. We currently retain all rights to sovleplenib worldwide.

Mechanism of Action

Syk is a key kinase upstream to PI3Kδ and BTK within the B-cell signaling pathway and therefore thought to be an important target for modulating B-cell signaling.

Syk, a target for autoimmune diseases

The central role of Syk in signaling processes is not only in cells of immune responses but also in cell types known to be involved in the expression of tissue pathology in autoimmune, inflammatory and allergic diseases. Therefore, interfering with Syk could represent a possible therapeutic approach for treating these disorders. Indeed, several studies have highlighted Syk as a key player in the pathogenesis of a multitude of diseases, including rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis.

Syk, a target for oncology

In hematological cancer, we believe Syk is a high potential target. In hematopoietic cells, Syk is recruited to the intracellular membrane by activated membrane receptors like B-cell receptors or another receptor called Fc and then binds to the intracellular domain of the receptors. Syk is activated after being phosphorylated by certain kinases and then further induces downstream intracellular signals including B-cell linker, PI3Kδ, BTK and Phospholipase C-y2 to regulate B-cell proliferation, growth, differentiation, homing, survival, maturation, and immune responses. Syk not only involves the regulation of lymphatic cells but also signal transduction of non-lymphatic cells such as mast cells, macrophages, and basophils, resulting in different immunological functions such as degranulation to release immune active substances, leading to immunological reaction and disease. Therefore, regulating B-cell signal pathways through Syk is expected to be effective for treating lymphoma.

Syk is upstream of both BTK and PI3Kδ, and we believe it could deliver the same outcome as inhibitors of BTK and PI3Kδ, assuming no unintentional toxicities are derived from Syk inhibition.

Sovleplenib Research Background

The threshold of safety for a Syk inhibitor in chronic disease is extremely high, with no room for material toxicity. The failure of Tavalisse in a global Phase III registration study in rheumatoid arthritis provided important insights for us in the area of toxicity. While Tavalisse clearly showed patient benefit in rheumatoid arthritis, a critical proof-of-concept for Syk modulation, it also caused high levels of hypertension which is widely believed to be due to the high levels of off-target kinase insert domain receptor inhibition. In addition, Tavalisse has also been shown to strongly inhibit the Ret kinase, and in pre-clinical trials it was demonstrated that inhibition of the Ret kinase was associated with developmental and reproductive toxicities.

The requirement for Syk kinase activity in inflammatory responses was first evaluated with Tavalisse, which was co-developed by AstraZeneca/Rigel Pharmaceuticals, Inc. In 2013, AstraZeneca announced results from pivotal Phase III clinical trials that Tavalisse statistically significantly improved ACR20 (a 20% improvement from baseline based on the study criteria) response rates of patients inadequately responding to conventional disease-modifying anti-rheumatic drugs and a single anti-TNFα (a key pro-inflammatory cytokine involved in rheumatoid arthritis pathogenesis) antagonist at 24 weeks, but failed to demonstrate statistical significance in comparison to placebo at 24 weeks. As a result, AstraZeneca decided not to proceed. Rigel Pharmaceuticals subsequently chose to develop Tavalisse for immune thrombocytopenia instead, for which it was approved by the FDA in 2018 and the EMA in 2020.

Tavalisse was also in trials for B-cell lymphoma and T-cell lymphoma. It demonstrated some clinical efficacy in diffused large B-cell lymphoma patients with an ORR of 22%. Entospletinib has features of high potency and good selectivity toward kinases. However, entospletinib shows some inhibition of the CYP3A4, CYP2D6, and CYP1A2 enzymes involved in the metabolism of certain drugs, and therefore their inhibition could increase the risk of drug-to-drug interaction when used in combined therapy. It is no longer in development.

Sovleplenib Pre-clinical Evidence

The safety profile of sovleplenib was evaluated in multiple in vitro and in vivo pre-clinical trials under good laboratory practice guidelines and found to be well tolerated following single dose oral administration. Toxic findings were seen in repeat dose animal safety evaluations in rats and dogs at higher doses and found to be reversible. These findings can be readily monitored in the clinical trials and fully recoverable upon drug withdrawal. The starting dose in humans was suggested to be 5 mg. This dose level is approximately 5% of the human equivalent dose extrapolated from the pre-clinical "no observed adverse event levels," which is below the 10% threshold recommended by FDA guidelines.

Sovleplenib Clinical Trials

The table below shows a summary of the clinical trials for sovleplenib.

Current Clinical Trials of Sovleplenib

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Sovleplenib monotherapy	ESLIM-01≥2L+ Immune thrombocytopenia	China	III	Fully enrolled; Breakthrough Therapy Designation	NCT05029635
Sovleplenib monotherapy	Indolent non-Hodgkin's lymphoma	U.S./ Europe	I/Ib	Ongoing; preliminary data presented at ASH 2021	NCT03779113
Sovleplenib monotherapy	Warm AIHA	China	II/III	Ongoing since 2022; Phase III decision in 2023 pending Phase II results	NCT05535933

ESLIM-01 Phase III study of sovleplenib in patients with immune thrombocytopenia (NCT05029635)

In October 2021, we initiated a randomized, double-blinded, placebo-controlled Phase III trial in China of sovleplenib in approximately 180 adult patients with primary ITP who have received at least one prior line of standard therapy. ITP is an autoimmune disorder that can lead to increased risk of bleeding. The primary endpoint of the study is the durable response rate. In January 2022, the NMPA granted Breakthrough Therapy Designation for this indication. Enrollment was completed in December 2022.

ESLIM-01 is supported by the results of a randomized, double-blind and placebo-controlled Phase Ib study of HMPL-523 in adult patients with primary immune thrombocytopenia were presented at the 63rd American Society for Hematology's (ASH) annual meeting. As of data cut-off date of September 30, 2021, a total of 34 patients were randomized to receive HMPL-523 and 11 patients to placebo. Among 16 patients who were randomized to receive the RP2D of 300mg once daily, 11 patients (68.8%) experienced response as defined by at least one incident of platelet count being $\geq 50\times10^9$/L in the initial 8-week double blinded phase of the study, compared to one out of 11 patients (9.1%) randomized to receive placebo. During the subsequent 16-week open-label phase of the study, one additional patient initially randomized to receive the RP2D experienced a response. Four patients randomized to placebo crossed over to receive treatment at RP2D after the initial 8-week double blinded phase of the study; all four of these patients experienced response. In total, 16 out of 20 patients (80%) experienced response during both phases of the study. Durable response, defined as platelet count being $\geq 50\times10^9$/L in at least 4 out of 6 last scheduled visits, were reported in 8 out of 20 patients (40%) who received RP2D in both phases of the study.

Safety data were presented for all 41 patients who received treatment at all doses, regardless of whether they were initially randomized to receive active treatment or crossed over during the open-label extension phase of the study. The median duration of treatment was 142 days (range: 23-170). No patients discontinued treatment due to treatment-related adverse events, and no cases of treatment-related serious adverse events were reported. There were 30 patients (73%) who experienced treatment-related adverse events, including 3 (7.3%) who experienced grade 3 or above treatment-related adverse events, one of whom received the RP2D. No treatment-related adverse events of grade 3 or above occurred in more than one patient.

Phase I/Ib study of sovleplenib in indolent non-Hodgkin's lymphoma (NCT03779113)

Based on extensive proof-of-concept clinical data in China and Australia, we have initiated a Phase I/Ib study in the United States and Europe. We presented preliminary results from this study at the ASH 2021 annual meeting, which support progressing sovleplenib into the ongoing dose expansion phase of the study to evaluate its safety and efficacy in multiple subtypes of B-cell and T-cell lymphoma at the RP2D of 700mg.

Phase II/III Trial of sovleplenib for warm AIHA (NCT05535933)

In September 2022, we initiated a Phase II/III trial of sovleplenib in adult patients with wAIHA in China. This is a randomized, double-blind, placebo-controlled Phase II/III study to evaluate the efficacy, safety, tolerability, and pharmacokinetics of sovleplenib in the treatment of warm AIHA. AIHA is the result of destruction of red blood cells due to the production of antibodies against red blood cells which bind to antigens on the red blood cell membrane in autoimmune disorders. If the results of the Phase II stage of the study indicate sufficiently satisfactory efficacy and safety, the Phase III stage will be initiated. The China IND was approved in July 2022. The first patient was enrolled in September 2022. The enrollment of Phase II part of the study is expected to be completed in 2023, and lead to a decision on whether to initiate Phase III.

5. Amdizalisib (HMPL-689), PI3Kδ Inhibitor

Amdizalisib is a novel, highly selective oral inhibitor targeting the isoform PI3Kδ, a key component in the B-cell receptor signaling pathway. Amdizalisib's pharmacokinetic properties have been found to be favorable with good oral absorption, moderate tissue distribution and low clearance in pre-clinical studies. We also expect that amdizalisib will have low risk of drug accumulation and drug-drug interactions, supporting feasibility of development in combination with other medicines. We currently retains all rights to amdizalisib worldwide.

Mechanism of Action

Targeting the B-cell signaling pathway is emerging as a potential means to treat both hematological cancer and immunological diseases. Inhibiting different kinases found along the B-cell signaling pathway has proven to have clinical efficacy in hematological cancers, with breakthrough therapies having been recently approved by the FDA.

The high efficacy and successful approvals of Bruton's tyrosine kinase, or BTK, inhibitors and PI3Kδ inhibitors are evidence that modulation of the B-cell signaling pathway is critical for the effective treatment of B-cell malignancies.

Class I phosphatidylinositide-3-kinases, or PI3Ks, are lipid kinases that, through a series of intermediate processes, control the activation of several important signaling proteins including the serine/threonine kinase AKT.

There are multiple sub-families of PI3K kinases, and PI3Kδ is a lipid kinase that, through a series of intermediate processes, controls the activation of several important signaling proteins, including the serine/threonine kinase B, or AKT. In most cells, AKT is a key PI3Kδ affector that regulates cell proliferation, carbohydrate metabolism, cell motility and apoptosis and other cellular processes. Upon an antigen binding to B-cell receptors, PI3Kδ can be activated through the Lyn and Syk signaling cascade.

Aberrant B-cell function has been observed in multiple immunological diseases and B-cell mediated malignancies. Therefore, PI3Kδ is considered to be a promising target for drugs that aim to prevent or treat hematologic cancer, autoimmunity and transplant organ rejection and other related inflammation diseases.

Amdizalisib Pre-clinical Evidence

Compared to other PI3Kδ inhibitors, amdizalisib shows higher potency and selectivity.

Enzyme Selectivity (IC_{50}, in nM) of amdizalisib Versus Competing PI3Kδ Inhibitors; This Shows amdizalisib is Approximately Five-fold More Potent than Zydelig on Whole Blood Level and, unlike Copiktra, does not Inhibit PI3K-γ.

Enzyme IC_{50} (nM)	HMPL-689	Zydelig	Copiktra	Aliqopa
PI3Kδ	0.8 (n = 3)	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 (142x)	104 (52x)	2 (2x)	6.4 (9x)
PI3Kα (fold vs. PI3Kδ)	>1,000 (>1,250x)	866 (433x)	143 (143x)	0.5 (1x)
PI3Kδ human whole blood CD63+	3	14	15	n/a
PI3Kβ (fold vs. PI3Kδ)	87 (109x)	293 (147x)	8 (8x)	3.7 (5x)

Source: Company.

Amdizalisib Clinical Development

The table below shows a summary of the clinical studies for amdizalisib.

Clinical Trials of Amdizalisib

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Amdizalisib monotherapy	Indolent non-Hodgkin's lymphoma PTCL	China	Ib	Ongoing; Expansion data presented at ESMO 2021	NCT03128164
Amdizalisib monotherapy	3L Relapsed/refractory follicular lymphoma	China	II registration-intent	Fully enrolled; Breakthrough Therapy Designation	NCT04849351
Amdizalisib monotherapy	2L Relapsed/refractory marginal zone lymphoma	China	II registration-intent	Ongoing since April 2021	NCT04849351
Amdizalisib monotherapy	Indolent non-Hodgkin's lymphoma	U.S./ Europe	I/Ib	De-prioritized	NCT03786926

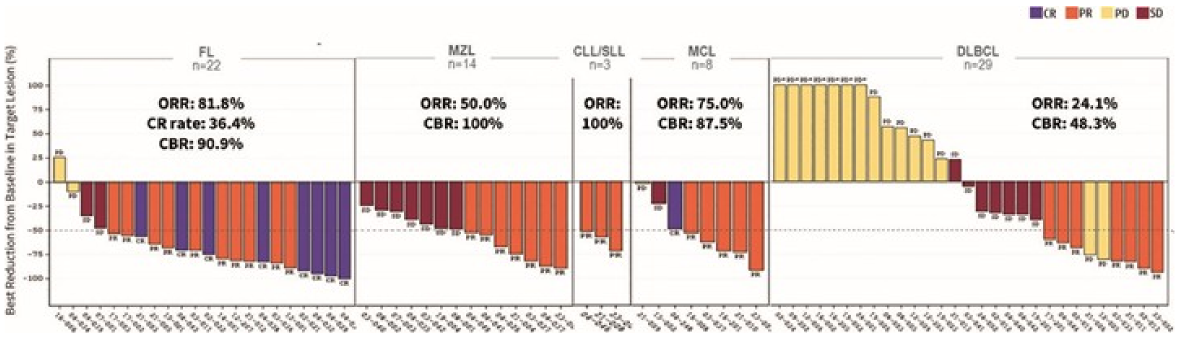
Phase Ib study of amdizalisib in patients with Indolent non-Hodgkin’s lymphoma in China (NCT03128164)

Our Phase I/Ib study of amdizalisib in China has successfully established a Phase II dose and has now expanded into multiple sub-categories of indolent non-Hodgkin’s lymphoma.

In ESMO 2021, we presented results from the Phase Ib study. In the efficacy evaluable population of 76 patients, the median time of follow-up was 5.6 months (95% CI: 5.5-8.3). Objective response rate was 53.9%, completed response rate was 11.8%, and clinical benefit rate was 76.3%. Median duration of response was not reached, and 6-months duration of response rate was 84.5% (95% CI: 62.9-94.1). Median time to response was 1.9 months (95% CI: 1.8-1.9). Amdizalisib showed promising single-agent clinical activity in patients with relapsed/refractory B-cell lymphoma, with high objective response rate and complete response rates noted particularly for follicular lymphoma patients.

In the 22 follicular lymphoma patients with efficacy evaluable, the median time of follow-up was 8.3 months (95% CI: 2.0-11.0). Objective response rate was 81.8%, complete response rate was 36.4% and clinical benefit rate was 90.9%. Median time to response was 1.8 months (95% CI: 1.8-1.9), 1-year duration of response was 59.7%, and progression-free survival rate was 75.8%. 77% of the patients remain on therapy.

Phase Ib Study of Amdizalisib in Chinese Patients with Relapsed/Refractory Lymphoma:
Best response of target lesion (N=76)



Notes: Data cut-off as of June 15, 2021. Target lesion SPD (sum of the product of perpendicular diameters) increased more over 100%. Efficacy evaluable population: received at least one tumor assessment. FL = follicular lymphoma; MZL = marginal zone lymphoma; CLL/SLL = chronic lymphocytic leukemia / small lymphocytic lymphoma; MCL = mantle cell lymphoma; DLBCL = diffuse large B cell lymphoma; n = number of patients; CR = complete response; PR = partial response; PD = progressive disease; SD = stable disease; ORR = objective response rate; CBR = clinical benefit rate (CR + PR + SD)

Source: CaoJN, et al. "A phase Ib study result of HMPL-689, a PI3Kδ inhibitor, in Chinese patients with relapsed/refractory lymphoma." Presented at the 2021 European Society for Medical Oncology (ESMO) Virtual Congress on September 20, 2021. Presentation #833O

Amdizalisib was well tolerated and demonstrated a manageable safety profile. The most frequent treatment-emergent adverse event was neutrophil count decreased (28.9%), and most frequent, non-hematologic, Grade 3 or above treatment-emergent adverse events were pneumonia (13.3%) and rash (5.6%). All liver enzyme elevation was mild to moderate (Grade 1-2). Grade 3 diarrhea was low (2.2%) and there were no colitis cases as of the data cut-off. Treatment discontinuation rate due to adverse events was 5.6%.

Phase II registration-intent study of amdizalisib in patients with relapsed/refractory follicular lymphoma and relapsed/refractory marginal zone lymphoma in China (NCT04849351)

Based on the highly promising preliminary results from the above Phase Ib expansion study, in April 2021, we commenced a registration-intent Phase II trial of amdizalisib in China in patients with relapsed or refractory follicular lymphoma and marginal zone lymphoma, two subtypes of non-Hodgkin's lymphoma. The clinical trial is a multi-center, single-arm, open-label clinical study to evaluate the efficacy and safety of amdizalisib once a day oral monotherapy in approximately 100 patients with relapsed/refractory follicular lymphoma and approximately 80 patients with relapsed/refractory marginal zone lymphoma. Relapsed/refractory is defined when a patient has not achieved response (complete response or partial response) after the latest line of systemic treatment, or has progressive disease or relapse after achieving response. The primary endpoint is ORR, with secondary endpoints including CR rate, PFS, TTR and duration of response. The trial is being conducted in over 35 sites in China, has fully enrolled the follicular lymphoma cohort and is expected to complete enrollment for the marginal zone lymphoma cohort around mid-year.

Phase I/Ib study of amdizalisib in patients with Indolent non-Hodgkin's lymphoma in the United States and Europe (NCT03786926)

In August 2019, we initiated an international Phase I/Ib study of amdizalisib in patients with relapsed or refractory lymphoma. The international clinical study, with multiple sites in the United States and Europe, is a multi-center, open-label, two-stage study, including dose escalation and expansion, investigating the effects of amdizalisib administered orally to patients with relapsed or refractory lymphoma. The primary outcome measures are safety and tolerability. Secondary outcomes include pharmacokinetic measurements and preliminary efficacy such as ORR.

6. Tazemetostat, EZH2 Inhibitor

Tazemetostat is an inhibitor of EZH2 developed by Ipsen that is approved by the U.S. FDA for the treatment of certain epithelioid sarcoma and follicular lymphoma patients. It received accelerated approval from the FDA based on ORR and DoR in January and June 2020 for epithelioid sarcoma and follicular lymphoma, respectively. In August 2021, we entered into a strategic collaboration with Epizyme, a subsidiary of Ipsen, to research, develop, manufacture and commercialize tazemetostat in Greater China, including the mainland, Hong Kong, Macau and Taiwan. We are developing and plan to seek approval for tazemetostat in various hematological and solid tumors, in Greater China. We are participating in Ipsen's SYMPHONY-1 (EZH-302) study, leading it in Greater China. We will generally be responsible for funding all clinical trials of tazemetostat in Greater China, including the portion of global trials conducted there. We are responsible for the research, manufacturing and commercialization of tazemetostat in Greater China.

In May 2022, tazemetostat was approved by the Health Commission and Medical Products Administration of Hainan Province of China to be used in the Hainan Boao Lecheng International Medical Tourism Pilot Zone, under the Clinically Urgently Needed Imported Drugs scheme, for the treatment of certain patients with epithelioid sarcoma and follicular lymphoma consistent with the label as approved by the FDA.

Mechanism of Action

EZH2 is one member of a class of histone methyltransferases ("HMTs"). It catalyzes the methylation of histone H3 at lysine 27 (H3K27) which controls expression of various genes and in turn plays a role in the normal physiology of many cell types. Dysregulation of EZH2 has been seen in a wide range of cancers and is associated with poor clinical prognosis and outcomes. Tazemetostat inhibits EZH2 which allows transcription of genes involved in functions such as cell cycle control and terminal differentiation and thus inhibits cancer cell proliferation.

Tazemetostat Clinical Trials

The table below shows a summary of our clinical trials for tazemetostat.

Clinical Trials of Tazemetostat

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
Tazemetotat monotherapy	Metastatic or locally advanced epithelioid sarcoma; Relapsed/refractory 3L+ follicular lymphoma	Hainan	N/A – Hainan Pilot Zone	Approved; Launched in 2022	N/A
Tazemetostat +lenalidomide + rituximab (R2)	SYMPHONY-1: 2L follicular lymphoma	Global	Ib/III	Ongoing: PhIb data at ASH 2022; China portion of global Phase III trial started H2 2022	NCT04224493
Tazemetotat monotherapy	Relapsed/refractory 3L+ follicular lymphoma	China	II registration-intent (bridging)	Ongoing since July 2022	NCT05467943
Tazemetost at + amdizalisib	Relapsed/refractory lymphoma	China	II	Ongoing since February 2023	NCT05713110

SYMPHONY-1 Phase Ib/III Trial of tazemetostat for follicular lymphoma (NCT04224493)

SYMPHONY-1 is a global, multicenter, randomized, double-blind, active-controlled, 3-stage, biomarker-enriched, Phase Ib/III study of tazemetostat in combination with R^2 (lenalidomide and rituximab) in patients with relapsed or refractory follicular lymphoma after at least one prior line of therapy. Ipsen conducted the Phase Ib portion of the study in 2021, which determined the recommended Phase III dose and also demonstrated potential efficacy in second-line follicular lymphoma. The safety profile of the combination was consistent with the previously reported safety information in the U.S. prescribing information for both tazemetostat and R^2, respectively.

An interim analysis of the Phase Ib portion of the study, based on 44 follicular lymphoma patients as of June 14, 2022, was presented at ASH 2022. The safety profile of the tazemetostat and R^2 combination was consistent with the prescribing information for both tazemetostat and R^2, respectively. Additionally, there was no clear dose response for treatment-emergent adverse events (TEAEs) or dose modifications. Of 41 evaluable patients, ORR was 97.6% with 51.2% complete response rate. Median PFS and DoR were not yet reached with a median follow-up of 11.2 months.

In the Phase III portion of the trial, approximately 500 patients are randomly assigned to receive the recommended Phase III dose of tazemetostat of tazemetostat + R^2 or placebo + R^2. The study will also include a maintenance arm with tazemetostat or placebo following the first year of treatment with tazemetostat + R^2 or placebo + R^2. The first patient was enrolled in May 2022 and the first China patient was enrolled in September 2022.

Phase II bridging study in relapsed/refractory follicular lymphoma (NCT05467943)

In July 2022, we initiated a multicenter, open-label, Phase II study to evaluate the efficacy, safety and pharmacokinetics of tazemetostat for the treatment of patients with relapsed/refractory follicular lymphoma intended to support conditional registration in China. The primary objective is to evaluate the efficacy of tazemetostat in patients with EZH2 mutation (Cohort 1). The secondary objectives are to evaluate the efficacy of tazemetostat in patients with EZH2 wild-type (Cohort 2) and to evaluate the safety and the pharmacokinetics of tazemetostat. Enrollment of cohort 2 is complete and cohort 1 is ongoing and is expected to be completed in 2023.

Phase II combination study in relapsed/refractory follicular lymphoma (NCT05713110.)

This is a multicenter, open-label, Phase II study to evaluate the safety, tolerability and preliminary anti-tumor efficacy of tazemetostat in combination with amdizalisib in patients with R/R lymphoma. The first patient was dosed in February 2023.

7. HMPL-453, FGFR Inhibitor

HMPL-453 is a novel, selective, oral inhibitor targeting FGFR 1/2/3. Aberrant FGFR signaling is associated with tumor growth, promotion of angiogenesis, as well as resistance to anti-tumor therapies. Approximately 10-15% of IHCC patients have tumors harboring FGFR2 fusion. We currently retain all rights to HMPL-453 worldwide.

Mechanism of Action

FGFR belongs to a subfamily of receptor tyrosine kinases. Four different FGFRs (FGFR1-4) and at least 18 ligand FGFs constitute the FGF/FGFR signaling system. Activation of the FGFR pathway through the phosphorylation of various downstream molecules ultimately leads to increased cell proliferation, migration and survival. FGF/FGFR signaling regulates a wide range of basic biological processes, including tissue development, angiogenesis, and tissue regeneration. Given the inherent complexity and critical roles in physiological processes, dysfunction in the FGF/FGFR signaling leads to a number of developmental disorders and is consistently found to be a driving force in cancer. Deregulation of the FGFR can take many forms, including receptor amplification, activating mutations, gene fusions, and receptor isoform switching, and the molecular alterations are found at relatively low frequencies in most tumors. The incidence of FGFR aberrance in various cancer types is listed in the table below.

Common FGFR Alterations in Certain Tumor Types

	Gene amplification	Gene translocation	Gene mutation
FGFR1	Lung squamous (7-15%) H&N squamous (10-17%) Esophageal squamous (9%) Breast (10-15%)	Lung squamous (n/a) Glioblastoma (n/a) Myeloproliferative syndrome (n/a) Breast (n/a)	Gastric (4%) Pilocytic astrocytoma (5-8%)
FGFR2	Gastric (5-10%) Breast (5-10%)	Intra-hepatic biliary tract cancer (14%) Breast (n/a)	Endometrial (12-14%) Lung squamous (5%)
FGFR3	Bladder (3%) Salivary adenoid cystic (n/a) Breast (1%)	Bladder (3-6%) Lung squamous (3%) Glioblastoma (3-7%) Myeloma (15-20%)	Bladder (60-80% NMIBC; 15-20% MIBC) Cervical (5%)

Notes: H&N = head and neck; NMIBC = non-muscle invasive bladder cancer; MIBC = muscle invasive bladder cancer; and n/a = data not available.

Source: M. Touat et al., "Targeting FGFR Signaling in Cancer," Clinical Cancer Research (2015); 21(12); 2684-94.

HMPL-453 Research Background

We noted a growing body of evidence has demonstrated the oncogenic potential of FGFR aberrations in driving tumor growth, promoting angiogenesis, and conferring resistance mechanisms to oncology therapies. Targeting the FGF/FGFR signaling pathway has therefore attracted attention from biopharmaceutical companies and has become an important exploratory target for new anti-tumor target therapies.

The main FGFR on-target toxicities observed to date in these compounds are all mild and manageable, including hyperphosphatemia, nail and mucosal disorder, and reversible retinal pigmented epithelial detachment. However, there are still many challenges in the development of FGFR-directed therapies. Uncertainties include the screening and stratifying of patients who are most likely to benefit from FGFR targeted therapy. Intra-tumor heterogeneity observed in FGFR amplified cancer may compromise the anti-tumor activity. In addition, the low frequency of specific FGFR molecular aberrance in each cancer type may hinder clinical trial enrollment.

HMPL-453 Pre-clinical Evidence

HMPL-453 is a highly selective and potent, small molecule that targets FGFR 1/2/3 with an IC_{50} in the low nanomolar range. Its good selectivity was revealed in the screening against 292 kinases. HMPL-453 exhibited strong anti-tumor activity that correlated with target inhibition in tumor models with abnormal FGFR activation.

HMPL-453 has good pharmacokinetic properties characterized by rapid absorption following oral dosing, good bioavailability, moderate tissue distribution and moderate clearance in all pre-clinical animal species. HMPL-453 was found to have little inhibitory effect on major cytochrome P450 enzymes, indicating low likelihood of drug-to-drug interaction issues.

HMPL-453 Clinical Development

The table below shows a summary of our clinical trials for HMPL-453.

Clinical Trials of HMPL-453

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
HMPL-453 monotherapy	2L Cholangiocarcinoma (IHCC with FGFR fusion)	China	II	Ongoing since 2020; Data submission planned in 2023; Preparing registration enabling study	NCT04353375
HMPL-453 + chemotherapies	Multiple	China	I/II	Ongoing since 2022	NCT05173142
HMPL-453 + Tuoyi (PD-1)	Multiple	China	I/II	Ongoing since 2022	NCT05173142

Phase II HMPL-453 monotherapy in advanced IHCC (NCT04353375)

In September 2020, we initiated a Phase II, single-arm, multi-center, open-label study, evaluating the efficacy, safety and pharmacokinetics of HMPL-453 in patients with advanced IHCC with FGFR2 fusion that had failed at least one line of systemic therapy. IHCC is a cancer that develops within the bile ducts, the second most common primary hepatic malignancy after hepatocellular carcinoma. Approximately 10-15% of IHCC patients have tumors that harbor FGFR2 fusion.

After consultation with the CDE, a monotherapy registration final design has been agreed, and preparations are under way.

Phase Ib/II HMPL-453 in combination with chemotherapies or toripalimab in advanced solid tumors (NCT05173142)

In January 2022, we initiated a Phase Ib/II, multi-center, two-stage, open-label clinical trial of HMPL-453 in combination with chemotherapy or the anti-PD-1 therapy, toripalimab, to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy profile of HMPL-453 combination therapy in patients with specific advanced or metastatic solid tumors. The first stage of the study is a dose escalation phase to determine the dose limiting toxicity (DLT) and recommended Phase II dose of HMPL-453 in combination with chemotherapy (gemcitabine and cisplatin) or toripalimab. The second stage of the study is a dose expansion phase in solid tumor patients with either gastric cancer, intrahepatic cholangiocarcinoma, or urothelial carcinoma, harboring specific FGFR gene alterations. Each solid tumor cohort will be treated with a specific combination of HMPL-453 and a chemotherapy or anti-PD-1 therapy to further evaluate the preliminary efficacy, safety and tolerability at the recommended Phase II dose.

8. HMPL-306, IDH1 and 2 Inhibitor

HMPL-306 is a novel dual-inhibitor of IDH1 and IDH2 enzymes. IDH1 and IDH2 mutations have been implicated as drivers of certain hematological malignancies, gliomas and solid tumors, particularly among acute myeloid leukemia patients. We currently retain all rights to HMPL-306 worldwide.

Mechanism of Action

IDHs are critical metabolic enzymes that help to break down nutrients and generate energy for cells. When mutated, IDH creates a molecule that alters the cell's genetic programming and prevents cells from maturing, 2-hydroxyglutarate ("2-HG"). Reduction in 2-HG levels can be used as a marker of target engagement by an IDH inhibitor. IDH1 or IDH2 mutations are common genetic alterations in various types of blood and solid tumors, including acute myeloid leukemia, with approximately 20% of patients having mutant IDH genes, myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPNs), low-grade glioma and intrahepatic cholangiocarcinoma. Mutant IDH isoform switching, either from cytoplasmic mutant IDH1 to mitochondrial mutant IDH2, or vice versa, is a mechanism of acquired resistance to IDH inhibition in acute myeloid leukemia and cholangiocarcinoma.

Cytoplasmic mutant IDH1 and mitochondrial mutant IDH2 have been known to switch to the other form when targeted by an inhibitor of IDH1 mutant alone or IDH2 mutant alone. By targeting both IDH1 and IDH2 mutations, HMPL-306 could potentially provide therapeutic benefits in cancer patients harboring either IDH mutation and may address acquired resistance to IDH inhibition through isoform switching.

HMPL-306 Clinical Trials

The table below shows a summary of our clinical trials for HMPL-306.

Clinical Trials of HMPL-306

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
HMPL-306 monotherapy	Hematological malignancies	China	I	Ongoing since 2020; RP2D determined	NCT04272957
HMPL-306 monotherapy	Solid tumors including but not limited to gliomas, chondrosarcomas or cholangiocarcinomas	U.S.	I	Ongoing since 2021; nominate RP2D in 2023	NCT04762602
HMPL-306 monotherapy	Hematological malignancies	U.S	I	Ongoing since 2021; nominate RP2D in 2023	NCT04764474

9. HMPL-760, BTK Inhibitor

HMPL-760 is an investigational, non-covalent, third-generation BTK inhibitor. It is a highly potent, selective, and reversible inhibitor with long target engagement against BTK, including wild-type and C481S-mutated BTK. We currently retain all rights to HMPL-760 worldwide.

Mechanism of Action

BTK is a key component of the B-cell receptor signaling pathway and is an important regulator of cell proliferation and cell survival in various lymphomas. The abnormal activation of B-cell receptor signaling is closely related to the development of B-cell type hematological cancers, which represent approximately 85% of all NHL cases. BTK is considered a validated target for drugs that aim to treat certain hematological cancers, however C481S mutation of BTK is a known resistance mechanism for first and second generation BTK inhibitors.

HMPL-760 Clinical Trials

The table below shows a summary of our clinical trials of HMPL-760.

Clinical Trials of HMPL-760

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
HMPL-760 monotherapy	CLL, SLL, other B-NHL	China	I	Ongoing since January 2022	NCT05190068
HMPL-760 monotherapy	CLL, SLL, other NHL	U.S.	I	De-prioritized	NCT05176691

10. HMPL-295, ERK Inhibitor

HMPL-295, a novel ERK inhibitor, is our tenth in-house discovered small molecule oncology drug candidate. ERK is a downstream component of the RAS-RAF-MEK-ERK signaling cascade (MAPK pathway). This is our first of multiple candidates in discovery addressing the MAPK pathway. We currently retain all rights to HMPL-295 worldwide.

Mechanism of Action

RAS-MAPK pathway is dysregulated in human diseases, particularly cancer, in which mutations or nongenetic events hyperactivate the pathway in up to 50% of cancers. Activating mutations in RAS genes occur in more than 30% of cancers. RAS and RAF mutations predict worse clinical prognosis in a wide variety of tumor types, mediate resistance to targeted therapies, and decrease the response to the approved standards of care, namely, targeted therapy and immunotherapy. On the MAPK pathway, KRAS inhibitors are under clinical evaluation, and acquired resistance develops for RAF/MEK targeted therapies. ERK inhibition has the potential to overcome or avoid the intrinsic or acquired resistance from the inhibition of RAS, RAF and MEK upstream mechanisms.

HMPL-295 Clinical Trials

The table below shows a summary of our clinical trial for HMPL-295.

Clinical Trial of HMPL-295

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
HMPL-295 monotherapy	Solid tumors	China	I	Ongoing since 2021	NCT04908046

We initiated our Phase I development in China in July 2021. This is a multi-center and open-label study to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy profile of HMPL-295, and to determine the maximum tolerated dose and RP2D in patients with advanced malignant solid tumors.

11. HMPL-653, CSF-1R Inhibitor

HMPL-653 is an investigational novel, highly selective, and potent CSF-1R inhibitor designed to target CSF-1R driven tumors as a monotherapy or in combination with other drugs. We currently retain all rights to HMPL-653 worldwide.

Mechanism of Action

CSF-1R is usually expressed on the surface of macrophages and can promote growth and differentiation of macrophages. Studies have shown that blocking the CSF-1R signaling pathway could effectively modulate the tumor microenvironment, relieve tumor immunosuppression, and synergize with other anti-cancer therapies such as immune checkpoint inhibitors to achieve tumor inhibition. It has been demonstrated in several clinical studies that CSF-1R inhibitors could treat tenosynovial giant cell tumors and treat a variety of malignancies combined with immuno-oncology or other therapeutic agents. Currently no CSF-1R inhibitor has been approved in China.

HMPL-653 Clinical Trials

The table below shows a summary of our clinical trial of HMPL-653.

Clinical Trial of HMPL-653

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
HMPL-653 monotherapy	Solid tumors & tenosynovial giant cell tumors	China	I	Ongoing since 2022, ~110 patients expected to be enrolled	NCT05190068

We initiated our Phase I development in China in January 2022, and the study is a multi-center, open-label and single-armed study to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy of HMPL-653 in patients with advanced or metastatic solid tumors and tenosynovial giant cell tumors. We expect to enroll around 110 patients in this study.

12. HMPL-A83, IgG4-type humanized anti-CD47 monoclonal antibody

HMPL-A83 is an investigational IgG4-type humanized anti-CD47 monoclonal antibody that exhibits high affinity for CD47. HMPL-A83 blocks CD47 binding to Signal regulatory protein (SIRP) α and disrupts the “do not eat me” signal that cancer cells use to shield themselves from the immune system. We currently retain all rights to HMPL-A83 worldwide.

Mechanism of Action and Preclinical Eridemia

CD47 is a cell surface transmembrane protein that is ubiquitously expressed on virtually all human cells. The overexpression of CD47 is reported in a variety of tumors and is believed to be associated with immune escape from macrophage-mediated phagocytosis. HMPL-A83 is an investigational IgG4-type humanized anti-CD47 monoclonal antibody that exhibits high affinity for CD47. HMPL-A83 blocks CD47 binding to Signal regulatory protein (SIRP) α and disrupts the “do not eat me” signal that cancer cells use to shield themselves from the immune system.

In preclinical studies, HMPL-A83 demonstrated weak affinity for red blood cells and no induction of hemagglutination, implying low risk of anemia. HMPL-A83 also demonstrated a high affinity for CD47 antigen on tumor cells and strong phagocytosis induction of multiple tumor cells. HMPL-A83 has also demonstrated strong anti-tumor activity in multiple animal models.

HMPL-A83 Clinical Trials

The table below shows a summary of our clinical trial of HMPL-A83.

Clinical Trial of HMPL-A83

Treatment	Trial Name, Patient Focus	Sites	Phase	Status/Plan	NCT #
HMPL-A83 monotherapy	Advanced malignant neoplasms	China	I	Ongoing since July 2022	NCT05429008

We initiated our Phase I development in China in July 2022, and the study is a multicenter, open-label study to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy of HMPL-A83 in patients with advanced malignant neoplasms. The primary endpoints are DLT, safety, tolerability, RP2D and MTD. The secondary endpoints include pharmacokinetics, pharmacodynamics, immunogenicity and preliminary efficacy profile. We expect to enroll around 100 patients in this study.

13. IMG-007 and IMG-004, Immunology Collaboration with Inmagene

In January 2021, we entered into a strategic partnership with Inmagene, a clinical development stage company with a focus on immunological diseases, to further develop four novel preclinical drug candidates we discovered for the potential treatment of multiple immunological diseases. Under the terms of the agreement, we granted Inmagene exclusive options to such drug candidates solely for the treatment of immunological diseases. Funded by Inmagene, we work together to move the drug candidates towards IND. If successful, Inmagene will then advance the drug candidates through global clinical development. INDs for the first two compounds were submitted in 2022.

Treatment	Name, Line, Patient Focus	Sites	Phase	Status/Plan	NCT #
IMG-007 (OX40 monoclonal antibody)	Healthy volunteers; adults with moderate to severe atopic dermatitis	Global	I	Ongoing since 2022	NCT05353972
IMG-004 (BTK inhibitor)	Healthy volunteers	Global	I	Ongoing since 2022	NCT05349097

IMG-007 in atopic dermatitis – This is a novel antagonistic monoclonal antibody targeting the OX40 receptor. OX40 is a costimulatory receptor member of the tumor necrosis factor receptor (TNFR) superfamily expressed predominantly on activated T cells. The Phase I study in healthy volunteers was initiated in July 2022 in Australia.

IMG-004 in immunological diseases – This is a non-covalent, reversible small molecule inhibitor targeting BTK. Designed specifically for inflammatory and autoimmune diseases that usually require long-term treatment, IMG-004 is potent, highly selective and brain permeable. The Phase I study in healthy volunteers in the United States was initiated in August 2022.

Our Research and Development Approach

Our core research and development philosophy is to take a holistic approach to the treatment of cancer and immunological diseases, through multiple modalities and mechanisms, including targeted therapies, immunotherapies and other pathways. A primary objective of our research efforts has been to develop next generation drug candidates with:

- unique selectivity to limit target-based toxicity;
- high potency to optimize the dose selection with the objective to lower the required dose and thereby limit compound-based toxicity;
- chemical structures deliberately engineered to improve drug exposure in the targeted tissue; and
- ability to be combined with other therapeutic agents, including targeted therapies, immunotherapies and chemotherapies.

We have built a drug discovery engine, with which we strive to create differentiated novel oncology and immunology treatments with global potential. These include furthering both small molecule and biologic therapies which address aberrant genetic drivers and cancer cell metabolism; modulate tumor immune microenvironment; and target immune cell checkpoints. We design drug candidates with profiles that enable them to be used in innovative combinations with other therapies, such as chemotherapy, immunotherapy and other targeted therapy in order to attack disease simultaneously through multiple modalities and pathways. We believe that this approach can significantly improve treatment outcomes for patients.

We believe our ability to successfully develop innovative drug candidates through our Oncology/Immunology operations will be the primary factor affecting our long-term competitiveness, as well as our future growth and development. Creating high quality global first-in-class or best-in-class drug candidates requires investment of resources over a prolonged period of time, and a core part of our strategy is to continue making sustained investments in this area. As a result of this commitment, our pipeline of drug candidates has been steadily advancing and expanding, with over a dozen drug candidates put into clinical development. See "– Our Clinical Pipeline" for more details.

Beyond these clinical candidates, we continue to conduct research into discovering new types of drug candidates, including among others, small molecules addressing cancer-related apoptosis, cell signaling, epigenetics and protein translation; biologic drug candidates including bispecific antibodies; and novel technologies including antibody-drug conjugates and heterobifunctional small molecules.

Our Collaborations

Collaborations and joint ventures with corporate partners have provided us with significant funding and access to our partners' scientific, development, regulatory and commercial capabilities. Our current oncology collaborations focus on savolitinib (collaboration with AstraZeneca) and fruquintinib (collaboration with Eli Lilly). When we entered into these collaborations, we had already conducted the discovery research and early clinical development of each drug candidate and, following our agreements, continued to conduct the clinical development and manage the engagement with regulatory authorities in China up to and including filing the NDAs with the NMPA. Our collaboration partners fund a significant portion of our research and development costs for drug candidates developed in collaboration with them. In addition, we may receive upfront payments upon our entry into these collaboration arrangements and upon the achievement of certain development milestones for the relevant drug candidate. We have received upfront payments, equity contributions and milestone payments totaling approximately $198.5 million mainly from our collaborations with AstraZeneca and Eli Lilly as of December 31, 2022. In return, our collaboration partners are entitled to a significant proportion of any future revenue from our drug candidates developed in collaboration with them, as well as a degree of influence over the clinical development process for such drug candidates. In addition, we have entered into other clinical collaborations for combination studies of fruquintinib and surufatinib with drug candidates belonging to BeiGene, Innovent and/or Junshi. We also have an immunology collaboration with Inmagene with respect to four novel pre-clinical drug candidates discovered by us and an in-licensing collaboration with Epizyme with respect to tazemetostat.

AstraZeneca

In 2008, our in-house teams started research on MET inhibitors, subsequently discovering our drug candidate, savolitinib, and conducting its pre-clinical development in-house. In 2011, we submitted applications for clinical development and initiated Phase I clinical trials. In December 2011, we entered into an agreement with AstraZeneca under which we granted to AstraZeneca co-exclusive, worldwide rights to develop, and exclusive worldwide rights to manufacture and commercialize savolitinib for all diagnostic, prophylactic and therapeutic uses. In August 2016, December 2020 and November 2021, we and AstraZeneca amended the terms of the agreement. We refer to this agreement, including the amendments thereto, as the AstraZeneca Agreement.

AstraZeneca paid $20.0 million upon execution of the AstraZeneca Agreement and agreed to pay royalties and additional amounts upon the achievement of development and sales milestones. Under the original terms of the AstraZeneca Agreement, we and AstraZeneca agreed to share the development costs for savolitinib in China, with AstraZeneca being responsible for the development costs for savolitinib in the rest of the world. With respect to certain clinical trials, we subsequently agreed with AstraZeneca on sharing development costs. As of December 31, 2022, we had received $64.9 million in milestone payments in addition to approximately $71.6 million in reimbursements for certain development costs. We may potentially receive future clinical development and first sales milestones payments for clinical development and initial sales of savolitinib, plus significant further milestone payments based on sales. Subject to approval of savolitinib in treating PRCC, under the amended AstraZeneca Agreement, AstraZeneca is obligated to pay us increased tiered royalties from 14% to 18% annually on all sales made of any product outside of China, which represents a five percentage point increase over the original terms, subject to a potential downward adjustment on such point increase based on the amount of any contribution by AstraZeneca to the Phase III development in patients with such indication. After total aggregate additional royalties have reached five times our contribution to the Phase III development in patients with such indication, this royalty will step down over a two-year period, to an ongoing royalty rate of 10.5% to 14.5%. AstraZeneca is also obligated to pay us a fixed royalty of 30% on all sales made of any product in China.

Development and collaboration under this agreement are overseen by a joint steering committee that is comprised of three of our senior representatives as well as three senior representatives from AstraZeneca. AstraZeneca is responsible for the development of savolitinib and all regulatory matters related to this agreement in all countries and territories other than China, and we are responsible for the development of savolitinib and all regulatory matters related to this agreement in China. Since entering the AstraZeneca Agreement, we have continued to lead the development of savolitinib in China.

Subject to earlier termination, the AstraZeneca Agreement will continue in full force and effect on a country-by-country basis as long as any collaboration product is being developed or commercialized. The AstraZeneca Agreement is terminable by either party upon a breach that is uncured, upon the occurrence of bankruptcy or insolvency of either party, or by mutual agreement of the parties. The AstraZeneca Agreement may also be terminated by AstraZeneca for convenience with 180 days' prior written notice. Termination for cause by us or AstraZeneca or for convenience by AstraZeneca will have the effect of, among other things, terminating the applicable licenses granted by us. Termination for convenience by AstraZeneca will have the effect of obligating AstraZeneca to grant to us all of its rights to regulatory approvals and other rights necessary to commercialize savolitinib. Termination by AstraZeneca for convenience will not have the effect of terminating any license granted by AstraZeneca to us.

Eli Lilly

In 2007, our in-house research into VEGFR inhibitors led to the discovery of our drug candidate, fruquintinib. We conducted pre-clinical development in-house and initiated a Phase I clinical trial in 2010. In October 2013, we entered into an agreement with Eli Lilly whereby we granted Eli Lilly an exclusive license to develop, manufacture and commercialize fruquintinib for all uses in China and Hong Kong. In December 2018, following the commercial launch of fruquintinib in China, we and Eli Lilly amended the terms of the agreement and further amended the terms of the agreement in July 2020. We refer to this agreement, including the amendments thereto, as the Eli Lilly Agreement.

Subsequent to the entering of the Eli Lilly Agreement, we continued to lead the development of fruquintinib, including all clinical trial development. Eli Lilly reimbursed us for a majority of the development costs and provided input over the course of the development of fruquintinib. Development, collaboration and manufacture of the products under this agreement are overseen by a joint steering committee comprised of equal numbers of representatives from each party.

Eli Lilly paid a $6.5 million upfront fee following the execution of the Eli Lilly Agreement in 2013, and agreed to pay royalties and additional amounts upon the achievement of development and regulatory approval milestones. As of December 31, 2022, Eli Lilly had paid us $37.2 million in milestone payments in addition to approximately $65.7 million in reimbursements for certain development costs.

We could potentially receive future milestone payments for the achievement of development and regulatory approval milestones in China. Additionally, Eli Lilly is obligated to pay us tiered royalties from 15% to 20% annually on sales made of fruquintinib in China and Hong Kong, the rate to be determined based upon the dollar amount of sales made for all products in that year. Under the terms of our 2018 amendment, upon the first commercial launch of fruquintinib in China in a new life cycle indication, these tiered royalties increased to 15% to 29%. Under the terms of our 2020 amendment, we and Eli Lilly share gross profits linked to sales target performance. Subject to meeting pre-agreed sales targets, Eli Lilly will pay us an estimated total of 70% to 80% of Elunate in-market sales in the form of royalties, manufacturing costs and service payments.

Under the terms of our 2018 amendment, we are entitled to determine and conduct future life cycle indication development of fruquintinib in China beyond the three initial indications specified in the original Eli Lilly Agreement. After the 2018 amendment, we assumed responsibility for all development activities and costs for fruquintinib in China in new life cycle indications, and we have the liberty to collaborate with third-parties to explore combination therapies of fruquintinib with various immunotherapy agents. Under the terms of our 2020 amendment, we took over development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in China.

We are responsible in consultation with Eli Lilly for the supply of, and have the right to supply, all clinical and commercial supplies for fruquintinib pursuant to an agreed strategy for manufacturing. For the term of the Eli Lilly Agreement, such supplies will be provided by us at a transfer price that accounts for our cost of goods sold.

The Eli Lilly Agreement is terminable by either party for breach that is uncured. The Eli Lilly Agreement is also terminable by Eli Lilly for convenience with 120 days' prior written notice or if there is a major unexpected safety issue with respect to a product. Termination by either us or Eli Lilly for any reason will have the effect of, among other things, terminating the applicable licenses granted by us, and will obligate Eli Lilly to transfer to us all regulatory materials necessary for us to continue development efforts for fruquintinib.

BeiGene

In May 2020, we entered into a clinical collaboration agreement with BeiGene to evaluate the safety, tolerability and efficacy of combining surufatinib and fruquintinib with BeiGene's anti-PD-1 antibody tislelizumab, for the treatment of various solid tumor cancers, in the United States, Europe, China and Australia. Under the terms of the agreement, we and BeiGene each plan to explore development of the combination of surufatinib with tislelizumab or fruquintinib with tislelizumab in different indications and regions. We have agreed to provide mutual drug supply and other support.

Inmagene

In January 2021, we and Inmagene entered into a strategic partnership to further develop four novel pre-clinical drug candidates (HMPL-A28, HMPL-727, HMPL-662 and HMPL-958) discovered by us for the potential treatment of multiple immunological diseases. We will work together to move the drug candidates towards IND submission. If successful, Inmagene will then move the drug candidates through global clinical development.

Under the terms of the agreement, we have granted Inmagene exclusive options to four drug candidates solely for the treatment of immunological diseases. If Inmagene exercises an option, it will have the right to further develop, manufacture and commercialize that specific drug candidate worldwide, while we retain first right to co-commercialization in China. For each of the drug candidates, we will be entitled to development milestones of up to $95 million and up to $135 million in commercial milestones, as well as up to double-digit royalties upon commercialization.

Epizyme (A Subsidiary of Ipsen Pharma SAS)

In August 2021, we entered into a licensing agreement with Epizyme Inc. (a subsidiary of Ipsen Pharma SAS) pursuant to which we obtained a co-exclusive license to develop, an exclusive license to commercialize and a co-exclusive license to manufacture tazemetostat in China, Hong Kong, Taiwan and Macau for all therapeutic and palliative uses in epithelioid sarcoma, follicular lymphoma (second line and third line), diffuse large b-cell lymphoma and any other indications that are approved according to the terms of the licensing agreement.

To date, we have paid Epizyme a $25.0 million upfront payment and an aggregate of $5.0 million milestone payments. We may be required to pay an additional aggregate amount of up to $105 million in development and regulatory milestone payments and up to an additional $175 million in sales milestone payments. Epizyme is also eligible to receive, across up to eight potential indications, certain tiered royalties (from mid-teen to low-twenties-percentage) based on annual net sales of tazemetostat in the licensed territory.

We have the right to manufacture the licensed product for development and commercialization in the licensed territory and are generally responsible for funding all clinical trials of tazemetostat, including the portion of global trials conducted in the licensed territory. The agreement with Epizyme will remain in effect until, on a licensed product-by-licensed product basis, the expiration of the royalty term for each licensed product in the licensed territory. We have the right to terminate the agreement for convenience at any time, subject to a certain notice period. Either party has the right to terminate the agreement if the other party or its affiliates challenge its patents. In addition, either party may terminate the agreement with written notice for the other party's material breach, subject to a certain cure period, or for the other party's bankruptcy or insolvency.

Takeda

On January 23, 2023, we entered into a license agreement with a subsidiary of Takeda to further the global development, commercialization and manufacture of fruquintinib outside of mainland China, Hong Kong and Macau, where it is marketed by us in partnership with Eli Lilly. We may receive up to $1.13 billion including $400 million upfront on closing as well as potential regulatory, development and commercial sales milestone payments, plus royalties on net sales. This deal is subject to customary closing conditions, including the completion of antitrust regulatory reviews. Following these clearances, Takeda will become solely responsible for the development and commercialization of fruquintinib in all included territories worldwide excluding mainland China, Hong Kong and Macau.

Other Collaborations

In October and November 2018, we entered into multiple collaborations to evaluate combinations of fruquintinib and surufatinib. These include a global collaboration with Innovent to evaluate the combination of fruquintinib with Tyvyt and a global collaboration with Junshi to evaluate the combination of surufatinib with Tuoyi. In September 2019, we expanded our global collaboration agreement with Innovent to evaluate the safety and efficacy of Tyvyt in combination with surufatinib.

Other Ventures

Other Ventures is our large-scale, profitable drug marketing and distribution platform covering about 290 cities and towns in China with over 2,900 manufacturing and commercial personnel as of December 31, 2022. Built over the past 20 years, it has been focused on the sale of prescription drugs products and consumer health products conducted through the following entities:

Shanghai Hutchison Pharmaceuticals

Shanghai Hutchison Pharmaceuticals, our non-consolidated joint venture, primarily engages in the manufacture and sale of prescription drug products originally contributed by our joint venture partner, as well as third-party prescription drugs with a focus on cardiovascular medicine. Shanghai Hutchison Pharmaceuticals' proprietary products are sold under the "Shang Yao" brand, literally meaning "Shanghai pharmaceuticals," a trademark that has been used for over 50 years in the pharmaceutical retail market, primarily in Shanghai and Eastern China. The trademark is owned by the joint venture and in January 2023, the Shanghai government recognized and awarded the brand as a Shanghai heritage brand. In early 2019, Shanghai Hutchison Pharmaceuticals was awarded the 2018 State Scientific and Technological Progress Award – Second Prize, which was presented by President Xi Jinping, Premier Li Keqiang and other state leaders of the PRC at the National Science and Technology Awards Ceremony. This award was one of only two such awards given that year to studies in the botanical drug industry.

Its key product is She Xiang Bao Xin pills, a vasodilator for the long-term treatment of coronary artery and heart disease and for rapid control and prevention of acute angina pectoris, a form of chest pain. There are over one million deaths due to coronary artery disease per year in China. She Xiang Bao Xin pill is the third largest botanical prescription drug in this indication in China, with market share in 2022 of 21.0% (2021 of 19.6%) nationally and 47.9% (2021: 43.6%) in Shanghai. She Xiang Bao Xin pills' sales represented 92.2% of all Shanghai Hutchison Pharmaceuticals sales in 2022.

She Xiang Bao Xin pills were first approved in 1983 and subsequently enjoyed 33 proprietary commercial protections under the prevailing regulatory system in China. In 2005, Shanghai Hutchison Pharmaceuticals was able to attain "Confidential State Secret Technology" status protection, as certified by China's Ministry of Science and Technology and State Secrecy Bureau, which extended proprietary protection in China until late 2016. The Science and Technology Commission of Shanghai Municipality has subsequently extended such protection. Shanghai Hutchison Pharmaceuticals holds an invention patent in China covering its formulation, which extends proprietary protection through 2029. She Xiang Bao Xin pill is one of less than two dozen proprietary prescription drugs represented on China's National Essential Medicines List, which means that all Chinese state-owned health care institutions are required to carry it. She Xiang Bao Xin pill is fully reimbursed in all of China.

Shanghai Hutchison Pharmaceuticals manufactures its products at its 78,000 square meter production facility located in Feng Pu district outside the center of Shanghai. Shanghai Hutchison Pharmaceuticals holds 74 drug product manufacturing licenses, of which 17 are included in the National Essential Medicines List, and three are in active production. The factory is operated by over 550 manufacturing staff.

As of December 31, 2022, Shanghai Hutchison Pharmaceuticals had a commercial team of about 2,300 medical sales representatives allowing for the promotion and scientific detailing of our products not just in hospitals in provincial capitals and medium-sized cities, but also in the majority of county-level hospitals in China. Shanghai Hutchison Pharmaceuticals, through its GSP-certified subsidiary, sells its products and its third-party licensed prescription drugs directly to distributors who on-sell such products to hospitals and clinics, pharmacies and other retail outlets in their respective areas, as well as to other local distributors. As of December 31, 2022, Shanghai Hutchison Pharmaceuticals engaged a group of approximately 530 primary distributors to cover China. These primary distributors in turn used over 2,300 secondary distributors to work directly with hospitals, on a local level, to manage logistics. Shanghai Hutchison Pharmaceuticals' own prescription drugs sales representatives promote its products to doctors and purchasing managers in hospitals, clinics and pharmacies as part of its marketing efforts.

Hutchison Sinopharm

Hutchison Sinopharm is our consolidated joint venture with Sinopharm. Based in Shanghai, Hutchison Sinopharm focuses on providing logistics services to, and distributing and marketing prescription drugs in China. As of December 31, 2022, Hutchison Sinopharm had a dedicated team of over 40 commercial staff that focus on marketing over 900 third-party prescription drug and other products directly to about 730 public and private hospitals in the Shanghai region and through a network of approximately 55 distributors to cover all other provinces in China.

Starting in 2015, Hutchison Sinopharm had been the exclusive marketing agent for Seroquel tablets in China. In June 2018, AstraZeneca sold and licensed its rights to Seroquel to Luye Pharma Group, Ltd., including its rights in China. The terms of our agreement with AstraZeneca were assigned to Luye Pharma Hong Kong Ltd., or Luye Pharma HK. In May 2019, we received a notice from Luye Pharma HK purporting to terminate our agreement. We believe that Luye Pharma HK had no basis for termination and commenced confidential legal proceedings to seek damages. In December 2021, the Hong Kong International Arbitration Centre made a final award in favor of Hutchison Sinopharm against Luye Pharma Hong Kong in the amount of RMB253.2 million plus costs we incurred in the legal proceedings and interest. An application was made by Luye on December 14, 2021 to set aside the final award which was heard by the High Court in Hong Kong on June 28, 2022 and dismissed by the judge on July 26, 2022. Luye have further applied and obtained leave to appeal the setting aside application to the Court of Appeal in Hong Kong and a hearing in the Court of Appeal has been set for June 6, 2023. We did not have any revenue from the distribution of Seroquel for the years ended December 31, 2020, 2021 and 2022.

In 2019, we began building an in-house oncology commercial sales and marketing team at Hutchison Sinopharm to support the launch of certain of our innovative oncology drugs. By December 31, 2022, this team had grown to over 870 commercial sales and marketing staff in mainland China and Hong Kong.

In 2021, a substantial portion of Hutchison Sinopharm's sales were made directly to hospitals and clinics, with the remaining sales being made through distributors. As of December 31, 2022, Hutchison Sinopharm had over 860 customers of which approximately 13% were distributors, and the revenue generated from these distributors accounted for approximately 25% of the revenue of Hutchison Sinopharm for the year ended December 31, 2022.

Hutchison Hain Organic

Hutchison Hain Organic is a consolidated joint venture with Hain Celestial, a Nasdaq-listed, natural and organic food and personal care products company. Hutchison Hain Organic distributes a broad range of over 500 imported organic and natural products. Pursuant to its joint venture agreement, Hutchison Hain Organic has rights to manufacture, market and distribute Hain Celestial's products within nine Asian territories. We believe the key strategic product for Hutchison Hain Organic is Earth's Best organic baby products, a leading brand in the United States. Hutchison Hain Organic's other products are distributed to hypermarkets, specialty stores and other retail outlets in Hong Kong, China and across seven other territories in Asia mainly through third-party local distributors, including retail chains owned by affiliates of CK Hutchison.

Hutchison Healthcare

Hutchison Healthcare is our wholly owned subsidiary and is primarily engaged in the manufacture and sale of health supplements. Hutchison Healthcare's major product is Zhi Ling Tong DHA capsules, a health supplement made from algae DHA oil for the promotion of brain and retinal development in babies and young children, which is distributed through Hutchison Sinopharm up till the end of September and from October 1, 2022 onwards, through our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals.

The majority of Hutchison Healthcare's products are contract manufactured at a dedicated and certified manufacturing facility operated by a third party.

HUTCHMED Science Nutrition

HUTCHMED Science Nutrition is our wholly owned subsidiary that is primarily engaged in the distribution of third-party consumer products in Asia.

Competition

Oncology/Immunology Competition

The biotechnology and pharmaceutical industries are highly competitive. While we believe that our highly selective drug candidates, experienced development team and chemistry-focused scientific approach provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies. Any drug candidates that we successfully develop and commercialize will compete with existing drugs and/or new drugs that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address inhibition of key biological pathways in cancer and immunological diseases. There are other companies working to develop kinase inhibitors and monoclonal antibodies as targeted therapies for cancer and immunological diseases. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our drug candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our drug candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

Below is a summary of existing therapies and therapies currently under development that may become available in the future which may compete with each of our clinical-stage drug candidates.

Savolitinib

Savolitinib is the only selective MET inhibitor currently approved in China, while two selective MET inhibitors are on the market in the US and Japan: Tepmetko (tepotinib) and Tabrecta (capmatinib) are approved for MET exon 14 skipping NSCLC with additional programs underway focused on lung cancer. Tepmetko (tepotinib)'s NDA for MET exon 14 skipping NSCLC is currently being reviewed by NMPA. Market Authorization Applications for Tabrecta and Tepmetko were approved in 2022 by the European Medicines Agency (EMA) for use in the treatment of MET exon 14 skipping NSCLC. Other selective MET inhibitors in development include telisotuzumab vedotin (in Phase II for advanced solid tumors, including NSCLC), elzovantinib (TPX-0022, in Phase I/II development for advanced solid tumors), REGN-5093 and REGN5093-M114 (in Phase I for NSCLC), glumetinib (NDA for MET exon 14 skipping NSCLC is currently being reviewed by NMPA) and bozitinib (NDA for MET exon 14 skipping NSCLC is currently being reviewed by NMPA). Sym-015 is a bi-specific antibody that binds to non-overlapping epitopes on the extracellular domain of the Met receptor tyrosine kinase (in Phase IIa development).

Approved compounds that inhibit MET as well as other kinases include Xalkori (crizotinib) (ALK, ROS1 and MET inhibitor marketed for NSCLC) and Cabometyx (cabozantinib) (VEGFR/MET/Ret inhibitor approved for RCC and liver cancer as well as in development for genitourinary cancers). Amivantamab (JNJ-61186372) (EGFR/MET bi-specific antibody) is approved for NSCLC harboring EGFR exon 20 insertion mutation and in late-stage development for EGFRm+ NSCLC. MCLA-129 (NCT03132155) is a EGFR/MET bispecific currently in early stage development.

Fruquintinib

Approved VEGF inhibitors on the market for the treatment of CRC include Avastin (anti-VEGF monoclonal antibody), Cyramza (anti-VEGFR2 monoclonal antibody), Stivarga (VEGFR/TIE2 inhibitor) and Zaltrap (ziv-aflibercept) (VEGF inhibitor). Cyramza (ramucirumab) was approved for the treatment of second-line gastric cancer in China in 2022. TAS-102 (trifluridine/tipiracil hydrochloride) was approved for mCRC in China in 2019. Avastin is approved for NSCLC and nintedanib is approved for the treatment of lung disease associated with fibrosis (under the name Ofev) as well asadeno-NSCLC in Europe (under the name Vargatef). Other VEGFR inhibitors being developed for the treatment of NSCLC include Cabometyx, Lenvima (lenvatinib), lucitanib and Caprelsa. VEGFR inhibitors being developed for the treatment of gastric cancer include dovitinib, telatinib and Stivarga. In China, Aitan (apatinib) has been approved for the treatment of third-line gastric cancer and Focus-V (anlotinib) has been approved for the treatment of third-line NSCLC.

Surufatinib

Sutent (VEGFR inhibitor) and Afinitor (mTOR inhibitor) have been approved for the treatment of pancreatic NETs. Somatuline Depot (Lanreotide) is a growth hormone release inhibitor that has been approved for the treatment of gastroenteropancreatic NETs. Sandostatin (octreotide) is a growth hormone and insulin-like growth factor-1 inhibitor that has also been approved for NETs. Lutathera (Lu-dotatate), a somatostatin receptor targeting radiotherapy, has been approved by the FDA for the treatment of somatostatin receptor positive gastroenteropancreatic NETs. Furthermore, small molecules, monoclonal antibodies and radiotherapies are being developed for the treatment of NETs. Compounds undergoing development for NETs include Inlyta (axitinib, tyrosine kinase inhibitor), and Vargatef (nintedanib, a tyrosine kinase inhibitor). Cometriq (an additional brand name for cabozantinib) has been marketed for thyroid cancer and is being studied for NETs. In addition, Avastin is an anti-VEGF monoclonal antibody being studied for NETs.

Sovleplenib and Amdizalisib

There has been extensive research on oral small-molecule Syk inhibitors due to the major unmet medical need in inflammation and oncology. However, many Syk inhibitors have failed in the development stage due to their off-target toxicity as a result of lower kinase selectivity and possibly poor pharmacokinetic properties. The only small molecule drug candidate targeting Syk specifically has been approved to date is Tavalisse for the treatment of chronic immune thrombocytopenia. Lanraplenib (GS-9876) is a Syk inhibitor that has been studied for autoimmune diseases, but not currently in active development for autoimmune diseases. Syk inhibitors currently in clinical studies for hematological cancers include lanraplenib and cerdulatinib (lymphoma).

Currently there are three PI3K inhibitors approved and on the market outside of China. Aliqopa (copanlisib, pan-PI3K inhibitor) was approved for relapsed follicular lymphoma as a monotherapy and is being studied in combination with rituximab as well as rituximab and chemotherapy in NHL. Zydelig (idelalisib) is approved for the treatment of chronic lymphocytic leukemia, globally. Copiktra (duvelisib, PI3K-δ/γ dual inhibitor) is approved for CLL/SLL. In China, during 2022, Copiktra and linperlisib (YY-20394) were approved for 3L+ follicular lymphoma. In January 2022, Incyte announced that it is withdrawing its NDA for parsaclisib due to the investment required to complete a post marketing confirmatory study within the timeframe required by the FDA. Parsaclisib's NDA for third-line follicular lymphoma is currently being reviewed by NMPA. In addition, several drug candidates that inhibit PI3Kδ are in clinical development for hematological cancers, including zandelisib (ME-401 discontinued outside of Japan) and ACP 319.

Tazemetostat

The most common treatments for follicular lymphoma are chemotherapies, usually combined with the monoclonal antibody Rituxan, or Gazyva, which is an antibody that acts against the same target as Rituxan, CD20. While Rituxan and a number of other widely used anti-cancer agents are labeled broadly for follicular lymphoma, no therapies are approved specifically for the treatment of tumors associated with EZH2 activating mutations. There are a number of companies currently evaluating investigational agents in the relapsed and refractory follicular lymphoma patient setting.

In the relapsed and refractory follicular lymphoma patient setting, both current and near-term competition exists. Current competition includes CD20 combinations along with multiple PI3K inhibitors. Near term competition includes companies currently evaluating investigational agents with varying mechanisms of action.

Other than tazemetostat, there are no therapies which have been approved specifically for the treatment of epithelioid sarcoma. Epithelioid sarcoma, an INI1-negative tumor, is typically treated with surgical resection when it presents as localized disease. When epithelioid sarcoma recurs or metastasizes, it may be treated with systemic chemotherapy or investigational agents because, other than tazemetostat, there are no approved systemic therapies specifically indicated for this disease. To the best of our knowledge there are no competitive products in development specifically for epithelioid sarcoma. However, we are aware of several clinical trials run by competitors that recruit patients with soft tissue sarcoma, which is inclusive of epithelioid sarcoma.

HMPL-453

To date, Balversa, Pemazyre and Truseltiq are the only approved therapies that specifically target the FGFR signaling pathway. Late-stage studies are underway for futibatinib and derazantinib. Additionally, a FGFR specific monoclonal antibody, bemarituzumab, is in Phase III development for gastric cancer and gastroesophageal junction (GEJ) adenocarcinoma. Several small molecule FGFR TKI are in clinical trials for solid tumors, including LOXO-435, AZD4547, rogaratinib, fisogatinib (BLU-554), famitinib, Debio 1347, E7090, ICP-192, ICP-105, ASP5878, FGF401, RLY-4008 and HH185.

HMPL-306

Tilbsovo (ivosidenib) and Rezlidnia (olutasidenib) are approved therapies that specifically inhibits IDH1 while Idhifa (enasidenib) is an approved therapy that specifically inhibits IDH2. To date, there are no approved therapies that inhibit both IDH1 and IDH2, which could be advantageous in deferring resistance to therapy. A pan-IDH inhibitor, vorasidenib, is currently in late stage development for glioma. An IDH 1/2 inhibitor, LY3410738, is in Phase 1 development for both hematological malignancies and solid tumors. Other IDH1 inhibitors in development include BAY1436032 and DS-1001b.

HMPL-760

Approved first and second generation BTK inhibitors include Imbruvica, Calquence, Tirabrutinib, Brukinsa and orelabrutinib. A third generation BTK inhibitor pirtobruntinib was approved for 3L+ in mantle cell lymphoma in January 2023. Nemtabrutinib, orelabrutinib, TG-1701 and JNJ-64264681 are in development for cancer. A number of other BTK inhibitors, such as evobrutinib, remibrutinib, tolebrutinib, rilzabrutinib, SAR444727 and fenebrutinib, are in development for immunological diseases.

HMPL-295

To date, no ERK inhibitor drug has been approved. A number of ERK inhibitors, including BVD-523, LY3214996 and LLT462, among others are being developed in clinical settings as a single agent and/or in combination with various therapeutical agents.

HMPL-653

Turalio is the only FDA approved CSF-1R inhibitor drug and currently there is no CSF-1R inhibitors approved in China. CSF-1R inhibitors in development globally include axatilimab, BLZ945, vimseltinib, AMB-05X, NMS-03592088, ARRY-382, JNJ-40346527, emactuzumab, AMG820 and IMC-CS4.

HMPL-A83

To date, no CD47 antibody drug has been approved. A number of antibodies, including magrolimab, evorpacept, lemzoparlimab, HX009, PF-07901801, AO-176, DSP107, and IBI188, among others are being developed in clinical settings as a single agent and/or in combination with various therapeutical agents.

Other Ventures Competition

Our Other Ventures operations which focus on prescription drugs compete in the pharmaceutical industry in China, which is highly competitive and is characterized by a number of established, large pharmaceutical companies, as well as some smaller emerging pharmaceutical companies. This business faces competition from other pharmaceutical companies in China engaged in the development, production, marketing or sales of prescription drugs, in particular cardiovascular drugs.

The barrier to entry for the PRC pharmaceutical industry primarily relates to regulatory requirements in connection with the production of pharmaceutical products and new product launches. The identities of the key competitors with respect to our prescription drugs business vary by product, and, in certain cases, different competitors that have greater financial resources than us may elect to focus these resources on developing, importing or in-licensing and marketing products in the PRC that are substitutes for our products and may have broader sales and marketing infrastructure with which to do so.

We believe that we compete primarily on the basis of brand recognition, pricing, sales network, promotion activities, product efficacy, safety and reliability. We believe our Other Ventures' continued success will depend on our business's capability to: maintain profitability of its products, obtain and maintain regulatory approvals, develop drug candidates with market potential, maintain an efficient operational model, apply technologies to production lines, attract and retain talented personnel, maintain high quality standards, and effectively market and promote the products sold by our prescription drugs business.

Our Other Ventures operations which focus on consumer health products competes in a highly fragmented market in Asia, particularly in our primary market in China. We believe that this business competes primarily on the basis of brand recognition, pricing, sales network, promotion activities, product safety and reliability. We believe our continued success will depend on our business's capability to: successfully market and distribute in-licensed products such as Earth's Best infant formula, maintain an efficient operational model, attract and retain talented personnel, maintain high quality standards, and effectively market and promote the products sold by our business.

Patents and Other Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our Oncology/Immunology drugs and drug candidates, our Other Ventures' products and other know-how. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in various jurisdictions related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

Patents

We and our joint ventures file patent applications directed to our Oncology/Immunology drugs and drug candidates and our Other Ventures' products in an effort to establish intellectual property positions with regard to new small molecule compounds and/or extracts of natural herbs, their compositions as well as their medical uses in the treatment of diseases. In relation to our Oncology/Immunology operations, we also file patent applications directed to crystalline forms, formulations, processes, key intermediates, and secondary uses as clinical trials for our drug candidates evolve. We file such patent applications in major market jurisdictions, including but not limited to the United States, Europe, Japan and China.

Our Oncology/Immunology Patents

As of December 31, 2022, we had 232 issued patents, including 18 Chinese patents, 22 U.S. patents and 12 European patents, 295 patent applications pending in the above major market jurisdictions, and 7 pending PCT patent applications relating to the drugs and drug candidates of our Oncology/Immunology operations. The intellectual property portfolios for our most advanced drug candidates are summarized below. With respect to most of the pending patent applications covering our drug candidates, prosecution has yet to commence. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office is often significantly narrowed by the time when they issue, if they issue at all. We expect this to be the case for our pending patent applications referred to below.

Savolitinib—The intellectual property portfolio for savolitinib contains two patent families.

The first patent family for savolitinib is directed to novel small molecule compounds as well as methods of treating cancers with such compounds. As of December 31, 2022, we owned 58 patents in this family, including patents in China, the United States, Europe and Japan, each expiring in 2030, and we also had 9 patent applications pending in various other jurisdictions.

The second patent family is directed to the method for the preparation of savolitinib. As of December 31, 2022, we owned one patent in this family in South Africa, which will expire in 2039. As of December 31, 2022, we also had 16 patent applications pending in this family in various jurisdictions, including China, the United States, Europe, and Japan, each of which, if issued, would have an expiration date in 2039. This patent family is co-owned by us and AstraZeneca.

Our collaboration partner AstraZeneca is responsible for maintaining and enforcing the intellectual property portfolio for savolitinib.

Surufatinib—The intellectual property portfolio for surufatinib contains nine patent families.

The first patent family for surufatinib is directed to novel small molecule compounds as well as methods of treating tumor angiogenesis-related disorders with such compounds. As of December 31, 2022, in this patent family we owned one Chinese patent expiring in 2027 and 12 patents in various other jurisdictions, including the United States expiring in 2031, and Europe and Japan, each expiring in 2028. As of December 31, 2022, we also had one patent application pending in Brazil.

The second patent family is directed to the compound and crystalline forms of surufatinib as well as methods of treating tumor angiogenesis-related disorders with such compound and forms. As of December 31, 2022, in this patent family we owned two patents in China expiring in 2029 and 2030, respectively, and we owned 15 patents in other jurisdictions, including the United States expiring in 2031 and Europe expiring in 2030. As of December 31, 2022, we also had one patent application pending in Brazil.

The third patent family is directed to the formulation of a micronized active pharmaceutical ingredient used in surufatinib as well as methods of treating tumor angiogenesis-related disorders with such formulation. As of December 31, 2022, we owned 14 patents in this family in various jurisdictions, including China, Europe and Japan, each of which will expire in 2036. We also had 5 patent applications pending in various other jurisdictions, each of which, if issued, would have an expiration date in 2036.

The fourth patent family is directed to clinical indications of surufatinib. With respect to this patent family, we had one patent application pending in Japan, which, if issued, would have an expiration date in 2036.

The fifth patent family is directed to impurities of surufatinib and their preparation methods. With respect to this family, we had one patent application pending in China, which, if issued, would have an expiration date in 2040.

The sixth patent family is directed to the pharmaceutical combinations of toripalimab and surufatinib. With respect to this family, we had one Chinese and one Taiwan applications pending, each of which, if issued, would have an expiration date in 2041. This patent family is co-owned by us and Shanghai Junshi Biosciences Co., Ltd.

The seventh patent family is directed to methods of using surufatinib in treating advanced pancreatic and extra-pancreatic neuroendocrine tumors. With respect to this family, we had one patent application pending in the United States, which, if issued, would have an expiration date in 2041.

The eighth patent family is directed to the therapeutic combinations of surufatinib and chemotherapeutic agents. With respect to this family, we had one patent application pending in China, which, if issued, would have an expiration date in 2041.

The ninth patent family is directed to solid dispersion of surufatinib. With respect to this family, we had one patent application pending in China, which, if issued, would have an expiration date in 2041.

Fruquintinib—The intellectual property portfolio for fruquintinib contains five patent families.

The first patent family for fruquintinib is directed to novel small molecule compounds as well as methods of treating tumor angiogenesis-related disorders with such compounds. As of December 31, 2022, we owned three U.S. patents, one Chinese patent and one Taiwanese patent in this family, each of which will expire in 2028. We also owned 16 patents in other jurisdictions including Europe and Japan, each of which will expire in 2029.

The second patent family is directed to crystalline forms of fruquintinib as well as methods of treating tumor angiogenesis-related disorders with such forms. As of December 31, 2022, we owned 22 patents in this family in various jurisdictions, including the United States, China, Europe and Japan, each of which will expire in 2035, and we had 5 patent applications pending in various other jurisdictions.

The third patent family is directed to the method of preparing one of the critical intermediates used in the manufacturing process of fruquintinib. With respect to this patent family, we had one patent in China expiring in 2034.

The fourth patent family is directed to the pharmaceutical composition of fruquintinib. As of December 31, 2022, we had 7 patent applications pending in this patent family in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2039.

The fifth patent family is directed to the pharmaceutical combinations of geptanolimab and fruquintinib. With respect to this family, we had one patent application pending in China, which, if issued, would have an expiration date in 2041. This patent family is co-owned by us and Genor Biopharma Co. Ltd.

Sovleplenib—The intellectual property portfolio for sovleplenib contains two patent families.

The first patent family is directed to novel small molecule compounds as well as methods of treating cancers, inflammatory diseases, allergic diseases, cell-proliferative diseases, and immunological diseases with such compounds. As of December 31, 2022, we owned 25 patents in this family in various jurisdictions, including the United States, China, Europe and Japan, each of which will expire in 2032.

The second patent family is directed to the salts of sovleplenib as well as crystalline forms thereof. As of December 31, 2022, we owned four patents in this family in various jurisdictions, including the United States and Japan, each of which will expire in 2038. As of December 31, 2022, we had 21 patent applications pending in this patent family in various jurisdictions, including China, the United States and Europe, each of which, if issued, would have an expiration date in 2038.

Amdizalisib—The intellectual property portfolio for amdizalisib contains three patent families.

The first patent family is directed to novel small molecule compounds as well as uses of such compounds. As of December 31, 2022, we owned 25 patents in this family in various jurisdictions, including the United States, Europe, China and Japan, each of which will expire in 2035. As of December 31, 2022, we also had two patent applications pending in this family in Argentina and Brazil.

The second patent family is directed to crystalline forms of amdizalisib. As of December 31, 2022, we had 23 patent applications pending in this family in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2039.

The third patent family is directed to the method of preparing one of the critical intermediates used in the manufacturing process of amdizalisib. With respect to this patent family, we had one patent in China expiring in 2038.

Tazemetostat—The intellectual property portfolio for Tazemetostat is licensed from Epizyme, Inc.

We entered into a licensing agreement with Epizyme pursuant to which we obtained a co-exclusive license to develop, an exclusive license to commercialize and a co-exclusive license to manufacture tazemetostat in China, Hong Kong, Taiwan and Macau for all therapeutic and palliative uses in epithelioid sarcoma, follicular lymphoma (second line and third line), diffuse large B-cell lymphoma and any other indications that are approved according to the terms of the licensing agreement. For more details, please see “—Our Collaborations—Epizyme.”

HMPL-306—The intellectual property portfolio for HMPL-306 contains one patent family.

The patent family is directed to novel small molecule compounds as well as methods of treating cancers with the compounds. As of December 31, 2022, we owned one patent in this family in the United States, which will expire in 2038. As of December 31, 2022, we also had 24 patent applications pending in this patent family in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2038.

HMPL-760—The intellectual property portfolio for HMPL-760 contains one patent family.

The patent family is directed to novel small molecule compounds as well as methods of treating cancers, inflammatory diseases or auto-immune diseases with such compounds. As of December 31, 2022, we owned one patent in this family in the United States, which will expire in 2041. As of December 31, 2022, we also had 23 patent applications pending in this patent family in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2041.

HMPL-453—The intellectual property portfolio for HMPL-453 contains two patent families.

The first patent family is directed to novel small molecule compounds as well as methods of treating cancers with the compounds. As of December 31, 2022, we owned 24 patents in this family in various jurisdictions, including China, Europe, Japan and the United States, each of which will expire in 2034. As of December 31, 2022, we had one patent application pending in Argentina.

The second patent family is directed to the salts of HMPL-453. As of December 31, 2022, we had 20 patent applications pending in this patent family in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2040.

HMPL-295—The intellectual property portfolio for HMPL-295 contains one patent family.

The patent family is directed to novel small molecule compounds as well as methods of treating cancers or auto-immune diseases with such compounds. As of December 31, 2022, in this patent family we had 24 patent applications pending in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2040.

HMPL-653—The intellectual property portfolio for HMPL-653 contains one patent family.

The patent family is directed to novel small molecule compounds as well as methods of treating cancers, inflammatory diseases or auto-immune diseases with such compounds. As of December 31, 2022, in this patent family we had 22 patent applications pending in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2041.

HMPL-A83—The intellectual property portfolio for HMPL-A83 contains two patent families.

The first patent family is directed to novel anti-CD47 antibodies as well as methods of treating cancers with such antibodies. As of December 31, 2022, in this patent family we had 22 patent applications pending in various jurisdictions, including China, the United States, Europe and Japan, each of which, if issued, would have an expiration date in 2041.

The second patent family is subject to confidential review by the patent authorities. As of December 31, 2022, in this patent family we had PCT, Argentina and Taiwan applications pending, each of which, if issued, would have an expiration date in 2042.

Other Ventures Patents

As of December 31, 2022, our joint venture Shanghai Hutchison Pharmaceuticals had (i) 75 issued patents in China, (ii) one patent granted in the U.S. and one granted patent in Canada under the Patent Cooperation Treaty, and (iii) 38 pending Chinese patent applications and seven patent applications under the Patent Cooperation Treaty, among them, two of which were filed in China, including patents for its key prescription products described below.

She Xiang Bao Xin Pills. As of December 31, 2022, Shanghai Hutchison Pharmaceuticals held an invention patent in China directed to the formulation of the She Xiang Bao Xin pill. Under PRC law, invention patents are granted for new technical innovations with respect to products or processes. Invention patents in China have a maximum term of 20 years. This patent will expire in 2029. The “Confidential State Secret Technology” status protection on the She Xiang Bao Xin pill technology held by Shanghai Hutchison Pharmaceuticals, as certified by China’s Ministry of Science and Technology and State Secrecy Bureau, is currently active.

Danning Tablets. As of December 31, 2022, Shanghai Hutchison Pharmaceuticals also held an invention patent in China directed to the formulation of the Danning tablet. This patent will expire in 2027.

Patent Term

The term of a patent depends upon the laws of the country in which it is issued. In most jurisdictions, a patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. In the future, if and when our drug candidates receive approval by the FDA or other regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each drug and other factors. There can be no assurance that any of our pending patent applications will be issued or that we will benefit from any patent term extension.

As with other pharmaceutical companies, our or our joint ventures' ability to maintain and solidify our proprietary and intellectual property position for our drugs and drug candidates or our or their products and technologies will depend on our or our joint ventures' success in obtaining effective patent claims and enforcing those claims if granted. However, our or our joint ventures' pending patent applications and any patent applications that we or they may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our or our joint ventures' patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of filing covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States, China or other markets that also claim technology or therapeutics to which we or our joint ventures have rights, we or our joint ventures may have to participate in interference proceedings, which could result in substantial costs to us, even if the eventual outcome is favorable to us, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

Trade Secrets

In addition to patents, we and our joint ventures rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our or their competitive position. We and our joint ventures seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees and consultants. We and our joint ventures have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we and our joint ventures enter into are designed to protect our or our joint ventures' proprietary information and the agreements or clauses requiring assignment of inventions to us or our joint ventures, as applicable, are designed to grant us or our joint ventures, as applicable, ownership of technologies that are developed through our or their relationship with the respective counterpart. We cannot guarantee, however, that these agreements will afford us or our joint ventures adequate protection of our or their intellectual property and proprietary information rights.

Trademarks and Domain Names

We conduct our business using trademarks with various forms of the "Hutchison", "Chi-Med", "Hutchison China MediTech", "HUTCHMED", "Elunate", "Sulanda", "Orpathys" and "Tazverik" brands, the logos used by HUTCHMED Limited, as well as domain names incorporating some or all of these trademarks. In April 2006, we entered into a brand license agreement (as amended and restated on June 15, 2021) with Hutchison Whampoa Enterprises Limited, an indirect wholly-owned subsidiary of CK Hutchison, pursuant to which we have been granted a non-exclusive, non-transferrable, royalty-free right to use the "Hutchison", "Hutchison China MediTech", "Chi-Med", "HUTCHMED" trademarks, domain names and other intellectual property rights owned by the CK Hutchison group in connection with the operation of our business worldwide. See "Connected Transactions" for further details. The Elunate and Orpathys trademarks are licensed to us in China by our collaboration partners Eli Lilly and AstraZeneca, respectively. The trademarks for the HUTCHMED Limited logo and "Sulanda" are owned by us. The Tazverik trademark is licensed to us in China, Hong Kong, Taiwan and Macau by our collaboration partner Epizyme.

In addition, our joint ventures seek trademark protection for their products. As of December 31, 2022, our joint venture Shanghai Hutchison Pharmaceuticals owned a total of 21 trademarks in China and one trademark in Canada related to products sold by it. For example, the name "Shang Yao" is a registered trademark of Shanghai Hutchison Pharmaceuticals in China for certain uses including pharmaceutical preparations.

Raw Materials and Supplies

Raw materials and supplies are ordered based on our or our joint ventures' respective sales plans and reasonable order forecasts and are generally available from our or our joint ventures' own cultivation operations and various third-party suppliers in quantities adequate to meet our needs. We typically order raw materials on short-term contract or purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

For our Oncology/Immunology operations, the active pharmaceutical ingredient used in our drug candidates are supplied to us from third-party vendors. Our ability to successfully develop our drug candidates, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the active pharmaceutical ingredients for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing.

We generally aim to identify and qualify one or more manufacturers to provide such active pharmaceutical ingredients prior to submission of an NDA to the FDA and/or NMPA. We contract with a single supplier to manufacture and supply us with the active pharmaceutical ingredient for fruquintinib for commercial purposes and are in the process of engaging a second supplier. We have already validated the second supplier's cGMP production processes and the application for this second supplier has been approved by the NMPA. We also contract with a single supplier to manufacture and supply us with the active pharmaceutical ingredient for surufatinib for commercial purposes. We contracted with a single supplier to provide active pharmaceutical ingredient and finished product for savolitinib. We manage the risk of price fluctuations and supply disruptions of active pharmaceutical ingredients by purchasing them in bulk quantities as these ingredients have a relatively long shelf life. Other than the foregoing, we do not currently have arrangements in place for a contingent or second-source supply of the active pharmaceutical ingredients for fruquintinib, surufatinib or savolitinib in the event any of our current suppliers of such active pharmaceutical ingredients or finished product cease their operations for any reason, which may lead to an interruption in our production and operations. However, to date, while we have experienced price fluctuations associated with our raw materials, we have not experienced any material disruptions in the supply of the active pharmaceutical ingredients or the other raw materials we and our joint venture partners use. See Item 3.D. "Risk Factors—Certain of our joint venture parties principal products involve the cultivation or sourcing of key raw materials including botanical products, and any quality control or supply failure or price fluctuations could adversely affect our ability to manufacture our products and/or could materially and adversely affect our operating results."

Quality Control and Assurance

We have our own independent quality control system and devote significant attention to quality control for the designing, manufacturing and testing of our products. We have established a strict quality control system in accordance with the NMPA regulations. Our laboratories fully comply with the Chinese manufacturing guidelines and are staffed with highly educated and skilled technicians to ensure quality of all batches of product release. We monitor in real time our operations throughout the entire production process, from inspection of raw and auxiliary materials, manufacture, delivery of finished products, clinical testing at hospitals, to ethical sales tactics. Our quality assurance team is also responsible for ensuring that we are in compliance with all applicable regulations, standards and internal policies. Our senior management team is actively involved in setting quality policies and managing internal and external quality performance of our company and our joint venture Shanghai Hutchison Pharmaceuticals.

Customers and Suppliers

For the years ended December 31, 2020, 2021 and 2022, we generated revenue of $102.3 million, $188.9 million and $185.0 million from our five largest customers, respectively. For the years ended December 31, 2020, 2021 and 2022, revenue from our five largest customers represented approximately 45%, 53% and 43% of our total revenue, respectively, and revenue from our largest customer in those periods represented approximately 16%, 16% and 16% of our revenue in the same periods, respectively. Save for Sinopharm, our five largest customers were independent third parties and none of our directors or their close associates or, to the knowledge of our directors, any shareholders who owned more than 5% of our issued ordinary shares had any interest in any of our five largest customers as of the date of the filing of this annual report.

In 2020, 2021 and 2022, Sinopharm, which jointly owns Hutchison Sinopharm with us, was one of our five largest customers. Sales to Sinopharm and/or its associates contributed 16%, 12% and 16% of our revenue in 2020, 2021 and 2022, respectively. Purchases from Sinopharm and/or its associates contributed less than 1% of our total purchases in 2020, 2021 and 2022, respectively.

For the years ended December 31, 2020, 2021 and 2022, the total purchases from our five largest suppliers were $58.0 million, $100.6 million and $90.9 million, respectively. For the years ended December 31, 2020, 2021 and 2022, our purchases from our five largest suppliers represented less than 20% of our total purchases. All of our five largest suppliers were independent third parties and none of our directors or their close associates or, to the knowledge of our directors, any shareholder who owned more than 5% of our issued ordinary shares had any interest in any of our five largest suppliers as of the date of the filing of this annual report.

Contract Research Organizations

Although we or our collaboration partners design the clinical trials for our drug candidates, CROs conduct most of the clinical trials. Our agreements with CROs are usually structured as master service agreements which set out the services to be performed, payment schedule, term and confirmation that all intellectual rights arising out of or made in performance of the services are owned by us. We and our collaboration partners work with major global and Chinese CROs.

Certificates and Permits

The following sets forth the material certificates and/or permits that we have obtained for our operations in China. We have received all material certificates and permits that are, or may be, required for our operations in China. No material certificate, permission or approval for our operations has been denied by relevant authorities in China. Given the uncertainties of interpretation and implementation of relevant laws and regulations and the enforcement practice by relevant government authorities, we may be required to obtain additional licenses, permits, filings or approvals for our products and business operations in China in the future, and may not be able to maintain or renew our current licenses, permits, filings or approvals. In addition, rules and regulations in China can change quickly with little advance notice. Uncertainties due to evolving laws and regulations could impede the ability of an issuer with significant operations in China, such as us, to obtain or maintain certificates, permits or licenses required to conduct business in China. In the absence of required certificates, permits or licenses, governmental authorities could impose material sanctions or penalties on us.

HUTCHMED (Suzhou) Limited holds a pharmaceutical manufacturing permit issued by its local regulatory authority expiring on September 13, 2025. It also complies with applicable GMP standards.

Hutchison Sinopharm holds a pharmaceutical trading license issued by its local regulatory authority expiring on July 30, 2024. Hutchison Sinopharm also holds a good supply practice, or GSP, certificate issued by its local regulatory authority which expires on July 30, 2024.

Shanghai Hutchison Pharmaceuticals holds a pharmaceutical manufacturing permit from its local regulatory authorities expiring on December 31, 2025.

Shanghai Shangyao Hutchison Whampoa GSP Company Limited, a subsidiary of Shanghai Hutchison Pharmaceuticals, holds a pharmaceutical trading license from its local regulatory authority expiring on November 17, 2024. It also holds a GSP certificate issued by its local regulatory authority expiring on November 17, 2024.

Regulations

This section sets forth a summary of the most significant rules and regulations affecting our business activities in China and the United States.

Government Regulation of Pharmaceutical Product Development and Approval

PRC Regulation of Pharmaceutical Product Development and Approval

Since China's entry to the World Trade Organization in 2001, the PRC government has made significant efforts to standardize regulations, develop its pharmaceutical regulatory system and strengthen intellectual property protection.

Regulatory Authorities

In the PRC, the NMPA is the authority that monitors and supervises the administration of pharmaceutical products and medical appliances and equipment as well as cosmetics. The NMPA's predecessor, the State Drug Administration, or the SDA, was established on August 19, 1998 as an organization under the State Council to assume the responsibilities previously handled by the Ministry of Health of the PRC, or the MOH, the State Pharmaceutical Administration Bureau of the PRC and the State Administration of Traditional Chinese Medicine of the PRC. The SDA was replaced by the State Food and Drug Administration, or the SFDA, in March 2003 and was later reorganized into the China Food and Drug Administration, or the CFDA, in March 2013. On March 17, 2018, the First Session of the Thirteenth National People's Congress approved the State Council Institutional Reform Proposal, according to which the duties of the CFDA were consolidated into the State Administration for Market Regulation, or the SAMR, and the NMPA was established under the management and supervision of the SAMR.

The primary responsibilities of the NMPA include:

- monitoring and supervising the administration of pharmaceutical products, medical appliances and equipment as well as cosmetics in the PRC;

- formulating administrative rules and policies concerning the supervision and administration of cosmetics and the pharmaceutical industry; evaluating, registering and approving of new drugs, generic drugs, imported drugs and traditional Chinese medicine;

- undertaking the standard, registration, quality and post marketing risk management of pharmaceutical products, medical appliances and equipment as well as cosmetics; and

- examining, evaluating and supervising the safety of pharmaceutical products, medical appliances and equipment as well as that of cosmetics.

The MOH is an authority at the ministerial level under the State Council and is primarily responsible for national public health. Following the establishment of the SFDA in 2003, the MOH was put in charge of the overall administration of national health in the PRC excluding the pharmaceutical industry. In March 2008, the State Council placed the SFDA under the management and supervision of the MOH. The MOH performs a variety of tasks in relation to the health industry such as establishing social medical institutes and producing professional codes of ethics for public medical personnel. The MOH is also responsible for overseas affairs, such as dealings with overseas companies and governments. In 2013, the MOH and the National Population and Family Planning Commission were integrated into the National Health and Family Planning Commission of the PRC, or the NHFPC. On March 17, 2018, the First Session of the Thirteenth National People's Congress approved the State Council Institutional Reform Proposal, according to which the responsibilities of NHFPC and certain other governmental authorities are consolidated into the NHC, and the NHFPC shall no longer be maintained. The responsibilities of the NHC include organizing the formulation of national drug policies, the national essential medicine system and the National Essential Medicines List and drafting the administrative rules for the procurement, distribution and use of national essential medicines.

Healthcare System Reform

The PRC government has promulgated several healthcare reform policies and regulations to reform the healthcare system. On March 17, 2009, the Central Committee of the PRC Communist Party and the State Council jointly issued the Guidelines on Strengthening the Reform of Healthcare System. On March 18, 2009, the State Council issued the Implementation Plan for the Recent Priorities of the Healthcare System Reform (2009-2011). On July 22, 2009, the General Office of the State Council issued the Five Main Tasks of Healthcare System Reform in 2009.

More recently, on May 5, 2022, the General Office of the State Council issued the Key Tasks for Deepening the Reform of the Medical and Health System in 2022 (the "**2022 PRC Health Care Reforms**").

Highlights of the 2022 PRC Health Care Reforms include the following:

- The overall objectives of the 2022 PRC Health Care Reforms are to comprehensively promote construction of a healthy China, deeply promote the experience of Sanming's medical reforms (which refers to certain medical reforms undertaken in Sanming, Fujian Province since 2012), promote the expansion and balanced distribution of high-quality medical resources, continue to promote the transition from centering on disease treatment to centering on people's health, and continue to promote solutions to lack of and cost of access to medical care.

- According to the Sanming People's Government website, the medical reforms that were undertaken in Sanming included but were not limited to (1) reforms to the personnel and salary system of public hospitals, whereby Sanming implemented target annual salaries for medical staff (being 3 times the average local salary), (2) introduction of competitive bidding processes in order to reduce the costs of medicines, and (3) integration of medical insurance management institutions to reduce coordination costs across departments. The 2022 PRC Health Care Reforms calls for promotion of Sanming's medical reform experience, including but not limited to (1) expansion of the scope of centralized procurement, whereby state and local governments in each province should strive to have a total of more than 350 common drugs purchased; (2) reform of medical service prices, whereby all provinces shall issue documents related to the establishment of a dynamic adjustment mechanism for medical service prices before the end of June 2022, and (3) reform of the personnel and salary system of public hospitals, whereby localities should be guided to make good use of staffing resources in light of their actual circumstances, and may explore the recruitment of the best external qualified professional and technical personnel via strict and standardized procedures such as open recruitment.

- The 2022 PRC Health Care Reforms also promote high-quality development in medicine and healthcare, including but not limited to (1) comprehensive and steady reform of public hospitals, whereby pilot provinces shall take the lead in exploring and reviewing reform paths of public hospitals at all levels; (2) giving a greater role to government investment incentives; (3) advancement of the national medical insurance program, such as promoting the improvement of the direct settlement of expenses of inter-provincial and remote medical treatments, and unifying the scope of drugs covered by national medical insurance across the country; (4) strengthening drug supply security, for example, by accelerating the granting of market authorization to innovative drugs of clinical value; and (5) promotion of pilot projects for the revitalization of traditional Chinese medicine. The 2022 PRC Health Care Reforms also call for (i) 35,000 general practitioners and 100,000 resident doctors (including postgraduates with a master degree) to be trained through various approaches within the year, (ii) for the enrollment of professional postgraduate students to be inclined towards areas facing skills shortages, such as general practice, pediatrics, and psychiatry, and (iii) the promotion of telemecine services, which shall cover 95% of the country's districts and counties.

Drug Administration Laws and Regulations

The PRC Drug Administration Law as promulgated by the Standing Committee of the National People's Congress in 1984 and the Implementing Measures of the PRC Drug Administration Law as promulgated by the MOH in 1989 have laid down the legal framework for the establishment of pharmaceutical manufacturing enterprises, pharmaceutical trading enterprises and for the administration of pharmaceutical products including the development and manufacturing of new drugs and medicinal preparations by medical institutions. The PRC Drug Administration Law also regulates the packaging, trademarks and the advertisements of pharmaceutical products in the PRC.

Certain revisions to the PRC Drug Administration Law took effect on December 1, 2001. They were formulated to strengthen the supervision and administration of pharmaceutical products, and to ensure the quality and the safety of pharmaceutical products for human use. The revised PRC Drug Administration Law applies to entities and individuals engaged in the development, production, trade, application, supervision and administration of pharmaceutical products. It regulates and prescribes a framework for the administration of pharmaceutical manufacturers, pharmaceutical trading companies, and medicinal preparations of medical institutions and the development, research, manufacturing, distribution, packaging, pricing and advertisements of pharmaceutical products.

The PRC Drug Administration Law was later amended on December 28, 2013 and April 24, 2015 by the Standing Committee of the National People's Congress. It provides the basic legal framework for the administration of the production and sale of pharmaceutical products in China and covers the manufacturing, distributing, packaging, pricing and advertising of pharmaceutical products.

On August 26, 2019, the Standing Committee of the National People's Congress promulgated the amended PRC Drug Administration Law, which took effect on December 1, 2019. The amendment brought a series of changes to the drug supervision and administration system, including but not limited to the clarification of the MAH system, pursuant to which the MAH shall assume responsibilities for non-clinical studies, clinical trials, manufacturing and marketing, post-marketing studies, monitoring, reporting and handling of adverse reactions of the drug. The amendment also stipulated that the PRC supports the innovation of drugs with clinical value and specific or special effects on human diseases, encourages the development of drugs with new therapeutic mechanisms and promotes the technological advancement of such drugs.

According to the PRC Drug Administration Law, no pharmaceutical products may be produced without a pharmaceutical production license. A manufacturer of pharmaceutical products must obtain a pharmaceutical production license from one of NMPA's provincial level branches in order to commence production of pharmaceuticals. Prior to granting such license, the relevant government authority will inspect the manufacturer's production facilities, and decide whether the sanitary conditions, quality assurance system, management structure and equipment within the facilities have met the required standards.

The PRC Drug Administration Implementation Regulations promulgated by the State Council took effect on September 15, 2002 and were later amended on February 6, 2016 and March 2, 2019 to provide detailed implementation regulations for the revised PRC Drug Administration Law. With respect to the latest revision of the PRC Drug Administration Law, promulgated on August 26, 2019 and effective on December 1, 2019, there are no corresponding revised PRC Drug Administration Implementation Regulations.

Examination and Approval of New Medicines

On January 22, 2020, the SAMR promulgated the Administrative Measures on the Registration of Pharmaceutical Products, or the Registration Measures, which became effective on July 1, 2020. According to the Registration Measures, an applicant who has obtained a drug registration certificate shall be a drug MAH. The approval process for medicines seeking marketing authorization mainly consists of the following steps:

- upon the completion of pharmaceutical, pharmacological and toxicological research and related activities, an application for clinical trial will be submitted to the Center for Drug Evaluation of the NMPA, or the Center for Drug Evaluation, for review. The Center for Drug Evaluation will organize pharmacists, medical personnel and other professionals to review the application for clinical trial. A decision on approval or non-approval of the application for clinical trial of drugs will be made within 60 working days from acceptance of the application, and the applicant shall be notified of the examination and approval result through the website of the Center for Drug Evaluation. If the applicant is not notified within the stipulated period, the application shall be deemed approved. The applicant who is approved to conduct clinical trial shall act as the sponsor for the clinical trial;

- if the application for clinical trial is approved, the sponsor shall, prior to conducting subsequent phases of the clinical trial, formulate a corresponding program for the clinical trial, carry out the clinical trial after the review and approval by the Ethics Committee, and submit the corresponding program for clinical trial and supporting materials on the website of the Center for Drug Evaluation. The applicant may proceed with the relevant clinical research (which is generally conducted in three phases for a new medicine under the Registration Measures) at institutions with appropriate qualification:

    - Phase I refers to the preliminary clinical trial for clinical pharmacology and body safety. It is conducted to observe the human body tolerance for new medicine and pharmacokinetics, so as to provide a basis for determining the prescription plan.

    - Phase I or II refers to the stage of preliminary evaluation of clinical effectiveness. The purpose is to preliminarily evaluate the clinical effectiveness and safety of the medicine used on patients with targeted indication, as well as to provide a basis for determining the Phase III clinical trial research plan and the volume under the prescription plan.

    - Phase III is a clinical trial stage to verify the clinical effectiveness. The purpose is to test and determine the clinical effectiveness and safety of the medicine used on patients with targeted indication, to evaluate the benefits and risks thereof and, eventually, to provide sufficient basis for review of the medicine registration application.

    - Phase IV refers to the stage of surveillance and research after the new medicines is launched. The purpose is to observe the clinical effectiveness and adverse effects of the medicine over a much larger patient population and longer time period than in Phase I to III clinical trials, and evaluate the benefits and risks when it is administered to general or special patient population in larger prescription volume;

- the sponsor shall submit a safety update report during the research and development period on the website of the NMPA on a regular basis. The safety update report during the research and development period shall be submitted once a year, and within two months of every full year after the clinical drug trial is approved. The NMPA may require the sponsor to adjust the reporting period if deemed necessary;

- after (i) completing relevant pharmaceutical, pharmacological and toxicological research, clinical drug trials, and other research supporting the marketing registration of a medicine, (ii) determining medicine quality standards, (iii) completing the verification of commercial scale manufacturing process, and (iv) making preparations for drug registration inspections, the applicant shall file the application for drug marketing authorization with the Center for Drug Evaluation;

- the Center for Drug Evaluation will organize pharmaceutical, medical and other professionals to review accepted drug marketing authorization applications in accordance with relevant requirements;

- upon acceptance of an application for drug registration, the Center for Drug Evaluation will conduct a preliminary examination within 40 working days from acceptance of the application; if there is a need to conduct an examination of manufacturing premises for drug registration, the Center for Drug Evaluation will notify the Centre for Food and Drug Inspection of the NMPA to organize an examination, provide the relevant materials required, and simultaneously notify the applicant as well as the provincial drug administrative authorities where the applicant or the manufacturing enterprise is located. The Centre for Food and Drug Inspection of the NMPA shall in principle complete the examination 40 working days before expiry of the review period, and give feedback to the Center for Drug Evaluation on the status and findings etc. of the examinations; and

- if the application is approved through the comprehensive review process, the drug shall be approved for marketing and a drug registration certificate shall be issued. The drug registration certificate will state the approval number for the drug, the holder of the certificate, and information of the manufacturing enterprise. A drug registration certificate for non-prescription drugs will also state the non-prescription drug category.

Any applicant who is not satisfied with the Center for Drug Evaluation's decision to deny an application during the application of the drug registration period can appeal within 15 working days after it is notified by the Center for Drug Evaluation of such decision. Upon termination for examination and approval of the application for drug registration, if the applicant is dissatisfied with the administrative licensing decision, the applicant may apply for administrative review or file an administrative lawsuit.

In accordance with the Provisions on the Administration of Special Examination and Approval of Registration of New Drugs promulgated by the SFDA, issued and effective on January 7, 2009, an NDA that meets certain requirements as specified below will be handled with priority in the review and approval process, so-called "green-channel" approval. In addition, the applicant is entitled to provide additional materials during the review period besides those requested by the SFDA, and will have access to enhanced communication channels with the SFDA. As of the date of this annual report, the SFDA has been succeeded by the SAMR and NMPA.

Applicants for the registration of the following new drugs are entitled to request priority treatment in review and approval: (i) active ingredients and their preparations extracted from plants, animals and minerals, and newly discovered medical materials and their preparations that have not been sold in the China market, (ii) chemical drugs and their preparations and biological products that have not been approved for sale at its origin country or abroad, (iii) new drugs with obvious clinical treatment advantages for such diseases as AIDS, therioma, and rare diseases, and (iv) new drugs for diseases that have not been treated effectively. Under category (i) or (ii) above, the applicant for drug registration may apply for special examination and approval when applying for the clinical trial of new drugs; under category (iii) or (iv) above, the applicant may only apply for special examination and approval when applying for manufacturing.

In addition, on July 7, 2020, the NMPA released the Priority Review and Approval Procedures for Drug Marketing Authorizations (for Trial Implementation), which further clarified that a fast track process for drug registration will be available to the following drugs with distinctive clinical value: (i) (a) drugs in urgent clinical demand and in shortage and (b) innovative drugs and modified new drugs for prevention and treatment of serious infectious diseases, rare diseases and other diseases; (ii) new varieties, dosage forms and specifications of children's drugs that conform to children's physiological characteristics; (iii) (a) vaccines that are in urgent need for disease prevention and control and (b) innovative vaccines; (iv) drugs that have been included in the procedures for Breakthrough Therapy Designation; (v) drugs that are subject to conditional approval; and (vi) other drugs which the NMPA deems applicable. It also specified that fast track status would be given to clinical trial applications for drugs with patent expiry within three years and manufacturing authorization applications for drugs with patent expiry within one year. Concurrent applications for new drug clinical trials which are already approved in the United States or E.U. are also eligible for fast track NMPA approval.

Drug Technology Transfer Regulations

On August 19, 2009, the SFDA promulgated the Administrative Regulations for Technology Transfer Registration of Drugs to standardize the registration process of drug technology transfer, which includes application for, and evaluation, examination, approval and monitoring of, drug technology transfer. Drug technology transfer refers to the transfer of drug production technology by the owner to a drug manufacturer and the application for drug registration by the transferee according to the provisions in the new regulations. Drug technology transfer includes new drug technology transfer and drug production technology transfer.

Conditions for the application for new drug technology transfer

Applications for new drug technology transfer may be submitted prior to the expiration date of the monitoring period of the new drugs with respect to:

- drugs with new drug certificates only; or
- drugs with new drug certificates and drug approval numbers.

For drugs with new drug certificates only and not yet in the monitoring period, or drug substances with new drug certificates, applications for new drug technology transfer should be submitted prior to the respective expiration date of the monitoring periods for each drug registration category set forth in the new regulations and after the issue date of the new drug certificates.

Conditions for the application of drug production technology transfer

Applications for drug production technology transfer may be submitted if:

- the transferor holds new drug certificates or both new drug certificates and drug approval numbers, and the monitoring period has expired or there is no monitoring period;
- with respect to drugs without new drug certificates, both the transferor and the transferee are legally qualified drug manufacturing enterprises, one of which holds over 50% of the equity interests in the other, or both of which are majority-owned subsidiaries of the same drug manufacturing enterprise;
- with respect to imported drugs with imported drug licenses, the original applicants for the imported drug registration may transfer these drugs to local drug manufacturing enterprises.

Application for, and examination and approval of, drug technology transfer

Applications for drug technology transfer should be submitted to the provincial drug administration. If the transferor and the transferee are located in different provinces, the provincial drug administration where the transferor is located should provide examination opinions. The provincial drug administration where the transferee is located is responsible for examining application materials for technology transfer and organizing inspections on the production facilities of the transferee. Medical examination institutes are responsible for testing three batches of drug samples.

The Center for Drug Evaluation should further review the application materials, provide technical evaluation opinions and form a comprehensive evaluation opinion based on the site inspection reports and the testing results of the samples. The SFDA (which, as of the date of this annual report, has been succeeded by the SAMR and NMPA) should determine whether to approve the application according to the comprehensive evaluation opinion of the Center for Drug Evaluation. An approval letter of supplementary application and a drug approval number will be issued to qualified applications. An approval letter of clinical trials will be issued when necessary. For rejected applications, a notification letter of the examination opinions will be issued with the reasons for rejection.

Permits and Licenses for Manufacturing and Registration of Drugs

Production Licenses

To manufacture pharmaceutical products in the PRC, a pharmaceutical manufacturing enterprise must first obtain a Pharmaceutical Manufacturing Permit issued by the relevant pharmaceutical administrative authorities at the provincial level where the enterprise is located. Among other things, such a permit must set forth the permit number, the name, legal representative and registered address of the enterprise, the site and scope of production, issuing institution, date of issuance and effective period.

Each Pharmaceutical Manufacturing Permit issued to a pharmaceutical manufacturing enterprise is effective for a period of five years. The enterprise is required to apply for renewal of such permit within six months prior to its expiry and will be subject to reassessment by the issuing authorities in accordance with then prevailing legal and regulatory requirements for the purposes of such renewal.

Business Licenses

In addition to a Pharmaceutical Manufacturing permit, the manufacturing enterprise must also obtain a business license from the administrative bureau of industry and commerce at the local level. The name, legal representative and registered address of the enterprise specified in the business license must be identical to that set forth in the Pharmaceutical Manufacturing Permit.

Registration of Pharmaceutical Products

All pharmaceutical products that are produced in the PRC must bear a registration number issued by the NMPA, with the exception of Chinese herbs and Chinese herbal medicines in soluble form. The medicine manufacturing enterprises must obtain the medicine registration number before manufacturing any medicine.

Good Manufacturing Practices

The Guidelines on Good Manufacturing Practices, as amended in 1998 and 2010, or the Guidelines, took effect on August 1, 1999 and set the basic standards for the manufacture of pharmaceuticals. These Guidelines cover issues such as the production facilities, the qualification of the personnel at the management level, production plant and facilities, documentation, material packaging and labeling, inspection, production management, sales and return of products and customers' complaints. On October 23, 2003, the SFDA issued the Notice on the Overall Implementation and Supervision of Accreditation of Good Manufacturing Practice Certificates for Pharmaceuticals, which required all pharmaceutical manufacturers to apply for the GMP certificates by June 30, 2004. Those enterprises that failed to obtain the GMP certificates by December 31, 2004 would have their Pharmaceutical Manufacturing Permit revoked by the drug administrative authorities at the provincial level. On October 24, 2007, the SFDA issued Evaluation Standard on Good Manufacturing Practices which became effective on January 1, 2008. On December 1, 2019, per the Announcement of the NMPA on Issues Concerning the Implementation of the PRC Drug Administration Law, GMP certificates were abolished, though manufacturers remain to be obligated to operate in accordance with the applicable requirements of the Guidelines. The Notice of the NMPA on Promulgation of the Administrative Measures for Drug Inspection (for Trial Implementation), or Trial Drug Inspection Measures, was released and effective on May 24, 2021, which regulates the inspection, investigation, evidence collection and disposal and other actions carried out by medical products administrative authorities with respect to the manufacturing, distribution and use of drugs. The Trial Drug Inspection Measures stipulate that where an application for a pharmaceutical manufacturing permit is filed for the first time, on-site inspection shall be carried out in accordance with the applicable requirements of the Guidelines. Where an application for re-issuance of a pharmaceutical manufacturing permit is filed, a compliance inspection may be carried out if necessary based on the principles of risk management, taking into consideration the enterprise's compliance with the laws and regulations on drug administration, the Guidelines, and the running of quality control systems.

Marketing Authorization Holder System

In May 2016, the State Council announced the piloting of the MAH system in ten provinces in China, where the market authorization/drug license holders are no longer required to be the actual manufacturers. The MAH system will allow for more flexibilities in contract manufacturing arrangements.

Under the authorization of the Standing Committee of the National People's Congress, the State Council issued the Pilot Plan for the Drug MAH Mechanism on May 26, 2016, providing a detailed pilot plan for the MAH system in ten provinces in China. Under the MAH system, domestic drug research and development institutions and individuals in the pilot regions are eligible to be holders of drug registrations without having to become drug manufacturers. The MAHs may engage contract manufacturers for manufacturing, provided that the contract manufacturers are licensed and are also located within the pilot regions. Drugs that qualify for the MAH system include: (1) new drugs (including biological products for curative uses of Class I, Class VII and biosimilars under the Administration of Drug Registration) approved after the implementation of the MAH system; (2) generic drugs approved as Category 3 or 4 drugs under the Reform Plan for Registration Category of Chemical Medicine issued by the NMPA on March 4, 2016; (3) previously approved generics that have passed equivalence assessments against their original drugs; and (4) previously approved drugs whose licenses were held by drug manufacturers originally located within the pilot regions but have moved out of the pilot regions due to corporate mergers or other reasons.

On August 15, 2017, the CFDA issued the Circular on the Matters Relating to Promotion of the Pilot Program for the Drug MAH System, clarifying that the MAH shall be responsible for managing the whole manufacturing and marketing chain and the whole life cycle of drugs and shall assume full legal liabilities for the non-clinical drug study, clinical trials, manufacturing, marketing and distribution and adverse drug reaction monitoring. The MAH is permitted to entrust several drug manufacturers under the drug quality management system established by the MAH. The MAH shall submit a report of drug manufacturing, marketing, prescription, techniques, pharmacovigilance, quality control measures and certain other matters to the CFDA (which, as of the date of this annual report, has been succeeded by the SAMR and NMPA) within 20 working days after the end of each year.

On December 1, 2019, the latest amendment of Drug Administration Law came into effect, marking the success of the pilot work, and the MAH system has become a national system. Pursuant to the latest amendment, the legal representative and the key person-in-charge of a drug MAH shall be fully responsible for the quality of drugs.

Administrative Protection for New Drugs

The Administrative Measures Governing the Production Quality of Pharmaceutical Products, or the Administrative Measures for Production, provides detailed guidelines on practices governing the production of pharmaceutical products. A manufacturer's factory must meet certain criteria in the Administrative Measures for Production, which include: institution and staff qualifications, production premises and facilities, equipment, hygiene conditions, production management, quality controls, product operation, maintenance of sales records and manner of handling customer complaints and adverse reaction reports.

Distribution of Pharmaceutical Products

According to the PRC Drug Administration Law and its implementing regulations and the Measures for the Supervision and Administration of Circulation of Pharmaceuticals, a manufacturer of pharmaceutical products in the PRC can only engage in the trading of the pharmaceutical products that the manufacturer has produced itself. In addition, such manufacturer can only sell its products to:

- wholesalers and distributors holding Pharmaceutical Distribution Permits;
- other holders of Pharmaceutical Manufacturing Permits; or
- medical practitioners holding Medical Practice Permits.

A pharmaceutical manufacturer in the PRC is prohibited from selling its products to end-users, or individuals or entities other than holders of Pharmaceutical Distribution Permits, the Pharmaceutical Manufacturing Permits or the Medical Practice Permits.

The granting of a Pharmaceutical Distribution Permit to wholesalers shall be subject to approval of the provincial level drug regulatory authorities, while the granting of a retailer permit shall be subject to the approval of the drug regulatory authorities above the county level. Unless otherwise expressly approved, no pharmaceutical wholesaler may engage in the retail of pharmaceutical products, nor may pharmaceutical retailers engage in wholesaling.

A pharmaceutical distributor shall satisfy the following requirements:

- personnel with pharmaceutical expertise as qualified according to law;
- business site, facilities, warehousing and sanitary environment compatible to the pharmaceutical products being distributed;
- quality management system and personnel compatible to the pharmaceutical products being distributed; and
- rules and regulations to ensure the quality of the pharmaceutical products being distributed.

Operations of pharmaceutical distributors shall be conducted in accordance with the Pharmaceutical Operation Quality Management Rules.

Pharmaceutical distributors must keep true and complete records of any pharmaceutical products purchased, distributed or sold with the generic name of such products, specification, approval code, term, manufacturer, purchasing or selling party, price and date of purchase or sale. A pharmaceutical distributor must keep such record at least until one year after the expiry date of such products and in any case, such record must be kept for no less than three years. Penalties may be imposed for any violation of record-keeping.

Pharmaceutical distributors can only distribute pharmaceutical products obtained from those with a Pharmaceutical Manufacturing Permit and a Pharmaceutical Distribution Permit.

On December 26, 2016, the Medical Reform Office of the State Council, the National Health and Family Planning Commission, the CFDA and other five government authorities promulgated the "Two-Invoice System" Opinions, which became effective on the same date. On April 25, 2017, the General Office of the State Council further promulgated the Notice on Issuing the Key Working Tasks for Deepening the Reform of Medicine and Health System in 2017. According to these rules, a two-invoice system is encouraged to be gradually adopted for drug procurement. The two-invoice system generally requires a drug manufacturer to issue only one invoice to its distributor followed by the distributor issuing a second invoice directly to the end customer hospital. Only one distributor is permitted to distribute drug products between the manufacturer and the hospital. The system also encourages manufacturers to sell drug products directly to hospitals. Public medical institutions are required to adopt the two-invoice system, and its full implementation nationwide is targeted for 2018. As of the date of the filing of this annual report, the relevant local rules with respect to the "Two-Invoice System" have been promulgated in some provinces and municipal cities in the PRC, and the reform is still in progress. Private medical institutions are encouraged but not yet required to adopt the two-invoice system. Pharmaceutical manufacturers and distributors who fail to implement the two-invoice system may be disqualified from attending future bidding events or providing distribution for hospitals and blacklisted for drug procurement practices. These rules aim to consolidate drug distribution and reduce drug prices. The impact on our company is that Shanghai Hutchison Pharmaceuticals was required to restructure its distribution and logistics network and Hutchison Sinopharm began to shift its prior Seroquel distribution model to a fee-for-service model. For more details, please refer to Item 4.B. "Business Overview—Other Ventures."

Foreign Investment and "State Secret" Technology Drugs

The interpretation of certain PRC laws and regulations governing foreign investment and "state secret" technology is uncertain. Under the Special Administrative Measures (Negative List) for Foreign Investment Access, or the Negative List, published by the MOFCOM and the China National Development and Reform Commission or the NDRC. Under the Catalogue, "manufacturing of modern Chinese medicines with confidential proprietary formula" has been deemed prohibited for any foreign investment. The technology and know-how of the She Xiang Bao Xin pill is classified as "state secret" technology by China's Ministry of Science and Technology, or the MOST, and the National Administration for the Protection of State Secrets, or NAPSS.

There are currently no PRC laws or regulations or official interpretations, and therefore there can be no assurance, as to whether the use of "state secret" technology constitutes the "manufacturing of Chinese medicines with confidential proprietary formula" under the Negative List. However, under the Rules on Confidentiality of Science and Technology promulgated by the State Science and Technology Commission (the predecessor of the MOST and the NAPSS) on January 6, 1995, cooperation with foreign parties or establishing joint ventures with foreign parties in respect of state secret technology is expressly allowed, provided that such cooperation has been duly approved by the relevant science and technology authorities. The establishment of Shanghai Hutchison Pharmaceuticals as a sino-foreign joint venture, including the re-registration of licenses for She Xiang Bao Xin pills in its name, was approved by the local counterpart of the MOFCOM and the Shanghai Drug Administration in 2001. Subsequently, the "Confidential State Secret Technology" status protection for She Xiang Bao Xin pills was also granted in 2005 to Shanghai Hutchison Pharmaceuticals as a sino-foreign joint venture by the MOST and NAPSS. Consequently, we believe Shanghai Hutchison Pharmaceuticals is in compliance with all applicable PRC laws and regulations governing foreign investment and "state secret" technology. Moreover, we believe that our other joint ventures and wholly-foreign owned enterprises in the PRC are also in compliance with all applicable PRC laws and regulations governing foreign investment.

U.S. Regulation of Pharmaceutical Product Development and Approval

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. The process of obtaining approvals and the subsequent compliance with appropriate federal, state and local rules and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. regulatory requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of enforcement correspondence, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the U.S. Department of Justice, or DOJ, or other governmental entities. Drugs are also subject to other federal, state and local statutes and regulations.

Our drug candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of extensive pre-clinical studies, sometimes referred to as pre-clinical laboratory tests, pre-clinical animal studies and formulation studies all performed in compliance with applicable regulations, including the FDA's good laboratory practice regulations;
- submission to the FDA of an IND application which must become effective before human clinical trials may begin and must be updated annually;
- IRB approval before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with study protocols, the applicable GCPs and other clinical trial-related regulations, to establish the safety and efficacy of the proposed drug product for its proposed indication;
- preparation and submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA whether the NDA is acceptable for filing; if the FDA determines that the NDA is not sufficiently complete to permit substantive review, it may request additional information and decline to accept the application for filing until the information is provided;
- in-depth review of the NDA by FDA, which may include review by a scientific advisory committee;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient and finished drug product are produced to assess compliance with the FDA's cGMP;
- potential FDA audit of the pre-clinical and/or clinical trial sites that generated the data in support of the NDA;
- payment of user fees and FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements, such as REMS and post-approval studies required by FDA.

Pre-clinical Studies

The data required to support an NDA is generated in two distinct development stages: pre-clinical and clinical. For new chemical entities, or NCEs, the pre-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, evaluating purity and stability, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the pre-clinical tests must comply with federal regulations, including good laboratory practices. The sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor must resolve with the FDA any outstanding concerns or questions before the clinical trial can begin. Some long-term pre-clinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, submission of an IND does not guarantee the FDA will allow clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

Clinical Studies

The clinical stage of development involves the administration of the drug product to human subjects or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that, in general, all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also reviews and approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. For example, information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Clinical trials are generally conducted in three sequential phases that may overlap or be combined, known as Phase I, Phase II and Phase III clinical trials.

- Phase I: In a standard Phase I clinical trial, the drug is initially introduced into a small number of subjects who are initially exposed to a range of doses of the drug candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, appropriate dosing, side effect tolerability and safety of the drug.

    - Phase Ib: Although Phase I clinical trials are not intended to treat disease or illness, a Phase Ib trial is conducted in patient populations who have been diagnosed with the disease for which the study drug is intended. The patient population typically demonstrates a biomarker, surrogate, or other clinical outcome that can be assessed to show "proof-of-concept." In a Phase Ib study, proof-of-concept typically confirms a hypothesis that the current prediction of a biomarker, surrogate or other outcome benefit is compatible with the mechanism of action of the study drug.

    - Phase I/II: A Phase I and Phase II trial for the same treatment is combined into a single study protocol. The drug is administered first to determine a maximum tolerable dose, and then additional patients are treated in the Phase II portion of the study to further assess safety and/or efficacy.

- Phase II: The drug is administered to a limited patient population to determine dose tolerance and optimal dosage required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy.

- Phase III: The drug is administered to an expanded number of patients, generally at multiple sites that are geographically dispersed, in well-controlled clinical trials to generate enough data to demonstrate the efficacy of the drug for its intended use, its safety profile, and to establish the overall benefit/risk profile of the drug and provide an adequate basis for drug approval and labeling of the drug product. Phase III clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a drug during marketing. Generally, two adequate and well-controlled Phase III clinical trials are required by the FDA for approval of an NDA. A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the drug. Generally, pivotal studies are also Phase III studies but may be Phase II studies if the trial design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need. Phase IV clinical trials are conducted after initial regulatory approval, and they are used to collect additional information from the treatment of patients in the intended therapeutic indication or to meet other regulatory requirements. In certain instances, FDA may mandate the performance of Phase IV clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk to human subjects. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. The FDA will typically inspect one or more clinical sites to assure compliance with GCPs and the integrity of the clinical data submitted. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, cGMPs impose extensive procedural, substantive and recordkeeping requirements to ensure and preserve the long-term stability and quality of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA Submission and FDA Review Process

Following trial completion, trial results and data are analyzed to assess safety and efficacy. The results of pre-clinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling for the drug, information about the manufacturing process and facilities that will be used to ensure drug quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain adequate evidence of safety and efficacy, which is demonstrated by extensive pre-clinical and clinical testing. The application includes both negative or ambiguous results of pre-clinical and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a drug, or from a number of alternative sources, including studies initiated by investigators. To support regulatory approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug product to the satisfaction of the FDA. Under federal law, the submission of most NDAs is subject to the payment of an application user fees; a waiver of such fees may be obtained under certain limited circumstances. FDA approval of an NDA must be obtained before a drug may be offered for sale in the United States.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by an application user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2021, the user fee for an application requiring clinical data, such as an NDA, is $2,875,842. PDUFA also imposes a program fee for prescription human drugs $336,432. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication. The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA conducts a preliminary review of an NDA within 60 days of receipt and informs the sponsor by the 74^{th} day after FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months from the filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the filing date for a "priority review" NDA. The FDA does not always meet its PDUFA goal dates for standard and priority review NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed drug is safe and effective for its intended use, and whether the drug is being manufactured in accordance with cGMP to assure and preserve the drug's identity, strength, quality and purity. The FDA may refer applications for drugs or drug candidates that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA may re-analyze the clinical trial data, which can result in extensive discussions between the FDA and us during the review process.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new drug to determine whether they comply with cGMPs. The FDA will not approve the drug unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the drug within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities where the drug product and/or its active pharmaceutical ingredient will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

If a drug receives regulatory approval, the approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited. Further, the FDA may require that certain contraindications, warnings or precautions be included in the drug labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved drugs. For example, the FDA may require Phase IV testing which involves clinical trials designed to further assess a drug's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved drugs that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a REMS to ensure that the benefits of a drug or biological product outweigh its risks. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of drugs. Drug approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA, which authorizes FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. Section 505(b)(2) allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations relied upon to show that the drug is safe and effective for the intended use "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain pre-clinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the pre-clinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." The Generic Drug User Fee Act (GDUFA), as reauthorized, sets forth performance goals for the FDA to review standard ANDA's within 10 months of their submission, and priority ANDA's within 8 months of their submission if they satisfy certain requirements.

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider an "AB" therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, FDA's designation of an "AB" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval, priority review and Breakthrough Therapy Designation, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. While these pathways can reduce the time it takes for the FDA to review an NDA, they do not guarantee that a product will receive FDA approval. In addition, the Right to Try Act of 2018 established a new regulatory pathway to increase access to unapproved, investigational treatments for patients diagnosed with life-threatening diseases or conditions who have exhausted approved treatment options and who are unable to participate in a clinical trial.

Fast Track Designation

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a drug is intended to treat a serious or life threatening disease or condition for which there is no effective treatment and demonstrates the potential to address an unmet medical need for the disease or condition. Under the fast track program, the sponsor of a drug candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the drug candidate. The FDA must make a fast track designation determination within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. A fast track drug also may be eligible for accelerated approval and priority review. In addition, the fast track designation may be withdrawn by the FDA if it believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority Review

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of 10 months under current PDUFA guidelines. These 6- and 10-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

Breakthrough Therapy Designation

Under the provisions of the new Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted by Congress in 2012, a sponsor can request designation of a drug candidate as a "breakthrough therapy," typically by the end of the drug's Phase II trials. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. For breakthrough therapies, the FDA may take certain actions, such as intensive and early guidance on the drug development program, that are intended to expedite the development and review of an application for approval.

Accelerated Approval

FDASIA also codified and expanded on FDA's accelerated approval regulations, under which FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit over existing treatments based on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. A surrogate endpoint is a marker that does not itself measure clinical benefit but is believed to predict clinical benefit. This determination takes into account the severity, rarity or prevalence of the disease or condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform Phase IV or post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for the FDA review or approval will not be shortened. Furthermore, fast track designation, priority review, accelerated approval and Breakthrough Therapy Designation, do not change the standards for approval and may not ultimately expedite the development or approval process.

Pediatric Trials

Under PREA, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With the enactment of FDASIA, a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must also submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase II meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early phase clinical trials, and/or other clinical development programs. The law requires the FDA to send a non-compliance letter to sponsors who do not submit their pediatric assessments as required.

Under the Best Pharmaceuticals for Children Act, or BPCA, certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested by the FDA, relating to the use of the active moiety of the product candidate in children. Although the FDA may issue a written request for studies on either approved or unapproved indications, it may only do so where it determines that information relating to that use of a product candidate in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

FDASIA permanently reauthorized PREA and BPCA, modifying some of the requirements under these laws, and established priority review vouchers for rare pediatric diseases. Pursuant to the Consolidated Appropriations Act of 2021, the FDA's authority to award rare pediatric disease vouchers has been extended until September 30, 2024, and until September 30, 2026 for products that receive rare pediatric disease designation by September 30, 2024.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, but the product will be entitled to orphan product exclusivity, meaning that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives regulatory approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. The 21st Century Cures Act, which became law in December 2016, expanded the types of studies that qualify for orphan drug grants. Orphan drug designation also may qualify an applicant for federal and possibly state tax credits relating to research and development costs.

Post-Marketing Requirements

Following approval of a new drug, a pharmaceutical company and the approved drug are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the drug, providing the regulatory authorities with updated safety and efficacy information, drug sampling and distribution requirements, and complying with applicable promotion and advertising requirements.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion, including standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may legally prescribe drugs for off-label uses, manufacturers may not market or promote such off-label uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Modifications or enhancements to the drug or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process. Any distribution of prescription drugs and pharmaceutical samples also must comply with the U.S. Prescription Drug Marketing Act, a part of the FDCA.

In the United States, once a drug is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that drugs be manufactured in specific approved facilities and in accordance with cGMP. Applicants may also rely on third parties for the production of clinical and commercial quantities of drugs, and these third parties must operate in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using third-party contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute drugs manufactured, processed or tested by them. Discovery of problems with a drug after approval may result in restrictions on a drug, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the drug from the market, and may require substantial resources to correct.

The FDA also may require Phase IV testing, risk minimization action plans and post-marketing surveillance to monitor the effects of an approved drug or place conditions on an approval that could restrict the distribution or use of the drug. Discovery of previously unknown problems with a drug or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our drugs under development.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Department of Justice, Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration for Controlled Substances, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Affordable Care Act. If drugs are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Drugs must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical drugs is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical drugs.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of drugs, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In 2018, the FDA advanced policies aimed at promoting drug competition and patient access to generic drugs, such as issuing guidance about making complex generic drugs and the circumstances in which approval of a generic product application may be delayed.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a NCE. A drug is a NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. Specifically, the applicant must certify with respect to each relevant patent that: the required patent information has not been filed; the listed patent has expired; the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration, or the listed patent is invalid, unenforceable or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant. To the extent that the Section 505(b)(2) applicant relies on prior FDA findings of safety and efficacy, the applicant is required to certify to the FDA concerning any patents listed for the previously approved product in the Orange Book to the same extent that an ANDA applicant would.

The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the pre-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Rest of the World Regulation of Pharmaceutical Product Development and Approval

For other countries outside of China and the United States, such as countries in Europe, Latin America or other parts of Asia, the requirements governing the conduct of clinical trials, drug licensing, pricing and reimbursement vary from country to country. In all cases the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and ethical principles.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Coverage and Reimbursement

PRC Coverage and Reimbursement

Historically, most of Chinese healthcare costs have been borne by patients out-of-pocket, which has limited the growth of more expensive pharmaceutical products. However, in recent years the number of people covered by government and private insurance has increased. According to the NHC, as of December 31, 2021, approximately 1.4 billion residents in China were enrolled in the national medical insurance program, with participation rates remaining steadily above 95%. In 2021, total income of the National Basic Medical Insurance Fund (including maternity insurance) reached RMB2,873.2 billion, an increase of 15.6% over the previous year.

Reimbursement under the National Medical Insurance Program

The National Medical Insurance Program was adopted pursuant to the Decision of the State Council on the Establishment of the Urban Employee Basic Medical Insurance Program issued by the State Council on December 14, 1998, under which all employers in urban cities are required to enroll their employees in the basic medical insurance program and the insurance premium is jointly contributed by the employers and employees. The State Council promulgated Guiding Opinions of the State Council about the Pilot Urban Resident Basic Medical Insurance on July 10, 2007, under which urban residents of the pilot district, rather than urban employees, may voluntarily join Urban Resident Basic Medical Insurance. The State Council expected the Pilot Urban Resident Basic Medical Insurance to cover the whole nation by 2010.

Participants of the National Medical Insurance Program and their employers, if any, are required to contribute to the payment of insurance premiums on a monthly basis. Program participants are eligible for full or partial reimbursement of the cost of medicines included in the NRDL. The Notice Regarding the Tentative Measures for the Administration of the Scope of Medical Insurance Coverage for Pharmaceutical Products for Urban Employees, jointly issued by several authorities including the Ministry of Labor and Social Security and the MOF, among others, on May 12, 1999, provides that a pharmaceutical product listed in the NRDL must be clinically needed, safe, effective, reasonably priced, easy to use, available in sufficient quantity, and must meet the following requirements:

- it is set forth in the Pharmacopoeia of the PRC;
- it meets the standards promulgated by the NMPA; and
- if imported, it is approved by the NMPA for import.

Factors that affect the inclusion of a pharmaceutical product in the NRDL include whether the product is consumed in large volumes and commonly prescribed for clinical use in the PRC and whether it is considered to be important in meeting the basic healthcare needs of the general public.

The PRC Ministry of Labor and Social Security, together with other government authorities, has the power to determine inclusion of medicines in the NRDL (also referred to as the “Drug Catalog”), which is divided into two parts, Category A and Category B. Per the Notice on the “National Basic Medical Insurance, Work Injury Insurance and Maternity Insurance Drug Catalog (2022)” issued by the National Healthcare Security Administration and the Ministry of Labor and Social Security, local authorities are required to strictly implement the Drug Catalog (2022) and must not adjust the categories of drugs, remarks and the classification of drugs in the Drug Catalog.

Patients purchasing medicines included in Category A of the NRDL are entitled to reimbursement of the entire amount of the purchase price. Patients purchasing medicines included in Category B of the NRDL are required to pay a certain percentage of the purchase price and obtain reimbursement for the remainder of the purchase price. The percentage of reimbursement for Category B medicines differs from region to region in the PRC.

The total amount of reimbursement for the cost of medicines, in addition to other medical expenses, for an individual participant under the National Medical Insurance Program in a calendar year is capped at the amounts in such participant's individual account under such program. The amount in a participant's account varies, depending on the amount of contributions from the participant and his or her employer.

National Essential Medicines List

On August 18, 2009, MOH and eight other ministries and commissions in the PRC issued the Provisional Measures on the Administration of the National Essential Medicines List, which was later amended in 2015, and the Guidelines on the Implementation of the Establishment of the National Essential Medicines System, which aim to promote essential medicines sold to consumers at fair prices in the PRC and ensure that the general public in the PRC has equal access to the drugs contained in the National Essential Medicines List. MOH promulgated the National Essential Medicines List (Catalog for the Basic Healthcare Institutions) on August 18, 2009, and promulgated the revised National Essential Medicines List on March 13, 2013 and September 30, 2018. According to these regulations, basic healthcare institutions funded by government, which primarily include county-level hospitals, county-level Chinese medicine hospitals, rural clinics and community clinics, shall store up and use drugs listed in the National Essential Medicines List. Per the Opinions of the General Office of the State Council on Improving the National Essential Medicines System, issued and effective on September 13, 2018, with respect to the qualifying drugs on the National Essential Medicines List, the medical insurance department shall prioritize their inclusion in the NDRL and adjust their classifications as Category A or B, respectively, in accordance with the stipulated procedures.

Price Controls

According to the PRC Drug Administration Law and the PRC Drug Administration Law Implementation Regulations, pharmaceutical products are subject to a directive pricing system or to be adjusted by the market. Per the Notice of the National Healthcare Security Administration on issuing the "Opinions on Doing a Good Job in the Current Drug Price Management", or the Notice on Current Drug Price Management, effective on November 26, 2019, government guidance prices are to be implemented for narcotic drugs and Class I psychotropic drugs, while prices of other drugs are to be determined by the market. Government guidance prices refer to prices as fixed by business operators according to benchmark prices and ranges of the prices as set by the government department in charge of pricing or other related departments. According to the Pricing Catalogue Initiated by the Central Government (2020 Edition), which was promulgated by the NDRC and effective on May 1, 2020, the National Healthcare Security Administration shall be responsible for setting prices of narcotic drugs and Class I psychotropic drugs.

Further, pursuant to the Notice Regarding Further Improvement of the Order of Market Price of Pharmaceutical Products and Medical Services, or the Market Price Notice, jointly promulgated by the NDRC, the State Council Legislative Affairs Office and the State Council Office for Rectifying, the MOH, the NMPA, the MOFCOM, the MOF and Ministry of Labor and Social Security on May 19, 2006, the PRC government exercises price control over pharmaceutical products included in the NRDL and made an overall adjustment of their prices by reducing the retail price of certain overpriced pharmaceutical products and increasing the retail price of certain underpriced pharmaceutical products in demand for clinical use but that have not been produced in large quantities by manufacturers due to their low retail price level. In particular, the retail price charged by hospitals at the county level or above may not exceed 115% of the procurement cost of the relevant pharmaceutical products or 125% for Chinese herbal pieces. The Market Price Notice has been abolished per the NDRC Decision to Abolish Standardized Pricing Directories, effective May 20, 2021.

On February 9, 2015, the General Office of the State Council issued the Guiding Opinion on Enhancing Consolidated Procurement of Pharmaceutical Products by Public Hospitals, or the Opinion. The Opinion encourages public hospitals to consolidate their demands and to play a more active role in the procurement of pharmaceutical products. Hospitals are encouraged to directly settle the prices of pharmaceutical products with manufacturers. Consolidated procurement of pharmaceutical products should facilitate hospital reform, reduce patient costs, prevent corrupt conducts, promote fair competition and induce the healthy growth of the pharmaceutical industry. According to the Opinion, provincial tendering processes will continue to be used for the pricing of essential drugs and generic drugs with significant demands, and transparent multi-party price negotiation will be used for some patented drugs and exclusive drugs.

On April 26, 2014, the NDRC issued the Notice on Issues concerning Improving the Price Control of Low Price Drugs, or the Low Price Drugs Notice, together with the Low Price Drug List, or LPDL. According to the Low Price Drugs Notice, for drugs with relatively low average daily costs within the current government-guided pricing scope (low price drugs), the maximum retail prices set by the government were cancelled. Within the standards of average daily costs, the specific purchase and sale prices are fixed by the producers and operators based on the drug production costs, market supply and demand and market competition. The standards of average daily costs of low price drugs were determined by the NDRC in consideration of the drug production costs, market supply and demand and other factors and based on the current maximum retail prices set by the government (or the national average bid-winning retail prices where the government does not set the maximum retail prices) and the average daily dose calculated according to the package insert. Under the Low Price Drugs Notice, the standards for the daily cost of low price chemical pharmaceuticals and of low price traditional Chinese medicine pharmaceuticals were less than RMB3.0 ($0.46) per day and RMB5.0 ($0.76) per day respectively. The Low Price Drugs Notice has been abolished per the NDRC Decision to Abolish Standardized Pricing Directories, effective May 20, 2021.

On May 4, 2015, the NDRC, the National Health and Family Planning Commission, the NMPA, MOFCOM and three other departments issued Opinions on Promoting Drug Pricing Reform. Under these opinions, beginning on June 1, 2015, the restrictions on the prices of the drugs that were subject to government pricing were cancelled except for narcotic drugs and Class I psychotropic drugs which remained subject to maximum factory prices and maximum retail prices set by the NDRC, and following the November 2019 Notice on Current Drug Price Management, narcotic drugs and Class I psychotropic drugs prices have transitioned towards government guidance prices. The medical insurance regulatory authority now has the power to prescribe the standards, procedures, basis and methods of the payment for drugs paid by medical insurance funds. The prices of patented drugs are set through transparent and public negotiation among multiple parties. The prices for blood products not listed in the NRDL, immunity and prevention drugs that are purchased by the Chinese government in a centralized manner, and AIDS antiviral drugs and contraceptives provided by the Chinese government for free, are set through a tendering process. Except as otherwise mentioned above, the prices for other drugs may be determined by the manufacturers and the operators on their own on the basis of production or operation costs and market supply and demand.

Centralized Procurement and Tenders

The Guiding Opinions concerning the Urban Medical and Health System Reform, promulgated on February 21, 2000, aim to provide medical services with reasonable price and quality to the public through the establishment of an urban medical and health system. One of the measures used to realize this aim is the regulation of the purchasing process of pharmaceutical products by medical institutions. Accordingly, the MOH and other relevant government authorities have promulgated a series of regulations and releases in order to implement the tender requirements.

According to the Notice on Issuing Certain Regulations on the Trial Implementation of Centralized Tender Procurement of Drugs by Medical Institutions promulgated on July 7, 2000 and the Notice on Further Improvement on the Implementation of Centralized Tender Procurement of Drugs by Medical Institutions promulgated on August 8, 2001, medical institutions established by county or higher level government are required to implement centralized tender procurement of drugs.

The MOH promulgated the Working Regulations of Medical Institutions for Procurement of Drugs by Centralized Tender and Price Negotiations (for Trial Implementation), or the Centralized Procurement Regulations, on March 13, 2002, and promulgated Sample Document for Medical Institutions for Procurement of Drugs by Centralized Tender and Price Negotiations (for Trial Implementation), or the Centralized Tender Sample Document in November 2001, as amended in 2010, to implement the tender process requirements and ensure the requirements are followed uniformly throughout the country. The Centralized Tender Regulations and the Centralized Tender Sample Document provide rules for the tender process and negotiations of the prices of drugs, operational procedures, a code of conduct and standards or measures of evaluating bids and negotiating prices. On January 17, 2009, the MOH, the NMPA and other four national departments jointly promulgated the Opinions on Further Regulating Centralized Procurement of Drugs by Medical Institutions. According to the notice, public medical institutions owned by the government at the county level or higher or owned by state-owned enterprises (including state-controlled enterprises) shall purchase pharmaceutical products through centralized procurement. Each provincial government shall formulate its catalogue of drugs subject to centralized procurement. Specifically, the procurement could be achieved through public tendering, online bidding, centralized price negotiations and online competition platform. Except for drugs in the National Essential Medicines List (the procurement of which shall comply with the relevant rules on the National Essential Medicines List), certain pharmaceutical products which are under the national government's special control and traditional Chinese medicines, in principle, all drugs used by public medical institutions shall be covered by the catalogue of drugs subject to centralized procurement. On July 7, 2010, the MOH and six other ministries and commissions jointly promulgated the Working Regulations of Medical Institutions for Centralized Procurement of Drugs to further regulate the centralized procurement of drugs and clarify the code of conduct of the parties in centralized drug procurement.

The centralized tender process takes the form of public tender operated and organized by provincial or municipal government agencies in principle is conducted once every year in all provinces and cities in China. Drug manufacturing enterprises, in principle, shall bid directly for the centralized tender process. Certain related parties, however, may be engaged to act as bidding agencies. Such intermediaries are not permitted to engage in the distribution of drugs and must have no conflict of interest with the organizing government agencies. The bids are assessed by a committee composed of pharmaceutical experts who will be randomly selected from a database of experts approved by the relevant government authorities. The committee members assess the bids based on a number of factors, including but not limited to, bid price, product quality, clinical effectiveness, qualifications and reputation of the manufacturer, and after-sale services. Only pharmaceuticals that have won in the centralized tender process may be purchased by public medical institutions funded by government in the relevant region.

4+7 Quality Consistency Evaluation

On November 15, 2018, China's Joint Procurement Office published its Paper on Centralized Drug Procurement in "4+7 Cities," known as the 4+7 Quality Consistency Evaluation process, or 4+7 QCE. The 4+7 QCE initiative is aimed at driving consolidation in the fragmented generic drug market in China. The 4+7 QCE initiative began as a pilot program in 11 cities: Beijing, Tianjin, Shanghai, Chongqing, Shenyang, Dalian, Xiamen, Guangzhou, Shenzhen, Chengdu and Xi'an. Under this pilot program, the public medical institutions in these 11 cities bulk-buy certain generic drugs together, forcing companies to bid for contracts and driving down prices. The 4+7 QCE initiative has expanded nationwide and now covers more varieties of drugs. On September 1, 2019, the Joint Procurement Office published its Paper on Centralized Drug Procurement in Alliance Areas (GY-YD2019-1), such areas covering 25 provinces and regions across China. On December 29, 2019, the Joint Procurement Office published its Paper on Nationwide Centralized Drug Procurement (GY-YD2019-2), promoting procurement nationwide, and on January 13, 2020, the National Healthcare Security Administration, the NHC, the NMPA, the Ministry of Industrial and Information Technology and the Logistics Support Department of the Central Military Commission promulgated the Notice on the Commencement of the Second Batch of State Organized Centralized Drug Procurement and Use, which states that the second batch of national organization of centralized procurement and use of drugs would not be carried out in selected areas but nationwide. On January 22, 2021, the General Office of the State Council issued the Opinions on Promoting the Normalization and Institutionalization of the Centralized and Quantitative Procurement of Drugs, stating that (i) the scope of procurement should focus on including drugs in the NDRL with large dosages and high purchase amounts and gradually cover all kinds of drugs that are clinically necessary and of reliable quality that are marketed in China, so as to ensure that all drugs that should be procured are exhausted, (ii) marketing authorization holders who have obtained drug registration certificates for drugs within the scope of centralized procurement can, in principle, participate in centralized drug procurement, provided they meet the requirements of centralized procurement in areas including but not limited to quality standards, production capacity and supply stability, and (iii) all public medical institutions (including military medical institutions) should participate in centralized drug procurement, and designated pharmacies shall follow the management requirements of designated agreements.

U.S. Coverage and Reimbursement

Successful sales of our products or drug candidates in the U.S. market, if approved, will depend, in part, on the extent to which our drugs will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. Patients who are provided with prescriptions as part of their medical treatment generally rely on such third-party payors to reimburse all or part of the costs associated with their prescriptions and therefore adequate coverage and reimbursement from such third-party payors are critical to new product success. These third-party payors are increasingly reducing reimbursements for medical drugs and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, requirements for substitution of generic drugs, and pricing transparency requirements. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug candidates, if approved, or a decision by a third-party payor to not cover our drug candidates could reduce physician usage of such drugs and have a material adverse effect on our sales, results of operations and financial condition.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Medicare payment for some of the costs of prescription drugs may increase demand for drugs for which we receive regulatory approval. However, any negotiated prices for our drugs covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the U.S. Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, if third-party payors do not consider a drug to be cost-effective compared to other available therapies, they may not cover such drugs as a benefit under their plans or, if they do, the level of payment may not be sufficient.

The Affordable Care Act, enacted in March 2010, has had a significant impact on the health care industry. The Affordable Care Act expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the Affordable Care Act, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which, beginning in 2019, manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. The Bipartisan Budget Act of 2018 made certain changes to Medicare Part D coverage, including changing the date when the Medicare Part D coverage gap is eliminated from 2020 to 2019, sunsetting the exclusion of biosimilars from the Medicare Part D coverage gap discount program in 2019 and reallocating responsibility for discounted pricing under the Medicare Part D coverage gap discount program from third-party payors to pharmaceutical companies. In December 2017, Congress also repealed the "individual mandate," which was an Affordable Care Act requirement that individuals obtain healthcare insurance coverage or face a penalty. This repeal could affect the total number of patients who have coverage from third-party payors that reimburse for use of our products. In July 2021, the U.S. Supreme Court dismissed a constitutional challenge to the Affordable Care Act brought by a group of Republican attorneys general seeking to invalidate the law in its entirety because of Congress's repeal of the individual mandate.

On December 14, 2018, a U.S. District Court judge in Texas ruled that the Affordable Care Act is unconstitutional in its entirety because of Congress's repeal of the individual mandate. On December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit affirmed the portion of the district court's ruling declaring the individual mandate unconstitutional and remanded for the district court to conduct analysis in the first instance on which provisions of the statute are severable from it and thus remain intact. The U.S. Supreme Court agreed to hear the case and a decision is expected by the spring of 2021.

In addition, other legislative and regulatory changes have been proposed and adopted in the United States since the Affordable Care Act was enacted that affect reimbursement for prescription drugs. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013. Section 4408 of the CARES Act temporarily suspended Medicare sequestration during the period of May 1, 2020 through December 31, 2021, while extending the Medicare sequestration sunset date through 2030. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Regulations adopted by the Centers for Medicare & Medicaid Services or CMS grant Medicare Part B plans authority to apply new cost control measures to steer patients toward lower-priced drug products prior to covering non-preferred, more expensive products. This could potentially have the result of reducing coverage of our products under Medicare Part B.

In addition, other proposed legislative and regulatory changes could affect reimbursement for prescription drugs. In January 2017, the Medicare Prescription Drug Price Negotiation Act was proposed in Congress, which would require the government to negotiate Medicare prescription drug prices with pharmaceutical companies. In October 2017, a similar bill, the Medicare Drug Price Negotiation Act of 2017 was proposed in Congress. In November 2017, the CMS announced a Final Rule that would adjust the applicable payment rate as necessary for certain separately payable drugs and biologicals acquired under the 340B Program from average sales price plus 6% to average sales price minus 22.5%. Congress and the U.S. administration continue to evaluate other proposals that could affect third-party reimbursement for our drug candidates, if approved.

In October 2020, the U.S. Department of Health and Human Services and the FDA issued a final rule and guidance concerning two new pathways for importing lower-cost drugs into the United States. The final rule allows certain prescription drugs to be imported from Canada, and the guidance describes procedures for drug manufacturers to facilitate the importation of FDA-approved drugs and biologics manufactured abroad and originally intended for sale in a foreign country into the United States.

In November 2020, the Department of Health and Human Services, under the outgoing Trump administration, issued a rule eliminating the safe harbor shielding Medicare Part D rebates to pharmacy benefit managers from the Anti-Kickback Statute. In response to litigation brought by a trade association on behalf of pharmacy benefit managers, the Biden administration agreed to delay the rule’s effective date until January 1, 2023. On November 15, 2021, President Biden signed into law the Infrastructure Investment and Jobs Act, which imposed a moratorium until January 1, 2026 at the earliest on the rule removing rebates from safe harbor protection under the Anti-Kickback Statute.

In November 2021, the U.S. House of Representatives passed the Build Back Better Act. Under this Act, the federal government would be permitted to negotiate prices for certain Medicare Part B and Part D drugs, and manufacturers would be required to pay Medicare rebates for some Part B and many Part D drugs if their prices increased faster than inflation. To date, the U.S. Senate has not passed the Act, and it is unclear whether the Act or component parts of the Act will ultimately be enacted. Such legislative and regulatory changes could have the effect of lowering the level of coverage or reimbursement for our products.

Rest of the World Coverage and Reimbursement

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the E.U. provides options for its member states to restrict the range of medicinal drugs for which their national health insurance systems provide reimbursement and to control the prices of medicinal drugs for human use. A member state may approve a specific price for the medicinal drug or it may instead adopt a system of direct or indirect controls on the profitability of our company placing the medicinal drug on the market. Historically, drugs launched in the E.U. do not follow price structures of the United States and generally tend to be significantly lower.

Other Healthcare Laws

Other PRC Healthcare Laws

Advertising of Pharmaceutical Products

In accordance with the Interim Administrative Measures for the Censorship of Advertisements for Drugs, Medical Devices, Health Food and Formula Food for Special Medical Purposes effective from March 1, 2020, the State Administration for Market Regulation is responsible for organizing and guiding the censorship of advertisements for drugs, medical devices, health foods and formula foods for special medical purposes. Any advertisement for drugs, medical devices, health food or formula food for special medical purposes shall indicate the advertisement approval number in a prominent position. The validity period of the advertisement approval number for drugs, medical devices, health food and formula food for special medical purposes shall be consistent with the shortest period of validity of the product registration certificate, record-filing certificate, or production license. Where no period of validity is prescribed in the product registration certificate, record-filing certificate or production license, the period of validity of the advertisement approval number shall be two years.

Packaging of Pharmaceutical Products

According to the Measures for The Administration of Pharmaceutical Packaging, effective on September 1, 1988, pharmaceutical packaging must comply with the provisions of the national standard and professional standard. If there are no standards, the enterprise can formulate its own standard after obtaining the approval of the provincial level drug administration or bureau of standards. The enterprise shall reapply to the relevant authorities if it needs to change the packaging standard. Drugs without packing must not be sold in PRC (except for drugs needed by the army).

Labor Protection

Under the Labor Law of the PRC, effective on January 1, 1995 and subsequently amended on August 27, 2009 and December 29, 2018, the Labor Contract Law of the PRC, effective on January 1, 2008 and subsequently amended on December 28, 2012, and the Implementing Regulations of the Labor Contract Law of the PRC, effective on September 18, 2008, employers must establish a comprehensive management system to protect the rights of their employees, including a system governing occupational health and safety to provide employees with occupational training to prevent occupational injury, and employers are required to truthfully inform prospective employees of the job description, working conditions, location, occupational hazards and status of safe production as well as remuneration and other conditions as requested by the Labor Contract Law of the PRC.

Pursuant to the Law of Manufacturing Safety of the People's Republic of China effective on November 1, 2002 and subsequently amended on December 1, 2014 and September 1, 2021, manufacturers must establish a comprehensive management system to ensure manufacturing safety in accordance with applicable laws and regulations. Manufacturers not meeting relevant legal requirements are not permitted to commence their manufacturing activities.

Pursuant to the Administrative Measures for Production effective on March 1, 2011, manufacturers of pharmaceutical products are required to establish production safety and labor protection measures in connection with the operation of their manufacturing equipment and manufacturing process.

Pursuant to applicable PRC laws, rules and regulations, including the Social Insurance Law which became effective on July 1, 2011 and subsequently amended on December 29, 2018, the Interim Regulations on the Collection and Payment of Social Security Funds which became effective on January 22, 1999 and subsequently amended on March 24, 2019, the Interim Measures concerning the Maternity Insurance which became effective on January 1, 1995 and the Regulations on Work-related Injury Insurance which became effective on January 1, 2004 and were subsequently amended on December 20, 2010, employers are required to contribute, on behalf of their employees, to a number of social security funds, including funds for basic pension insurance, unemployment insurance, basic medical insurance, work-related injury insurance, and maternity insurance. If an employer fails to make social insurance contributions timely and in full, the social insurance collecting authority will order the employer to make up outstanding contributions within the prescribed time period and impose a late payment fee at the rate of 0.05% per day from the date on which the contribution becomes due. If such employer fails to make social insurance registration, the social insurance collecting authority will order the employer to correct within the prescribed time period. The relevant administrative department may impose a fine equivalent to three times the overdue amount and management personnel who are directly responsible can be fined RMB500 ($76.43) to RMB3,000 ($458.02) if the employer fails to correct within the prescribed time period.

Commercial Bribery

Medical production and operation enterprises involved in criminal, investigation or administrative procedure for commercial bribery will be listed in the Adverse Records of Commercial Briberies by provincial health and family planning administrative department. Pursuant to the Provisions on the Establishment of Adverse Records of Commercial Briberies in the Medicine Purchase and Sales Industry issued by the National Health and Family Planning Commission and effective on March 1, 2014, if medical production and operation enterprises are listed into the Adverse Records of Commercial Briberies for the first time, their production shall not be purchased by public medical institutions, and medical and health institutions receiving financial subsidies in local provincial regions for a period of two years following the publication of the Adverse Records, and public medical institutions, and medical and health institutions receiving financial subsidies in other provinces shall lower their rating in bidding or purchasing process. If medical production and operation enterprises are listed into the Adverse Records of Commercial Briberies twice or more times in five years, their production may not be purchased by public medical institutions, and medical and health institutions receiving financial subsidies nationwide in two years from public of the record.

As advised by our PRC legal advisor, from a PRC law perspective, a pharmaceutical company will not be penalized by the relevant PRC government authorities merely by virtue of having contractual relationships with distributors or third-party promoters who are engaged in bribery activities, so long as such pharmaceutical company and its employees are not utilizing the distributors or third-party promoters for the implementation of, or acting in conjunction with them in, the prohibited bribery activities. In addition, a pharmaceutical company is under no legal obligation to monitor the operating activities of its distributors and third-party promoters, and will not be subject to penalties or sanctions by relevant PRC government authorities as a result of failure to monitor their operating activities.

Product Liability

In addition to the strict new drug approval process, certain PRC laws have been promulgated to protect the rights of consumers and to strengthen the control of medical products in the PRC. Under current PRC law, manufacturers and vendors of defective products in the PRC may incur liability for loss and injury caused by such products. Pursuant to the Civil Code of the PRC, or the PRC Civil Code, promulgated on May 28, 2020 and effective on January 1, 2021, a defective product which causes property damage or physical injury to any person may subject the manufacturer or vendor of such product to civil liability for such damage or injury.

On February 22, 1993, the Product Quality Law of the PRC, or the Product Quality Law, was promulgated aiming to define responsibilities for product quality, to protect the legitimate rights and interests of the end-users and consumers and to strengthen the supervision and control of the quality of products. The Product Quality Law was amended by the Ninth National People’s Congress on July 8, 2000 and was later amended by the Eleventh National People’s Congress on August 27, 2009 and the Thirteenth National People’s Congress on December 29, 2018. Pursuant to the amended Product Quality Law, manufacturers who produce defective products may be subject to civil or criminal liability and have their business licenses revoked.

The Law of the PRC on the Protection of the Rights and Interests of Consumers was promulgated on October 13, 1993 and was amended on October 25, 2013 to protect consumers’ rights when they purchase or use goods and accept services. All business operators must comply with this law when they manufacture or sell goods and/or provide services to customers. Under the amendment on October 25, 2013, all business operators shall pay high attention to protect the customers’ privacy which they obtain during the business operation. In addition, in extreme situations, pharmaceutical product manufacturers and operators may be subject to criminal liabilities under applicable laws of the PRC if their goods or services lead to the death or injuries of customers or other third parties.

Pursuant to the PRC Civil Code, if damages to other persons are caused by defective products that are resulted from the fault of a third party such as the parties providing transportation or warehousing, the producers and the sellers of the products have the right to recover their respective losses from such third parties. If defective products are identified after they have been put into circulation, the producers or the sellers shall take remedial measures such as issuance of warning, and recall of products, etc. in a timely manner. The producers or the sellers shall be liable under tort if they cause damages due to their failure to take remedial measures in a timely manner or have not made efforts to take remedial measures, thus causing damages. If the products are produced and sold with known defects, causing deaths or severe damage to the health of others, the infringed party shall have the right to claim respective punitive damages in addition to compensatory damages.

Other PRC National and Provincial-Level Laws and Regulations

We are subject to changing regulations under many other laws and regulations administered by governmental authorities at the national, provincial and municipal levels, some of which are or may become applicable to our business. Our hospital customers are also subject to a wide variety of laws and regulations that could affect the nature and scope of their relationships with us.

For example, regulations control the confidentiality of patients' medical information and the circumstances under which patient medical information may be released for inclusion in our databases, or released by us to third parties. These laws and regulations governing both the disclosure and the use of confidential patient medical information may become more restrictive in the future.

We also comply with numerous additional state and local laws relating to matters such as safe working conditions, manufacturing practices, environmental protection and fire hazard control. We believe that we are currently in compliance with these laws and regulations; however, we may be required to incur significant costs to comply with these laws and regulations in the future. Unanticipated changes in existing regulatory requirements or adoption of new requirements could therefore have a material adverse effect on our business, results of operations and financial condition.

Other U.S. Healthcare Laws

We may also be subject to healthcare regulation and enforcement by the U.S. federal government and the states where we may market our drug candidates, if approved. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations.

Anti-Kickback Statute

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service, or the purchase or order of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare, pharmaceutical, and biotechnology companies based on a range of financial arrangements with physicians and other healthcare industry entities. A person or entity does not need to have actual knowledge of the Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations of the Anti-Kickback Statute can result in criminal, civil, or administrative liability. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for the purposes of the federal False Claims Act.

False Claims

Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the U.S. Attorney General or as a qui tam action by a private individual in the name of the government. Analogous state law equivalents may apply and may be broader in scope than the federal requirements. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the United States, for example, in connection with the violations of the Anti-Kickback Statute, the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions and corporate resolutions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, also created new federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Payments to Physicians

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers were required to begin collecting data on August 1, 2013 and submit reports to the government by March 31, 2014 and June 30, 2014, and the 90^{th} day of each subsequent calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians. The federal government has begun to impose penalties on companies that fail to appropriately report required information.

Data Privacy and Security

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of personal health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

PRC Regulation of Foreign Currency Exchange, Offshore Investment and State-Owned Assets

PRC Foreign Currency Exchange

Foreign currency exchange regulation in China is primarily governed by the following rules:

- Foreign Currency Administration Rules (1996), as last amended on August 5, 2008, or the Exchange Rules; and
- Administration Rules of the Settlement, Sale and Payment of Foreign Exchange (1996), or the Administration Rules.

Under the Exchange Rules, the renminbi is convertible for current account items, including the distribution of dividends, interest payments, trade and service-related foreign exchange transactions. Conversion of renminbi for capital account items, such as direct investment, loan, security investment and repatriation of investment, however, is still subject to the SAFE's scrutiny.

Under the Administration Rules, foreign-invested enterprises may only buy, sell and/or remit foreign currencies at those banks authorized to conduct foreign exchange business after providing valid commercial documents and, in the case of capital account item transactions, obtaining approval from the SAFE. Capital investments by foreign-invested enterprises outside of China are also subject to limitations, which include approvals by the MOFCOM, the SAFE and the NDRC.

Pursuant to the Circular on Further Improving and Adjusting the Direct Investment Foreign Exchange Administration Policies, or Circular 59, promulgated by the SAFE on November 19, 2012, effective on December 17, 2012, and amended in 2015, 2018 and 2019, approval is not required for the opening of and payment into foreign exchange accounts under direct investment, for domestic reinvestment with legal income of foreign investors in China. Circular 59 also simplified the capital verification and confirmation formalities for Chinese foreign-invested enterprises and the foreign capital and foreign exchange registration formalities required for the foreign investors to acquire the equities of Chinese party and other items. Circular 59 further improved the administration on exchange settlement of foreign exchange capital of Chinese foreign-invested enterprises.

Foreign Exchange Registration of Offshore Investment by PRC Residents

In July 2014, the SAFE issued the Notice on Relevant Issues Concerning Foreign Exchange Administration for PRC Residents to Engage in Offshore Investment and Financing and Round Trip Investment via Special Purpose Vehicles, or Circular 37, and its implementation guidelines, which abolishes and supersedes the SAFE's Circular on Relevant Issues Concerning Foreign Exchange Administration for PRC Residents to Engage in Financing and Round Trip Investment via Overseas Special Purpose Vehicles, or Circular 75. Pursuant to Circular 37 and its implementation guidelines, PRC residents (including PRC institutions and individuals) must register with local branches of the SAFE in connection with their direct or indirect offshore investment in an overseas special purpose vehicle, or SPV, directly established or indirectly controlled by PRC residents for the purposes of offshore investment and financing with their legally owned assets or interests in domestic enterprises, or their legally owned offshore assets or interests. Such PRC residents are also required to amend their registrations with the SAFE when there is a significant change to the SPV, such as changes of the PRC individual resident's increase or decrease of its capital contribution in the SPV, or any share transfer or exchange, merger, division of the SPV. Failure to comply with the registration procedures set forth in Circular 37 may result in restrictions being imposed on the foreign exchange activities of the relevant onshore company, including the payment of dividends and other distributions to its offshore parent or affiliate, the capital inflow from the offshore entities and settlement of foreign exchange capital, and may also subject relevant onshore company or PRC residents to penalties under PRC foreign exchange administration regulations.

In February 2012, the SAFE promulgated the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Stock Incentive Plans of Overseas Publicly Listed Companies. Based on this regulation, directors, supervisors, senior management and other employees of domestic subsidiaries or branches of a company listed on an overseas stock market who are PRC citizens or who are non-PRC citizens residing in China for a continuous period of not less than one year, subject to a few exceptions, are required to register with the SAFE or its local counterparts by following certain procedures if they participate in any stock incentive plan of the company listed on an overseas stock market. Foreign exchange income received from the sale of shares or dividends distributed by the overseas listed company may be remitted into a foreign currency account of such PRC citizen or be exchanged into renminbi. Our PRC citizen employees who have been granted share options have been subject to these rules due to our admission to trading on the AIM market and the listing of our ADSs on Nasdaq.

Regulation on Investment in Foreign-invested Enterprises

Pursuant to PRC law, the registered capital of a limited liability company is the total capital contributions subscribed for by all the shareholders as registered with the company registration authority. A foreign-invested enterprise's total investment limit was previously approved by or filed with the MOFCOM or its local counterpart by reference to both its registered capital and expected investment scale. A foreign-invested enterprise was required to obtain approval from or file with the MOFCOM or its local counterpart for any increases to its total investment limit.

During 2019 and 2020, a series of reforms concerning foreign-invested enterprises came into effect, including but not limited to the Foreign Investment Law of the PRC, effective January 1, 2020; the Implementation Rules for the Foreign Investment Law, effective January 1, 2020, and Measures on Reporting of Foreign Investment Information, effective January 1, 2020. The reformed rules do not require foreign-invested enterprises to complete the abovementioned filing or approval with the MOFCOM in relation to total investment limits; rather, pursuant to Measures on Reporting of Foreign Investment Information, during enterprise incorporation and subsequent changes in commercial registration, foreign investors and foreign-invested enterprises (as applicable) shall submit investment information to the MOFCOM or its local counterpart.

The difference between the total investment limit and the registered capital of a foreign-invested enterprise or the cross-border financing risk weighted balance calculated based on a formula by the PBOC represents the foreign debt financing quota to which the foreign-invested enterprise is entitled (i.e., the maximum amount of debt which the company may borrow from a foreign lender).

In accordance with these regulations, we and our joint venture partners have contributed financing to our PRC subsidiaries and joint ventures in the form of capital contributions up to the registered capital amount and/or in the form of shareholder loans up to the foreign debt quota. According to the financing needs of our PRC subsidiaries and joint ventures, we and our joint venture partners have requested and received approvals (where necessary) from the government authorities for increases to the total investment limit for certain of our PRC subsidiaries and joint ventures from time to time. As a result, these regulations have not had a material impact to date on our ability to finance such entities.

Regulation on Dividend Distribution

The principal regulations governing distribution of dividends paid by wholly foreign-owned enterprises include:

- Company Law of the PRC (1993), as amended in 1999, 2004, 2005, 2013 and 2018;
- Foreign Investment Law of the PRC; and
- Implementation Rules for the Foreign Investment Law.
- Under these laws and regulations, foreign-invested enterprises in China may pay dividends only out of their accumulated profits, if any, determined in accordance with PRC accounting standards and regulations. In addition, a wholly foreign-owned enterprise in China is required to set aside at least 10.0% of its after-tax profit based on PRC accounting standards each year to its general reserves until the accumulative amount of such reserves reach 50.0% of its registered capital. These reserves are not distributable as cash dividends. The board of directors of a foreign-invested enterprise has the discretion to allocate a portion of its after-tax profits to staff welfare and bonus funds, which may not be distributed to equity owners except in the event of liquidation.

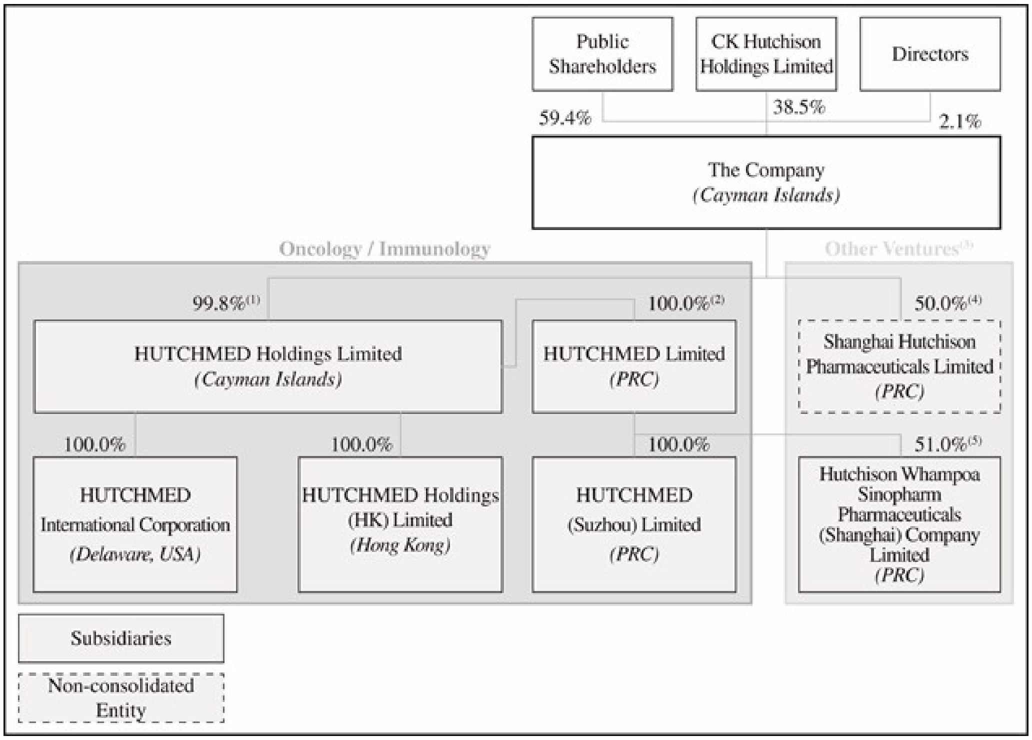
Filings and Approvals Relating to State-Owned Assets

Pursuant to applicable PRC state-owned assets administration laws and regulations, incorporating a joint venture that will have investments of assets that are both state-owned and non-state-owned, investing in an entity that was previously owned by a state-owned enterprise and restructuring an enterprise ultimately owned by the general public require the performance of an assessment of the relevant state-owned assets and the filing of the assessment results with the competent state-owned assets administration, finance authorities or other regulatory authorities and, if applicable, the receipt of approvals from such authorities.

Our joint venture partners were required to perform a state-owned asset assessment when Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan were incorporated and our joint venture partners contributed state-owned assets, and when we invested in Hutchison Sinopharm, which was previously wholly-owned by Sinopharm, a state-owned enterprise. In addition, Hutchison Sinopharm was required to perform a state-owned asset assessment when Hutchison Sinopharm restructured from an enterprise ultimately owned by the general public into a limited liability enterprise. In all four instances, our joint venture partners have informed us that they or Hutchison Sinopharm have duly filed the relevant state-owned asset assessment results with, and obtained the requisite approvals from, the relevant governmental authorities as required by the foregoing laws and regulations. Accordingly, we believe that such joint ventures are in full compliance with all applicable laws and regulations governing the administration and restructuring of state-owned assets, although we are currently unable to obtain copies of certain filing and approval documents from our joint venture partners due to their internal confidentiality constraints. We have not received any notice of warning or been subject to any penalty or other disciplinary action from the relevant governmental authorities with respect to the applicable laws and regulations governing the administration and restructuring of state-owned assets.

C. Organizational Structure

The chart below shows our organizational structure, including our principal subsidiaries and joint ventures, as of January 31, 2023.



Notes:

(1) Employees and former employees of HUTCHMED Limited hold the remaining 0.2% shareholding in HUTCHMED Holdings Limited.

(2) Held through HUTCHMED Investment (HK) Limited, a 100.0% subsidiary of HUTCHMED Holdings Limited. HUTCHMED Limited's revenue generated by sales of, and royalties, manufacturing costs and services fees in connection with, our current and future internally developed drug candidates are allocated to the Oncology/Immunology operations.

(3) Our Other Ventures also include Hutchison Hain Organic Holdings Limited, a consolidated joint venture with The Hain Celestial Group, Inc., which wholly-owns Hutchison Hain Organic (Hong Kong) Limited and Hutchison Hain Organic (Guangzhou) Limited.

(4) Held through our 100.0% subsidiary Shanghai HUTCHMED Investment (HK) Limited. Shanghai Pharmaceuticals Holding Co., Limited is the other 50.0% joint venture partner.

(5) Sinopharm Group Co. Limited is the other 49.0% joint venture partner.

D. Property, Plants and Equipment

We are headquartered in Hong Kong where we have our main administrative offices.

We rent and operate a 4,968 square meter manufacturing facility that complies with applicable GMP standards for fruquintinib and surufatinib in Suzhou, Jiangsu Province in Eastern China, and own a 5,024 square meter facility in Shanghai which houses research and development operations. We lease 9,080 square meters of office and lab space in Shanghai which houses HUTCHMED Limited's management and staff. In 2020, we entered into a 50-year land use rights agreement for a 28,771 square meter site in Shanghai. We have commenced construction of an almost 55,000 square meter large-scale manufacturing facility for innovative drugs on the site. The construction and qualification of the Shanghai facility is expected to be completed in mid-2023 and technology transfer will start for some projects into the facility in late 2023. The Shanghai factory will be our largest manufacturing facility, with a production capacity estimated to be five times that of our facility in Suzhou. The first phase will be primarily for small molecule production, with an expected production capacity of 250 million tablets and capsules per years.

We also lease a 26,989 square foot facility in Florham Park, New Jersey where we house our U.S.-based clinical and regulatory staff.

Our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, operates a 78,000 square meter large-scale research and development and manufacturing facility in Shanghai for which it has obtained land use rights and property ownership certificates.

Our and our joint ventures' manufacturing operations consist of bulk manufacturing and formulation, fill, and finishing activities that produce products and drug candidates for both clinical and commercial purposes. Our manufacturing capabilities have a large operation scale for our own-brand products. We and our joint ventures manufacture and sell about 2.8 billion doses of medicines a year, in the aggregate, through our well-established manufacturing base. See "—Other Ventures—Shanghai Hutchison Pharmaceuticals" for more details on our manufacturing operations.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis of our financial condition and results of operations together with Item 3.A. "Selected Financial Data," our consolidated financial statements and the related notes and our non-consolidated joint ventures' consolidated financial statements and the related notes appearing elsewhere in this annual report. This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act, including, without limitation, statements regarding our expectations, beliefs, intentions or future strategies that are signified by the words "expect," "anticipate," "intend," "believe," or similar language. All forward-looking statements included in this annual report are based on information available to us on the date hereof, and we assume no obligation to update any such forward-looking statements. In evaluating our business, you should carefully consider the information provided under Item 3.D. "Risk Factors." Actual results could differ materially from those projected in the forward-looking statements.

A. Operating Results.

Overview

We are a global commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies and immunotherapies for the treatment of patients with cancer and immunological diseases. We conduct our business through our Oncology/Immunology and Other Ventures operations.

Through our Oncology/Immunology operations, our team of approximately 960 scientists and staff has created, developed and in-licensed a deep portfolio of 14 drug candidates. We have advanced 14 oncology drug candidates to clinical trials in China, with four also in active clinical development in the United States and Europe. In China, we have brought three of our internally developed drugs, Elunate (fruquintinib), Sulanda (surufatinib) and Orpathys (savolitinib), to patients, have all been approved and launched in China and the fourth, tazemetostat, has been approved and launched in Hainan Pilot Zone and submitted for registration in Hong Kong. All three drugs are also in late-stage development outside of China. We have additional drug candidates in earlier stage clinical development (Phase I/Ib and Phase Ib/II proof-of-concept studies) and several advanced pre-clinical drug candidates. These drug candidates are being developed to treat a wide spectrum of diseases, including solid tumors, hematological malignancies and immunological diseases which we believe may address unmet medical needs and represent large commercial opportunities. Our success in research and development has led to partnerships with leading global pharmaceutical companies, including AstraZeneca and Eli Lilly. We and our collaboration partners have invested over $1,590 million in our Oncology/Immunology operations as of December 31, 2022, with almost all of these funds used for research and development expenses for the development of our drug candidates. Net loss attributable to our company from our Oncology/Immunology operations was $175.5 million, $291.7 million and $385.4 million for the years ended December 31, 2020, 2021 and 2022, respectively.

In addition, we have built large-scale and profitable drug marketing and distribution capabilities through subsidiaries and joint ventures in our Other Ventures, which primarily manufacture, market and distribute prescription drugs and consumer health products in China. Net income attributable to our company generated from our Other Ventures operations was $72.8 million, $142.9 million and $54.6 million for the years ended December 31, 2020, 2021 and 2022, respectively. In addition to helping to fund our Oncology/Immunology operations, we utilize the know-how from our Other Ventures to support the launch of our internally developed Oncology/Immunology products in China. Our Other Ventures also include our businesses focused on a range of health-focused consumer products.

Our consolidated revenue was $228.0 million, $356.1 million and $426.4 million for the years ended December 31, 2020, 2021 and 2022, respectively. Net loss attributable to our company was $125.7 million, $194.6 million and $360.8 million for the years ended December 31, 2020, 2021 and 2022, respectively.

Basis of Presentation

Our consolidated statements of operations data presented herein for the years ended December 31, 2022, 2021 and 2020 and our consolidated balance sheet data presented herein as of December 31, 2022 and 2021 have been derived from our audited consolidated financial statements, which were prepared in accordance with U.S. GAAP, and should be read in conjunction with those statements which are included elsewhere in this annual report.

We have two strategic operations, Oncology/Immunology and Other Ventures, that offer different products and services. Our Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan (until September 28, 2021 when the disposal of our shareholding interest in Hutchison Baiyunshan was completed) joint ventures under our Other Ventures operations are accounted for under the equity accounting method as non-consolidated entities in our consolidated financial statements, and their consolidated financial statements were prepared in accordance with IFRS as issued by the IASB and audited under auditing standards generally accepted in the United States and included elsewhere in this annual report. The presentation of financial data for our business units excludes certain unallocated costs attributed to expenses incurred by our corporate head office. For more information on our corporate structure, see Item 4.A. “History and Development of the Company.”

Factors Affecting our Results of Operations

Research and Development Expenses

We believe our ability to successfully develop innovative drug candidates through our Oncology/Immunology operations will be the primary factor affecting our long-term competitiveness, as well as our future growth and development. Creating high quality global first-in-class or best-in-class drug candidates requires significant investment of resources over a prolonged period of time, and a core part of our strategy is to continue making sustained investments in this area. As a result of this commitment, our pipeline of drug candidates has been steadily advancing and expanding, with 12 in clinical development. In addition, we are proactively making a strategic shift to focus on the most advanced assets from our internal developed pipeline, that are most likely to drive near-term value. For more information on the nature of the efforts and steps necessary to develop our drug candidates, see Item 4.B. “Business Overview—Our Clinical Pipeline” and “Business Overview—Regulations.”

The drug candidates of our Oncology/Immunology operations are still in development, and we have incurred and will continue to incur significant research and development costs for pre-clinical studies and clinical trials. We expect that our research and development expenses will significantly increase in future periods in line with the advancement and expansion of the development of our drug candidates.

Research and development expenses include:

- employee compensation related expenses, including salaries, benefits and equity compensation expense;
- expenses incurred for payments to CROs, investigators and clinical trial sites that conduct our clinical studies;
- the cost of acquiring, developing, and manufacturing clinical study materials;
- facilities, depreciation, and other expenses, which include office leases and other overhead expenses; and
- costs associated with pre-clinical activities and regulatory operations.

Research and development expenses incurred by our Oncology/Immunology operations totaled $174.8 million, $299.1 million and $386.9 million for the years ended December 31, 2020, 2021 and 2022, respectively, representing approximately 76.7%, 84.0% and 90.7% of our total consolidated revenue for the respective period. These research and development figures do not include payments made by our collaboration partners directly to third parties to help fund the research and development of our drug candidates.

We have been able to fund the research and development expenses for our Oncology/Immunology operations via a range of sources, including revenue generated from our commercialized drugs, payments received from our collaboration partners, cash flows generated from and dividend payments from our Other Ventures, the proceeds raised from our initial public offering on the AIM, initial public offering and follow-on offerings on Nasdaq, initial public offering on the SEHK, investments from other third parties and bank borrowings.

This diversified approach to funding allows us to not depend on any one method of funding for our research and development activities, thereby reducing the risk that sufficient financing will be unavailable as we continue to accelerate the development of our drug candidates.

For more information on the research and development expenses incurred for the development of our drug candidates, see "—Key Components of Results of Operations—Cost of Revenues and Operating Expenses—Research and Development Expenses."

Our Ability to Commercialize Our Drug Candidates

Our ability to generate revenue from our drug candidates depends on our ability to successfully complete clinical trials for our drug candidates and obtain regulatory approvals for them in the United States, Europe, China and other major markets.

We believe that our globally-facing strategy of focusing on drug development for novel but relatively well-characterized targets and for validated targets, in combination with our development of multiple drug candidates concurrently and testing them for multiple indications and in combinations with other drugs, enhances the likelihood that our research and development efforts will yield successful drug candidates. Nonetheless, we cannot be certain if any of our drug candidates will receive regulatory approvals. Even if such approvals are granted, we will need to thereafter establish manufacturing supply and engage in extensive marketing prior to generating any revenue from such drugs. The effectiveness of our marketing will depend on the efforts of our dedicated oncology team in China and our collaboration partners in the rest of the world. The ultimate commercial success of our drugs will depend on their acceptance by patients, the medical community and third-party payors and their ability to compete effectively with other therapies on the market.

To date, fruquintinib, surufatinib and savolitinib have been approved for sale in China.

Our manufacturing site in Suzhou produces commercial supplies of fruquintinib and surufatinib. Our commercial supplies of savolitinib are outsourced and manufactured by a third-party manufacturer based in Shanghai, China. Beginning in October 2020, we assumed responsibility for the development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities in China for Elunate. Sulanda is marketed by us in China without the support of a collaboration partner. However, we have a limited history of successfully commercializing our internally developed drug candidates, which makes it difficult to evaluate our future prospects.

The competitive environment is also an important factor with the commercial success of our potential global first-in-class products, such as sovleplenib, depending on whether we are able to gain regulatory approvals and quickly bring such products to market ahead of competing drug candidates being developed by other companies.

For our drug candidates where we retain all rights worldwide, which currently include surufatinib, sovleplenib, amdizalisib, HMPL-306, HMPL-760, HMPL-453, HMPL-295, HMPL-653, and HMPL-A83, we will be able to retain all the profits if any of them are successfully commercialized if they remain unpartnered, though we will need to bear all the costs associated with such drug candidates. Conversely, as discussed below, for our drug candidates which are subject to collaboration partnerships, our collaboration partners provide funding for development of the drug candidates but are entitled to retain a significant portion of any revenue generated by such drug candidates.

Our Collaboration Partnerships

Our results of operations have been, and we expect them to continue to be, affected by our collaborations with third parties for the development and commercialization of certain of our drug candidates. Currently, these include savolitinib (global collaboration with AstraZeneca) and fruquintinib (collaboration with Eli Lilly in China and expected collaboration with Takeda outside of China). In addition to providing us with clinical and regulatory support, the payments received from these collaborations have been critical to our ability to develop and quickly advance the pre-clinical and clinical studies of multiple drug candidates concurrently.

In particular, our partners cover a portion of our research and development costs for drug candidates developed in collaboration with them. In addition, under our collaboration agreements with AstraZeneca and Eli Lilly, we received upfront payments upon our entry into such agreements and milestone payments upon the achievement of certain development, regulatory and commercial milestones payments for our provision of research and development services for the relevant drug candidate as well as royalties. In the future, we expect to receive such payments from our recently agreed Takeda collaboration as well. Revenue recognized in our consolidated financial statements from such agreements with AstraZeneca and Eli Lilly totaled $29.7 million, $107.1 million and $129.4 million for the years ended December 31, 2020, 2021 and 2022, respectively.

Moreover, we have entered into and may consider entering in the future in-licensing arrangements to expand and complement our existing portfolio of novel oncology assets under which we may be obligated to make upfront, milestone and royalty payments. For example, in August 2021, we entered into an in-licensing agreement with Epizyme (a subsidiary of Ipsen Pharma SAS) to collaborate in research, development, manufacturing and commercialization of tazemetostat in Greater China, the licensed territory. In connection with this collaboration, Epizyme received a $25 million upfront payment and an aggregate of $5 million milestone payment to date and is eligible to receive up to an additional $105 million in development and regulatory milestone payments and up to an additional $175 million in sales milestone payments. Epizyme is also eligible to receive tiered royalties of mid-teen to low-twenties percent based on annual net sales of tazemetostat in the licensed territory.

The achievement of milestones for our and in-licensed drug candidates, which is dependent on the outcome of clinical studies, is subject to a high degree of uncertainty and, as a result, we cannot reasonably estimate when we can expect to receive or incur future milestone payments, revenue from related product sales, or other relevant income or expenses or at all. If we are unable to achieve development milestones for our drug candidates or if our partners were to terminate their collaborative agreements with us, payments for research and development services could also be affected.

For more information regarding our collaboration agreements, see Item 4.B. “Business Overview—Overview of Our Collaborations.”

China Government Insurance Reimbursement and Drug Pricing Policies

Our revenue is affected by the sales volume and pricing of our current and future internally developed drug candidates, if approved. Eligible participants in the government-sponsored medical insurance programs in China are entitled to reimbursement for varying percentages of the cost for any medicines that are included in applicable reimbursement lists. Factors that affect the inclusion of medicines in China's NRDL and any other applicable reimbursement list may include whether the medicine is consumed in large volumes and commonly prescribed for clinical use in China and whether it is considered to be important in meeting the basic healthcare needs of the general public. For more information, see Item 4.B. "Business Overview—Coverage and Reimbursement—PRC Coverage and Reimbursement." The inclusion of a medicine in the NRDL or other applicable reimbursement lists can substantially improve the sales volume of the medicine due to the availability of third-party reimbursements. On the other hand, such inclusion may also subject it to centralized procurement processes. The National Healthcare Security Administration has stated that centralized procurement will focus on NRDL-listed and costly-to-procure drugs. Centralized procurement may negatively affect the retail price of our drug candidates. On balance, we believe that, if priced appropriately, the benefit of the inclusion of our drug candidates in the NRDL and other applicable reimbursement lists outweighs the cost of such inclusion. Elunate was added to the NRDL in January 2020 at approximately 60% discount to its initial retail price, and such inclusion was renewed for an additional two-year term starting in January 2022 at a discount of 5% relative to the prior NRDL price. Sulanda was included in the NRDL starting in January 2022 at a 52% discount on its main dosage form, relative to its 2021 initial retail price. Orpathys will be included as a Category B medicine in the updated NRDL, effective from March 1, 2023.

Revenue from our Other Ventures, including the revenue of our non-consolidated joint venture Shanghai Hutchison Pharmaceuticals, is affected by the sales volume and pricing of their own-brand and third-party prescription pharmaceutical products. The sales volume of the products sold by these businesses is driven in part by the level of Chinese government spending on healthcare and the coverage of Chinese government medical insurance schemes, which is correlated with patient reimbursements for drug purchases, all of which have increased significantly in recent years as part of healthcare reforms in China. The sales volume of pharmaceutical products in China is also influenced by their representation on the NRDL, which determines eligibility for drug reimbursement, as well as their representation on the National Essential Medicines List, which mandates distribution of drugs in China. Substantially all pharmaceutical products manufactured and sold by Shanghai Hutchison Pharmaceuticals in 2021 were capable of being reimbursed under the NRDL as of December 31, 2022. There were 17 of its drugs included in the National Essential Medicine List, of which two were in active production as of December 31, 2022. She Xiang Bao Xin pills, Shanghai Hutchison Pharmaceuticals' top-selling drug, is one of the few proprietary drugs included on the National Essential Medicines List.

The NRDL and the National Essential Medicines List are subject to revision by the government from time to time, and our results could be materially and adversely affected if any of our products are removed from the NRDL or the National Essential Medicines List. For more information, see Item 3.D. "Risk Factors—Risks Relating to Sales of our Internally Developed Drugs and other Drugs—Reimbursement may not be available for the products currently sold through our Oncology/Immunology and Other Ventures operations or our drug candidates in China, the U.S. or other countries, which could diminish our sales or affect our profitability."

In addition, the pricing of Shanghai Hutchison Pharmaceuticals' prescription drugs is influenced by the outcomes of periodic provincial and municipal tender processes organized by the various provincial or municipal government agencies in China. For more information, see Item 4.B. "Business Overview—Coverage and Reimbursement—PRC Coverage and Reimbursement."

Ability to Effectively Market Own-Brand and Third-Party Drugs

A key component of our Other Ventures operations is the extensive prescription drugs marketing network operated by our joint ventures Shanghai Hutchison Pharmaceuticals and Hutchison Sinopharm, which includes approximately 2,900 medical sales representatives covering hospitals in about 290 cities and towns in China. Our results of operations are impacted by the effectiveness of this network, including the ability of Shanghai Hutchison Pharmaceuticals to generate sales of She Xiang Bao Xin pills, which represented approximately 90%, 92% and 92% of its total revenue for the years ended December 31, 2020, 2021 and 2022, respectively. In addition, in recent years Hutchison Sinopharm has been increasingly focused on providing distribution and commercialization services for prescription drugs licensed from third parties, and we have established and continue to expand our oncology drug sales team which we utilize for our internally developed drugs for which we have commercialization rights, if approved, throughout China.

If the marketing efforts of these joint ventures to doctors and hospitals are not successful, our revenue and profitability may be negatively affected. Moreover, if we are unsuccessful in marketing any third party drugs, it may adversely affect our ability to enter into commercialization arrangements on acceptable terms, gain rights to market additional third-party drugs or prevent us from expanding the geographic scope of existing arrangements.

Seasonality

The results of operations of our Other Ventures operations are also affected by seasonal factors. Our Other Ventures operations typically experience higher profits in the first half of the year due to the sale cycles of our distributors, whereby they typically increase their inventories at the beginning of each year. In addition, in the second half of each year, our Other Ventures operations typically spend more on marketing activities to help reduce such inventory held by distributors. We do not experience material seasonal variations in the results of our Oncology/Immunology operations.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of operating results and financial condition are based upon our consolidated financial statements. The preparation of consolidated financial statements requires us to estimate the effect of various matters that are inherently uncertain as of the date of the consolidated financial statements. Each of these required estimates varies with regard to the level of judgment involved and its potential impact on our reported financial results. Estimates are deemed critical when a different estimate could have reasonably been used or where changes in the estimates are reasonably likely to occur from period to period, and a different estimate would materially impact our financial position, changes in financial position or results of operations. Our significant accounting policies are discussed under note 3 to our consolidated financial statements included in this annual report. We believe the following critical accounting policies are affected by significant judgments and estimates used in the preparation of our consolidated financial statements and that the judgments and estimates are reasonable.

Revenue Recognition— Goods and Services

We generate revenue from (1) sales of goods, which are the manufacture or purchase and distribution of pharmaceutical products and other consumer health products and (2) provision of services, which are the provision of sales, distribution and marketing services to pharmaceutical manufacturers. We evaluate whether we are the principal or agent for these contracts. Where we obtain control of the goods for distribution, we are the principal (i.e. recognizes sales of goods on a gross basis). Where we do not obtain control of the goods for distribution, we are the agent (i.e. recognizes provision of services on a net basis). Control is primarily evidenced by taking physical possession and inventory risk of the goods.

Revenue from sales of goods is recognized when the customer takes possession of the goods. We have determined that this usually occurs upon completed delivery of the goods to the customer site. The amount of revenue recognized is adjusted for expected sales incentives as stipulated in the contract, which are generally issued to customers as direct discounts at the point of sale or indirectly in the form of rebates. Sales incentives are estimated using the expected value method. Additionally, sales are generally made with a limited right of return under certain conditions. Revenues are recorded net of provisions for sales discounts and returns.

Revenue from provision of services is recognized when the benefits of the services transfer to the customer over time, which is based on the proportionate value of services rendered as determined under the terms of the relevant contract. Additionally, when the amounts that can be invoiced correspond directly with the value to the customer for performance completed to date, we recognize revenue from provision of services based on amounts that can be invoiced to the customer.

Revenue Recognition— License and Collaboration Contracts

Our Oncology/Immunology reportable segment includes revenue from license and collaboration contracts. The license and collaboration contracts generally contain multiple performance obligations including (1) the license to the commercialization rights of a drug compound and (2) the research and development services for each specified treatment indication, which are accounted for separately if they are distinct, i.e. if a product or service is separately identifiable from other items in the arrangement and if a customer can benefit from it on its own or with other resources that are readily available to the customer.

The transaction price generally includes fixed and variable consideration in the form of upfront payment, research and development cost reimbursements, contingent milestone payments and sales-based royalties. Contingent milestone payments are not included in the transaction price until it becomes probable that a significant reversal of revenue will not occur, which is generally when the specified milestone is achieved. The allocation of the transaction price to each performance obligation is based on the relative standalone selling prices of each performance obligation determined at the inception of the contract. We estimate the standalone selling prices based on the income approach.

Control of the license to the drug compounds transfers at the inception date of the collaboration agreements and consequently, amounts allocated to this performance obligation are generally recognized at a point in time. Conversely, research and development services for each specified indication are performed over time and amounts allocated to these performance obligations are generally recognized over time using cost inputs as a measure of progress. We have determined that research and development expenses provide an appropriate depiction of measure of progress for the research and development services. Changes to estimated cost inputs may result in a cumulative catch-up adjustment. Royalty revenues are recognized as future sales occur as they meet the requirements for the sales-usage based royalty exception.

Deferred revenue is recognized if allocated consideration is received in advance of the rendering of research and development services. Accounts receivable is recognized based on the terms of the contract and when we have an unconditional right to bill the customer, which is generally when research and development services are rendered.

Share-based Compensation

We recognize share-based compensation expense on share options granted to employees and directors based on their estimated grant date fair value using the polynomial model. Determining the fair value of share options requires the use of subjective assumptions. This polynomial pricing model uses various inputs to measure fair value, including the market value of our underlying ordinary shares at the grant date, contractual terms, estimated volatility, risk-free interest rates and expected dividend yields. The assumptions in determining the fair value of share options are highly subjective and represent our best estimates, which involve inherent uncertainties and the application of judgment. As a result, if factors change and different assumptions are used, our level of share-based compensation could be materially different in the future.

We recognize share-based compensation expense in the consolidated statements of operations on a graded vesting basis over the requisite service period, and account for forfeitures as they occur.

Impairment of Long-lived Assets

We evaluate the recoverability of long-lived assets in accordance with authoritative guidance on accounting for the impairment or disposal of long-lived assets.

We evaluate long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Indicators that we consider in deciding when to perform an impairment review include significant under-performance of a business or product line in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in our use of the assets.

If indicators of impairment exist, the first step of the impairment test is performed to assess if the carrying value of the net assets exceeds the undiscounted cash flows of the assets. If yes, the second step of the impairment test is performed in order to determine if the carrying value of the net assets exceeds the fair value. If yes, impairment is recognized for the excess.

Allowance for Current Expected Credit Losses ("CECLs")

Effective from January 1, 2020, we adopted Accounting Standards Update 2016-13 “Financial Instruments – Credit Losses (Topic 326), Measurement of Credit Losses on Financial Instruments.” We estimate our allowance for current expected credit losses ("CECLs") based on an expected loss model, which requires the consideration of forward-looking economic variables and conditions in the reserve calculation across the portfolio.

We estimate our allowances for CECLs for accounts and other receivables (except for prepayments) by considering past events, including any historical default, current economic conditions and certain forward-looking information, including reasonable and supportable forecasts. From January 1, 2020 onwards, the methodologies that the Group uses to estimate the allowance for CECLs for accounts and other receivables are as follows:

Individually evaluated—we review all accounts and other receivables considered at risk on a timely basis and perform an analysis based upon current information available about the customers and other debtors, which may include financial statements, news reports, published credit ratings as well as collateral net of repossession cost, prior collection history and current and future expected economic conditions. Using this information, we determine the expected cash flow for the accounts and other receivables and calculate an estimate of the potential loss and the probability of loss. For those accounts for which the loss is probable, we record a specific allowance.

Collectively evaluated—we determine our allowance for CECLs for collectively evaluated accounts and other receivables based on appropriate groupings.

We consider forward-looking macroeconomic variables, which may include gross domestic product, unemployment rates, equity prices and corporate profits when quantifying the impact of economic forecasts on our allowance for expected credit losses. Macroeconomic variables may vary based on historical experiences, portfolio composition and current environment. We also consider the impact of current conditions and economic forecasts relating to specific industries and client-credit ratings, in addition to performing a qualitative review of credit risk factors across the portfolio. Forward-looking estimates require the use of judgment, particularly in times of economic uncertainty.

Recent Accounting Pronouncements

See note 3 to our consolidated financial statements included in this annual report for information regarding recent accounting pronouncements.

Key Components of Results of Operations

The following tables set forth our selected consolidated financial data. We have derived the selected consolidated statements of operations data for the years ended December 31, 2022, 2021 and 2020 and the selected consolidated balance sheet data as of December 31, 2022 and 2021 from our audited consolidated financial statements, which were prepared in accordance with U.S. GAAP and are included elsewhere in this annual report. The following selected consolidated financial data for the years ended December 31, 2019 and 2018 and as of December 31, 2020, 2019 and 2018 have been derived from our audited consolidated financial statements for those years, which were prepared in accordance with U.S. GAAP and are not included in this annual report.

	Year Ended December 31,				
	2022	2021	2020	2019	2018
	$'000 (except share and per share data)				
Consolidated statement of operations data:					
Revenues					
Goods—third parties	314,329	266,199	203,606	175,990	156,234
—related parties	5,293	4,256	5,484	7,637	8,306
Services —commercialization—third parties	41,275	27,428	3,734	2,584	11,660
—collaboration research and development —third parties	23,741	18,995	9,771	15,532	17,681
—research and development—related parties	507	525	491	494	7,832
Other collaboration revenue —royalties—third parties	26,310	15,064	4,890	2,653	261
—licensing—third parties	14,954	23,661	—	—	12,135
Total revenues	**426,409**	**356,128**	**227,976**	**204,890**	**214,109**
Operating expenses					
Costs of goods—third parties	(268,698)	(229,448)	(178,828)	(152,729)	(129,346)
Costs of goods—related parties	(3,616)	(3,114)	(3,671)	(5,494)	(5,978)
Costs of services—commercialization —third parties	(38,789)	(25,672)	(6,020)	(1,929)	(8,620)
Research and development expenses	(386,893)	(299,086)	(174,776)	(138,190)	(114,161)
Selling expenses	(43,933)	(37,827)	(11,334)	(13,724)	(17,736)
Administrative expenses	(92,173)	(89,298)	(50,015)	(39,210)	(30,909)
Total operating expenses	**(834,102)**	**(684,445)**	**(424,644)**	**(351,276)**	**(306,750)**
	(407,693)	**(328,317)**	**(196,668)**	**(146,386)**	**(92,641)**
Gain on divestment of an equity investee	—	121,310	—	—	—
Other (expense)/income					
Interest income	9,599	2,076	3,236	4,944	5,978
Other income	1,833	2,426	4,600	1,855	1,798
Interest expense	(652)	(592)	(787)	(1,030)	(1,009)
Other expense	(13,509)	(12,643)	(115)	(488)	(781)
Total other (expense)/income	**(2,729)**	**(8,733)**	**6,934**	**5,281**	**5,986**
Loss before income taxes and equity in earnings of equity investees	**(410,422)**	**(215,740)**	**(189,734)**	**(141,105)**	**(86,655)**
Income tax benefit/(expense)	283	(11,918)	(4,829)	(3,274)	(3,964)
Equity in earnings of equity investees, net of tax	49,753	60,617	79,046	40,700	19,333
Net loss	**(360,386)**	**(167,041)**	**(115,517)**	**(103,679)**	**(71,286)**
Less: Net income attributable to non-controlling interests	(449)	(27,607)	(10,213)	(2,345)	(3,519)
Net loss attributable to the Company	**(360,835)**	**(194,648)**	**(125,730)**	**(106,024)**	**(74,805)**
Losses per share attributable to the Company—basic and diluted (US$ per share)	(0.43)	(0.25)	(0.18)	(0.16)	(0.11)
Number of shares used in per share calculation—basic and diluted	847,143,540	792,684,524	697,931,437	665,683,145	664,263,820
Net loss	**(360,386)**	**(167,041)**	**(115,517)**	**(103,679)**	**(71,286)**
Other comprehensive (loss)/income					
Foreign currency translation (loss)/gain	(8,469)	2,964	9,530	(4,331)	(6,626)
Total comprehensive loss	**(368,855)**	**(164,077)**	**(105,987)**	**(108,010)**	**(77,912)**
Less: Comprehensive loss/(income) attributable to non-controlling interests	545	(28,029)	(11,413)	(1,620)	(2,566)
Total comprehensive loss attributable to the Company	**(368,310)**	**(192,106)**	**(117,400)**	**(109,630)**	**(80,478)**

	2022	2021	2020	2019	2018
Consolidated balance sheet data:					
Cash and cash equivalents	313,278	377,542	235,630	121,157	86,036
Short-term investments	317,718	634,158	199,546	96,011	214,915
Total assets	1,029,445	1,372,661	724,118	465,122	532,118
Total current liabilities	353,903	311,658	158,397	113,101	85,479
Total non-current liabilities	38,672	21,489	46,772	39,118	34,384
Total shareholders' equity	636,870	1,039,514	518,949	312,903	412,255

Revenues

We derive our consolidated revenue primarily from (i) the sales of goods and services to Eli Lilly as well as royalties on in-market sales of Elunate by Eli Lilly, (ii) the sales of goods to AstraZeneca as well as royalties on in-market sales of Orpathys by AstraZeneca, (iii) sales of our unpartnered drug Sulanda, (iv) licensing and collaboration projects conducted by our Oncology/Immunology operations, which generate revenue in the form of upfront payments, milestone payments, payments received for providing research and development services for our collaboration projects; and (v) the sales of goods by our Other Ventures, which generate revenue from the distribution and marketing of prescription pharmaceutical and consumer health products.

The following table sets forth the components of our consolidated revenue for the years indicated, which does not include the revenue from our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals. In September 2021, we sold our interest in our non-consolidated joint venture, Hutchison Baiyunshan, and its historical financial results and the gain on its divestment are reflected in our consolidated financial statements. Our revenue from research and development projects for related parties is attributable to income for research and development services that we received from Shanghai Hutchison Pharmaceuticals. Our revenue from sales to related parties is attributable to sales by our Other Ventures to indirect subsidiaries of CK Hutchison.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Revenues						
Oncology/Immunology:						
Goods—third parties	57,057	13.4	33,937	9.5	11,329	5.0
Services:						
Services—Commercialization—third parties	41,275	9.7	27,428	7.7	3,734	1.7
Collaboration R&D—third parties	23,741	5.5	18,995	5.3	9,771	4.3
R&D services—related parties	507	0.1	525	0.2	491	0.2
Other collaboration revenue:						
Royalties—third parties	26,310	6.2	15,064	4.2	4,890	2.1
Licensing—third parties	14,954	3.5	23,661	6.7	—	—
Subtotal	163,844	38.4	119,610	33.6	30,215	13.3
Other Ventures:						
Goods—third parties	257,272	60.3	232,262	65.2	192,277	84.3
Goods—related parties	5,293	1.3	4,256	1.2	5,484	2.4
Subtotal	262,565	61.6	236,518	66.4	197,761	86.7
Total	426,409	100.0	356,128	100.0	227,976	100.0

Revenue from Oncology/Immunology primarily comprises revenue from Elunate, Sulanda and Orpathys in China. The revenue we generate from Elunate is primarily comprised of revenue from the sales of Elunate to Eli Lilly which we manufacture and sell at cost, promotion and marketing services to Eli Lilly and royalty revenue. The revenue we generate from Sulanda, an unpartnered drug, is primarily comprised of revenue from sales of Sulanda to distributors. The revenue we generate from Orpathys is primarily comprised of revenue from the sales of Orpathys to AstraZeneca as well as royalty revenue. Additionally, Oncology/Immunology revenue includes revenue from licensing, co-development and commercialization agreements for upfront, milestone and research and development services payments for our drug candidates developed in collaboration with AstraZeneca and Eli Lilly.

The following table sets forth the components of revenues of our Other Ventures by product type for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Revenues—Other Ventures						
Prescription drug products	237,293	90.4	204,091	86.3	165,072	83.5
Consumer health products	25,272	9.6	32,427	13.7	32,689	16.5
Total	262,565	100.0	236,518	100.0	197,761	100.0

Revenue from our Other Ventures primarily comprises revenue from prescription drugs including the commercial services, logistics and distribution business of our consolidated Hutchison Sinopharm joint venture with Sinopharm, a leading distributor of pharmaceutical and healthcare products and a leading supply chain service provider in China.

Revenue from our Other Ventures also comprises revenue from sales of organic and natural products by Hutchison Hain Organic, Zhi Ling Tong infant nutrition and other health supplement products manufactured by Hutchison Healthcare and distributed through Hutchison Sinopharm up till the end of September and from October 1, 2022 onwards, through our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, and certain third-party consumer products distributed and marketed by HUTCHMED Science Nutrition.

The revenue of our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, the accounts of which are prepared in accordance with IFRS as issued by the IASB and whose revenue is not included in our consolidated revenue, was $276.4 million, $332.6 million and $370.6 million for the years ended December 31, 2020, 2021 and 2022, respectively. Shanghai Hutchison Pharmaceuticals is a joint venture with Shanghai Pharmaceuticals, a leading pharmaceuticals company in China, and primarily focuses on the manufacture and sale of prescription pharmaceutical products in China. We and Shanghai Pharmaceuticals each own 50% of this joint venture. We have the right to nominate the general manager and other management of this joint venture and run its day-to-day operations. The effect of Shanghai Hutchison Pharmaceuticals on our consolidated financial results is discussed below under "—Equity in Earnings of Equity Investees."

The revenue of our former non-consolidated joint venture, Hutchison Baiyunshan, the accounts of which are prepared in accordance with IFRS as issued by the IASB and whose financial results up to September 28, 2021 are reflected in our consolidated financial statements, was $232.4 million and $209.5 million for the year ended December 31, 2020 and the period ended September 28, 2021, respectively. Hutchison Baiyunshan was a joint venture with Guangzhou Baiyunshan, a leading China-based pharmaceutical company. We sold our interest in this joint venture on September 28, 2021 and recognized a gain on divestment attributable to our Group, net of taxes, of $82.9 million from this transaction. The effect of Hutchison Baiyunshan on our consolidated financial results is discussed under "—Equity in Earnings of Equity Investees."

Cost of Revenues and Operating Expenses

Cost of Revenues

Our cost of revenues is primarily attributable to the cost of revenues of Hutchison Sinopharm and HUTCHMED Limited. Our cost of revenues to related parties is attributable to sales to indirect subsidiaries of CK Hutchison. The following table sets forth the components of our cost of revenues attributable to third parties and related parties for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Cost of Revenues						
Costs of goods—third parties	268,698	86.4	229,448	88.9	178,828	94.9
Costs of goods—related parties	3,616	1.1	3,114	1.2	3,671	1.9
Costs of services—third parties	38,789	12.5	25,672	9.9	6,020	3.2
Total	311,103	100.0	258,234	100.0	188,519	100.0

The following table sets forth the components of cost of revenues of our Other Ventures by product type for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Cost of Revenues—Other Ventures						
Prescription drug products	228,968	94.6	196,375	92.0	158,910	90.1
Consumer health products	12,943	5.4	17,053	8.0	17,500	9.9
Total	241,911	100.0	213,428	100.0	176,410	100.0

Research and Development Expenses

Our research and development expenses are attributable to our Oncology/Immunology operations. These costs primarily comprise the cost of research and development for our drug candidates, including clinical trial related costs such as payments to third-party CROs, personnel compensation and related costs, and other research and development expenses. The following table sets forth the components of our research and development expenses and the clinical trial related costs incurred for the development of our main drug candidates for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
R&D Expenses						
Oncology/Immunology:						
Savolitinib (targeting MET)	48,249	12.5	26,152	8.7	5,341	3.1
Fruquintinib (targeting VEGFR1/2/3)	52,115	13.5	57,707	19.3	28,254	16.2
Surufatinib (targeting VEGFR/FGFR1/CSF-1R)	37,635	9.7	47,971	16.0	32,106	18.4
Sovleplenib (targeting Syk)	23,138	6.0	8,602	2.9	7,422	4.2
Amdizalisib (targeting PI3Kδ)	27,046	7.0	21,044	7.0	7,383	4.2
HMPL-453 (targeting FGFR)	2,776	0.7	1,708	0.6	1,356	0.8
HMPL-306 (targeting IDH 1/2)	14,865	3.8	10,073	3.4	5,389	3.1
HMPL-295 (targeting ERK)	1,362	0.4	692	0.2	—	—
HMPL-760 (targeting BTK)	4,954	1.3	5,288	1.8	—	—
HMPL-653 (targeting CSF-1R)	1,778	0.5	132	—	—	—
HMPL-A83 (IgG4-type humanized anti-CD47 monoclonal antibody)	2,840	0.7	—	—	—	—
Tazemetostat (targeting EZH2)	19,019	4.9	12,139	4.1	—	—
Epitinib (targeting EGFRm+ with brain metastasis)	—	—	—	—	808	0.5
Theliatinib (targeting EGFR wild-type)	—	—	—	—	(74)	—
Others and government grant	20,158	5.2	(1,457)	(0.4)	17,884	10.1
Total clinical trial related costs	255,935	66.2	190,051	63.6	105,869	60.6
Personnel compensation and related costs	119,306	30.8	91,639	30.6	63,542	36.3
Other research and development costs	11,652	3.0	17,396	5.8	5,365	3.1
Total	386,893	100.0	299,086	100.0	174,776	100.0

The following table summarizes our research and development expenses by location for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
PRC	215,963	55.8	159,038	53.2	111,473	63.8
U.S. and others	170,930	44.2	140,048	46.8	63,303	36.2
Total	386,893	100.0	299,086	100.0	174,776	100.0

We cannot determine with certainty the duration and completion costs of the current or future pre-clinical or clinical studies of our drug candidates or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our drug candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our drug candidates currently under development. The duration, costs, and timing of clinical studies and development of our drug candidates will depend on a variety of factors, including:

- the scope, rate of progress and expense of our ongoing as well as any additional clinical studies and other research and development activities;
- future clinical study results;
- uncertainties in clinical study enrollment rate;

- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a drug candidate could mean a significant change in the costs and timing associated with the development of that drug candidate.

For more information on the risks associated with the development of our drug candidates, see Item 3.D. “Risk Factors—Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates—All of our drug candidates, other than fruquintinib, surufatinib and savolitinib for approved indications in China, are still in development. If we are unable to obtain regulatory approval and ultimately commercialize our drug candidates, or if we experience significant delays in doing so, our business will be materially harmed.”

Selling Expenses

The following table sets forth the components of our selling expenses for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$’000	%	$’000	%	$’000	%
Selling Expenses						
Oncology/Immunology	33,862	77.1	24,627	65.1	237	2.1
Other Ventures	10,071	22.9	13,200	34.9	11,097	97.9
Total	43,933	100.0	37,827	100.0	11,334	100.0

Our selling expenses primarily comprise selling expenses incurred by our Oncology/Immunology operations by HUTCHMED Limited for sales and marketing expenses and related personnel expenses for our unpartnered drug Sulanda and sales of Elunate to third parties other than Eli Lilly. It also includes sales and marketing expenses and related personnel expenses incurred by our Other Ventures in their distribution and marketing of pharmaceutical and consumer health products.

Administrative Expenses

The following table sets forth the components of our administrative expenses for the years indicated.

Administrative expenses are also incurred by our corporate head office, which are not allocated to either Oncology/Immunology or Other Ventures.

	Year Ended December 31,					
	2022		2021		2020	
	$’000	%	$’000	%	$’000	%
Administrative Expenses						
Oncology/Immunology	58,395	63.3	48,359	54.2	19,144	38.3
Other Ventures	3,482	3.8	7,712	8.6	6,129	12.3
Corporate Head Office	30,296	32.9	33,227	37.2	24,742	49.4
Total	92,173	100.0	89,298	100.0	50,015	100.0

Oncology/Immunology’s administrative expenses are comprised of the salaries and benefits of administrative staff, office leases and other overhead expenses incurred by HUTCHMED Limited.

Our Other Ventures’ administrative expenses primarily comprise the salaries and benefits of administrative staff, office leases and other overhead expenses incurred by Hutchison Sinopharm, Hutchison Hain Organic and Hutchison Healthcare.

Our corporate head office administrative expenses primarily comprise the salaries and benefits of our corporate head office employees and directors, office leases and other overhead expenses.

Equity in Earnings of Equity Investees

We have historically derived a significant portion of our net income from our equity in earnings of equity investees, which was primarily attributable to our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals and former non-consolidated joint venture, Hutchison Baiyunshan. Our equity in earnings of equity investees, net of tax, contributed by Shanghai Hutchison Pharmaceuticals was $33.5 million, $44.7 million and $49.7 million for the years ended December 31, 2020, 2021 and 2022 respectively. Our equity in earnings of equity investees, net of tax, contributed by Hutchison Baiyunshan was $45.6 million and $15.9 million for the year ended December 31, 2020 and the period ended September 28, 2021, respectively. Equity in earnings of Hutchison Baiyunshan for year ended December 31, 2020 included a one-time gain of $36.0 million from land compensation for a return of land-use rights to the Guangzhou government and for the period ended September 28, 2021 included a one-time gain of $7.0 million for additional land compensation.

The following table shows the revenue of Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan for the periods indicated. The consolidated financial statements of these joint ventures are prepared in accordance with IFRS as issued by the IASB and are presented separately elsewhere in this annual report.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Revenue						
Other Ventures:						
Shanghai Hutchison Pharmaceuticals	370,600	100.0	332,648	61.4	276,354	54.3
Hutchison Baiyunshan (1)	—	—	209,528	38.6	232,368	45.7
Total	370,600	100.0	542,176	100.0	508,722	100.0

(1) On September 28, 2021, we completed the disposal of our equity interest in Hutchison Baiyunshan. Revenue in 2021 reflects the period from January 1, 2021 to September 28, 2021.

The following table shows the amount of equity in earnings of equity investees, net of tax, of our non-consolidated joint ventures for the years indicated.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Equity in earnings of equity investees, net of tax						
Other Ventures:						
Shanghai Hutchison Pharmaceuticals(1)	49,748	100.0	44,678	73.7	33,502	42.4
Hutchison Baiyunshan(2)	—	—	15,919	26.3	45,641	57.7
Oncology/Immunology:						
Others	5	—	20	—	(97)	(0.1)
Total	49,753	100.0	60,617	100.0	79,046	100.0

(1) The amount for the years ended December 31, 2021 and 2022 includes elimination of unrealized profits on transactions with the Group of $36,000 and $110,000 respectively.

(2) The amount for the year ended December 31, 2020 and for the period ended September 28, 2021 includes a one-time gain of $36.0 million and $7.0 million, respectively, from land compensation for a return of land use rights to the Guangzhou government. On September 28, 2021, we completed the divestment of our shareholding interest in Hutchison Baiyunshan. Equity in earnings of Hutchison Baiyunshan reflects the period from January 1, 2021 to September 28, 2021.

Investments in equity investees mainly consisted of our investment in Shanghai Hutchison Pharmaceuticals. The fluctuation in the investments in equity investees was primarily due to recording our equity in earnings of Shanghai Hutchison Pharmaceuticals, net of tax, offset by dividends declared.

The following table shows our investments in our equity investees as of the dates indicated.

	As of December 31, 2022	As of December 31, 2021
	$'000	
Shanghai Hutchison Pharmaceuticals	73,461	75,999
Others	316	480
Total	73,777	76,479

The following table shows the financial position of Shanghai Hutchison Pharmaceuticals as of the dates indicated.

	As of December 31, 2022	As of December 31, 2021
	$'000	
Current assets	214,267	190,260
Non-current assets	80,062	91,605
Current liabilities	(147,952)	(128,993)
Non-current liabilities	(4,944)	(7,131)
Net assets	141,433	145,741

Results of Operations

The following table sets forth a summary of our consolidated results of operations for the years indicated, both in absolute amounts and as percentages of our revenues. This information should be read together with our consolidated financial statements and related notes included elsewhere in this annual report. Our operating results in any period are not necessarily indicative of the results that may be expected for any future period.

	Year Ended December 31,					
	2022		2021		2020	
	$'000	%	$'000	%	$'000	%
Revenues	426,409	100.0	356,128	100.0	227,976	100.0
Cost of revenues	(311,103)	(73.1)	(258,234)	(72.5)	(188,519)	(82.7)
Research and development expenses	(386,893)	(90.7)	(299,086)	(84.0)	(174,776)	(76.7)
Selling expenses	(43,933)	(10.3)	(37,827)	(10.6)	(11,334)	(5.0)
Administrative expenses	(92,173)	(21.6)	(89,298)	(25.1)	(50,015)	(21.9)
Gain on divestment of an equity investee	—	—	121,310	34.1	—	—
Other (expense)/income	(2,729)	(0.6)	(8,733)	(2.5)	6,934	3.0
Income tax benefit/ (expense)	283	0.1	(11,918)	(3.3)	(4,829)	(2.1)
Equity in earnings of equity investees, net of tax	49,753	11.7	60,617	17.0	79,046	34.7
Net loss	(360,386)	(84.5)	(167,041)	(46.9)	(115,517)	(50.7)
Net loss attributable to our company	(360,835)	(84.6)	(194,648)	(54.7)	(125,730)	(55.2)

Taxation

Cayman Islands

HUTCHMED (China) Limited is incorporated in the Cayman Islands. The Cayman Islands currently levies no taxes on profits, income, gains or appreciation earned by individuals or corporations. In addition, our payment of dividends, if any, is not subject to withholding tax in the Cayman Islands. For more information, see Item 10.E. "Taxation—Overview of Tax Implications of Various Other Jurisdictions—Cayman Islands Taxation."

People’s Republic of China

Our subsidiaries and a joint venture incorporated in the PRC are governed by the EIT Law and regulations. Under the EIT Law, the standard EIT rate is 25% on taxable profits as reduced by available tax losses. Tax losses may be carried forward to offset any taxable profits for the following five years (extended to ten years for those with HNTE status, with effective from January 1, 2018). HUTCHMED Limited and our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, have been successful in their respective applications to renew their HNTE status for three years from January 1, 2020 to December 31, 2022. Accordingly, these entities are eligible to a preferential EIT rate of 15% for the years ended/ending December 31, 2020, 2021 and 2022. HUTCHMED (Suzhou) Limited, a wholly owned subsidiary of HUTCHMED Limited, successful renewed its HNTE status for another three years from January 1, 2021 to December 31, 2023. Accordingly, it is eligible for a preferential EIT rate of 15% for the years ended December 31, 2021, 2022 and 2023.

For more information, see Item 10.E. “Taxation—Taxation in the PRC.” Please also see Item. 3 “Key Information—Risk Factors—Other Risks and Risks Relating to Doing Business in China—Our business benefits from certain PRC government tax incentives. The expiration of, changes to, or our PRC subsidiaries/joint venture failing to continuously meet the criteria for these incentives could have a material adverse effect on our operating results by significantly increasing our tax expenses.”

According to the EIT Law and its implementation regulations, dividends declared after January 1, 2008 and paid by PRC foreign-invested enterprises to their non-PRC parent companies will be subject to PRC withholding tax at 10% unless there is a tax treaty between the PRC and the jurisdiction in which the overseas parent company is a tax resident and which specifically exempts or reduces such withholding tax, and such tax exemption or reduction is approved by the relevant PRC tax authorities. Pursuant to the tax arrangement between PRC and Hong Kong, if a shareholder of the PRC enterprise is a Hong Kong tax resident and directly holds a 25% or more equity interest in the PRC enterprise and is considered to be the beneficial owner of dividends paid by the PRC enterprise, such withholding tax rate may be lowered to 5%, subject to approval by the relevant PRC tax authorities. For more information, see Item 10.E. “Taxation—Taxation in the PRC” and “Taxation—Overview of Tax Implications of Various Other Jurisdictions— Hong Kong Taxation.”

Hong Kong

Our company and certain of its subsidiaries are subject to Hong Kong Profits Tax laws and regulations. Hong Kong has a two-tiered Profits Tax rates regime under which the first HK$2.0 million ($0.3 million) of assessable profits of qualifying corporations will be taxed at 8.25%, with the remaining assessable profits taxed at 16.5%. Hong Kong Profits Tax has been provided for at the relevant rates on the estimated assessable profits less estimated available tax losses, if any, of these entities as applicable.

Period-to-Period Comparison of Results of Operations

Year Ended December 31, 2022 Compared to Year Ended December 31, 2021

Revenues

Our revenue increased by 19.7% from $356.1 million for the year ended December 31, 2021 to $426.4 million for the year ended December 31, 2022, which resulted from increased revenue primarily in the Oncology/Immunology operations.

Revenue from Oncology/Immunology increased by 37.0% from $119.6 million for the year ended December 31, 2021 to $163.8 million for the year ended December 31, 2022, primarily due to an increase in revenue related to the sales of Sulanda from $11.6 million for the year ended December 31, 2021 to $32.3 million for the year ended December 31, 2022. The increase was also attributable to the sales of Elunate from $53.5 million for the year ended December 31, 2021 (of which $15.8 million was revenue from sales of goods primarily to Eli Lilly, $10.3 million was royalty revenue and $27.4 million was revenue from promotion and marketing services to Eli Lilly) to $69.9 million for the year ended December 31, 2022 (of which $14.7 million was revenue from sales of goods primarily to Eli Lilly, $13.9 million was royalty revenue and $41.3 million was revenue from promotion and marketing services to Eli Lilly). Sales of Orpathys have also contributed to the increase in revenue from $11.3 million for the year ended December 31, 2021 (of which $6.5 million was revenue from sales of goods and $4.8 million was royalty revenue) to $22.3 million for the year ended December 31, 2022 (of which $9.9 million was revenue from sales of goods and $12.4 million was royalty revenue). The increase has been netted off by reduction in revenue related to collaboration research and development services which have decreased from $42.7 million for the year ended December 31, 2021 to $38.7 million for the year ended December 31, 2022, primarily attributable to receipt of a $25.0 million milestone payment from AstraZeneca upon the commercial launch of Orpathys in August 2021 compared to the receipt of a $15.0 million milestone payment upon initiating start-up activities for a Global Phase III study of Orpathys in Lung Cancer in March 2022. Such decrease has been netted off by the increase in revenue from other collaboration research and development from $17.7 million for the year ended December 31, 2021 to $23.7 million for the year end December 31, 2022.

Revenue from our Other Ventures increased by 11.0% from $236.5 million for the year ended December 31, 2021 to $262.6 million for the year ended December 31, 2022, primarily due to an increase in sales of prescription drugs products. Revenue from sales of prescription drugs increased by 16.3% from $204.1 million for the year ended December 31, 2021 to $237.3 million for the year ended December 31, 2022, primarily due to increased sales by our consolidated joint venture Hutchison Sinopharm. Revenue from sales of our consumer health products on the other hand has decreased by 22.1% from $32.4 million for the year ended December 31, 2021 to $25.3 million for the year ended December 31, 2022, primarily due to decreased sales by our consolidated joint venture Hutchison Hain Organic.

Cost of Revenues

Our cost of revenues increased by 20.5% from $258.2 million for the year ended December 31, 2021 to $311.1 million for the year ended December 31, 2022. This increase was due to increased sales by the Oncology/Immunology and Other Ventures operations.

Cost of revenues from Oncology/Immunology increased by 54.4% from $44.8 million for the year ended December 31, 2021 to $69.2 million for the year ended December 31, 2022, primarily due to an increase in sales of Sulanda, Elunate (including the provision of promotion and marketing services to Eli Lilly), and Orpathys.

Cost of revenues from our Other Ventures increased by 13.3% from $213.4 million for the year ended December 31, 2021 to $241.9 million for the year ended December 31, 2022, which was primarily due to increased sales.

Cost of revenues as a percentage of our revenues increased from 72.5% to 73.0% across these periods.

Research and Development Expenses

Our research and development expenses incurred by Oncology/Immunology increased by 29.4% from $299.1 million for the year ended December 31, 2021 to $386.9 million for the year ended December 31, 2022, which was primarily due to a $65.9 million increase in CROs and other clinical trial related costs and a $21.9 million increase in employee compensation related and other costs. These increased costs were due to an expansion of clinical activities. In particular, this increase was attributable to the expansion of the clinical activities of fruquintinib, savolitinib, amdizalisib and sovleplenib. Such increase was also attributable to the decrease in government grants recognized. As a result, research and development expenses as a percentage of our revenue increased from 84.0% to 90.7% across these periods.

Selling Expenses

Our selling expenses increased by 16.1% from $37.8 million for the year ended December 31, 2021 to $43.9 million for the year ended December 31, 2022, primarily due to the increased marketing activities. Selling expenses as a percentage of our revenues decreased from 10.6% to 10.3% across these periods.

Administrative Expenses

Our administrative expenses increased by 3.2% from $89.3 million for the year ended December 31, 2021 to $92.2 million for the year ended December 31, 2022. This was primarily due to a $10.0 million increase in administrative expenses incurred by Oncology/Immunology, which was mainly related to increased staff costs and other office expenses to support our expanded clinical activities. Administrative expenses as a percentage of our revenues decreased from 25.1% to 21.6% across these periods.

Gain on Divestment of an Equity Investee

We had a gain on divestment of an equity investee of $121.3 million for the year ended December 31, 2021, before applicable capital gain taxes and amounts attributable to non-controlling interests, which is related to the disposal of our shareholding interest in Hutchison Baiyunshan.

Other (Expense)/ Income

Our net other expenses decreased by 68.8% from $8.7 million for the year ended December 31, 2021 to $2.7 million for the year ended December 31, 2022 primarily due to higher interest income of $7.5 million.

Income Tax Benefit/(Expense)

Our income tax expense decreased from $11.9 million for the year ended December 31, 2021 to $0.3 million income tax benefit for the year ended December 31, 2022, primarily due to the capital gains taxes related to the disposal of our shareholding interest in Hutchison Baiyunshan on September 28, 2021.

Equity in Earnings of Equity Investees

Our equity in earnings of equity investees, net of tax, decreased by 17.9% from $60.6 million for the year ended December 31, 2021 to $49.8 million for the year ended December 31, 2022, primarily due to the disposal of Hutchison Baiyunshan on September 28, 2021.

Shanghai Hutchison Pharmaceuticals

The following table shows a summary of the results of operations of Shanghai Hutchison Pharmaceuticals for the years indicated. The consolidated financial statements of Shanghai Hutchison Pharmaceuticals are prepared in accordance with IFRS as issued by the IASB and are presented separately elsewhere in this annual report.

	Year Ended December 31,			
	2022		2021	
	($'000)	%	($'000)	%
Revenue	370,600	100.0	332,648	100.0
Cost of sales	(89,487)	(24.1)	(77,559)	(23.3)
Selling expenses	(144,979)	(39.1)	(131,821)	(39.6)
Administrative expenses	(21,727)	(5.9)	(22,627)	(6.8)
Other net operating income	2,126	0.5	4,759	1.4
Taxation charge	(16,738)	(4.5)	(15,896)	(4.8)
Profit for the year	99,683	26.9	89,388	26.9
Equity in earnings of equity investee attributable to our company(1)	49,748	13.4	44,678	13.4

(1) The amount for the years ended December 31, 2021 and 2022 includes elimination of unrealized profits on transactions with the Group of $36,000 and $110,000 respectively.

Shanghai Hutchison Pharmaceuticals' revenue increased by 11.4% from $332.6 million for the year ended December 31, 2021 to $370.6 million for the year ended December 31, 2022, primarily due to an increase in sales of She Xiang Bao Xin pills, a vasodilator used in the treatment of heart conditions. Sales of She Xiang Bao Xin pills increased by 11.2% from $307.1 million for the year ended December 31, 2021 to $341.6 million for the year ended December 31, 2022.

Cost of sales increased by 15.4% from $77.6 million for the year December 31, 2021 to $89.5 million for the year ended December 31, 2022, primarily due to higher sales of She Xiang Bao Xin pills. Shanghai Hutchison Pharmaceuticals' revenue increased at a lower rate than the cost of sales due to shut down costs associated with the temporary shutdown of the factory during the COVID-19 outbreak.

Selling expenses increased by 10.0% from $131.8 million for the year ended December 31, 2021 to $145.0 million for the year ended December 31, 2022, as a result of increased spending on marketing and promotional activities to support the increase in sales.

Administrative expenses decreased by 4.0% from $22.6 million for the year ended December 31, 2021 to $21.7 million for the year ended December 31, 2022, primarily due to a decrease in research and development expenses for new products.

Other net operating income decreased by 55.3% from $4.8 million for the year ended December 31, 2021 to $2.1 million for the year ended December 31, 2022, primarily due to a decrease in government grants and interest income.

Taxation charge increased by 5.3% from $15.9 million for the year ended December 31, 2021 to $16.7 million for the year ended December 31, 2022, primarily due to an increase in taxable profit.

As a result of the foregoing, profit increased by 11.5% from $89.4 million for the year ended December 31, 2021 to $99.7 million for the year ended December 31, 2022. Our equity in earnings of equity investees contributed by this joint venture was $44.7 million and $49.7 million for the years ended December 31, 2021 and 2022, respectively.

For more information on the financial results of our non-consolidated joint ventures, see "—Key Components of Results of Operations—Equity in Earnings of Equity Investees."

Net Loss

As a result of the foregoing, our net loss increased from $167.0 million for the year ended December 31, 2021 to $360.4 million for the year ended December 31, 2022. Net loss attributable to our company increased from $194.6 million for the year ended December 31, 2021 to $360.8 million for the year ended December 31, 2022.

Year Ended December 31, 2021 Compared to Year Ended December 31, 2020

For a discussion of our results of operations for the year ended December 31, 2021 compared to the year ended December 31, 2020, see Item 5.A. "Operating Results" of our annual report on Form 20-F for the year ended December 31, 2021, filed with the SEC on March 3, 2022.

B. Liquidity and Capital Resources

To date, we have taken a multi-source approach to fund our operations, including through cash flows generated and dividend payments from our Oncology/Immunology and Other Ventures operations, service and milestone and upfront payments from our collaboration partners, bank borrowings, investments from other third parties, proceeds from our listings on various stock exchanges and follow-on offerings.

Our Oncology/Immunology operations have historically not generated significant profits or have operated at a net loss, as creating potential global first-in-class or best-in-class drug candidates requires a significant investment of resources over a prolonged period of time. As a result, we anticipate that we may need additional financing for our Oncology/Immunology operations in future periods. See Item 3.D. "Risk Factors—Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates—Historically, our in house research and development division, which is included in our Oncology/Immunology operations, has not generated significant profits or has operated at a net loss. Our future profitability is dependent on the successful commercialization of our drug candidates."

As of December 31, 2022, we had cash and cash equivalents of $313.3 million and short-term investments of $317.7 million and unutilized bank facilities of $140.3 million. Substantially all of our bank deposits are at major financial institutions, which we believe are of high credit quality. As of December 31, 2022, we had $18.1 million in bank loans, all of which was related to a fixed asset loan from BOC. The total weighted average cost of bank borrowings for the year ended December 31, 2022 was 1.73% per annum. For additional information, see "—Loan Facilities."

Certain of our subsidiaries and joint ventures, including those registered as wholly foreign-owned enterprises in China, are required to set aside at least 10.0% of their after-tax profits to their general reserves until such reserves reach 50.0% of their registered capital. In addition, certain of our joint ventures are required to allocate certain of their after-tax profits as determined in accordance with related regulations and their respective articles of association to the reserve funds upon their board approval. Profit appropriated to the reserve funds for our subsidiaries and joint ventures incorporated in the PRC was approximately $44,000, $89,000 and $318,000 for the years ended December 31, 2020, 2021 and 2022, respectively.

In addition, as a result of PRC regulations restricting dividend distributions from such reserve funds and from a company's registered capital, our PRC subsidiaries are restricted in their ability to transfer a certain amount of their net assets to us as cash dividends, loans or advances. This restricted portion amounted to $0.1 million as of December 31, 2022. Although we do not currently require any such dividends, loans or advances from our PRC subsidiaries to fund our operations, should we require additional sources of liquidity in the future, such restrictions may have a material adverse effect on our liquidity and capital resources. For more information, see Item 4.B. "Business Overview—Regulation—PRC Regulation of Foreign Currency Exchange, Offshore Investment and State-Owned Assets—Regulation on Investment in Foreign invested Enterprises—Regulation on Dividend Distribution."

In addition, our non-consolidated joint venture Shanghai Hutchison Pharmaceuticals held $33.9 million in cash and cash equivalents and no bank borrowings as of December 31, 2022. Such cash and cash equivalents are only accessible by us through dividend payments from the joint venture. The level of dividends declared by the joint venture is subject to agreement each year between us and our joint venture partner based on the profitability and working capital needs of the joint venture. As a result, we cannot guarantee that the joint venture will continue to pay dividends to us in the future at the same rate we have enjoyed in the past, or at all, which may have a material adverse effect on our liquidity and capital resources. For more information, see Item 3.D. "Risk Factors—Risks Relating to Sales of our Internally Developed Drugs and Other Drugs—As a significant portion of the operations of our Other Ventures is conducted through joint venture, we are largely dependent on the success of our joint venture and our receipt of dividends or other payments from our joint venture for cash to fund our operations and our investment in joint venture subject to liquidity risk."

We believe that our current levels of cash and cash equivalents, short-term investments, along with cash flows from operations, dividend payments and unutilized bank borrowings, will be sufficient to meet our anticipated cash needs for at least the next 12 months. In the long term, we believe that we can meet our need for cash through revenues generated from marketed products, public and private sales of our securities and the potential disposals of our remaining non-core businesses. However, we may require additional financing in order to fund all of the clinical development efforts that we plan to undertake to accelerate the development of our clinical-stage drug candidates. For more information, see Item 3.D. "Risk Factors—Risks Relating to Our Financial Position and Need for Capital."

	Year Ended December 31,		
	2022	2021	2020
		($'000)	
Cash Flow Data:			
Net cash used in operating activities	(268,599)	(204,223)	(62,066)
Net cash generated from/(used in) investing activities	296,588	(306,320)	(125,441)
Net cash (used in)/generated from financing activities	(82,763)	650,028	296,434
Net (decrease)/increase in cash and cash equivalents	(54,774)	139,485	108,927
Effect of exchange rate changes	(9,490)	2,427	5,546
Cash and cash equivalents at beginning of the year	377,542	235,630	121,157
Cash and cash equivalents at end of the year	313,278	377,542	235,630

Net Cash used in Operating Activities

Net cash used in operating activities was $204.2 million for the year ended December 31, 2021, compared to net cash used in operating activities of $268.6 million for the year ended December 31, 2022. The net change of $64.4 million was primarily attributable to higher operating expenses of $149.7 million from $684.4 million for the year ended December 31, 2021 to $834.1 million for the year ended December 31, 2022. The foregoing was partially offset by an increase in revenue of $70.3 million from $356.1 million for the year ended December 31, 2021 to $426.4 million for the year ended December 31, 2022 and an increase in changes of working capital of $26.2 million from $32.5 million for the year ended December 31, 2021 to $58.7 million for the year ended December 31, 2022.

For a discussion of our net cash used in operating activities for the years ended December 31, 2021 and 2020, see Item 5.B. “Liquidity and Capital Resources” of our annual report on Form 20-F for the year ended December 31, 2021, filed with the SEC on March 3, 2022.

Net Cash generated from/(used in) Investing Activities

Net cash used in investing activities was $306.3 million for the year ended December 31, 2021, compared to net cash generated from investing activities of $296.6 million for the year ended December 31, 2022. The net change of $602.9 million was primarily attributable to short-term investments which had net deposits of $434.6 million for the year ended December 31, 2021 as compared to net withdrawals of $316.4 million for the year ended December 31, 2022. The net change was partially offset by the proceeds received from divestment of Hutchison Baiyunshan of $159.1 million during the year ended December 31, 2021, compared to a dividend of $16.5 million received from divestment of the equity investee during the year ended December 31, 2022.

For a discussion of our net cash (used in)/generated from investing activities for the years ended December 31, 2021 and 2020, see Item 5.B. “Liquidity and Capital Resources” of our annual report on Form 20-F for the year ended December 31, 2021, filed with the SEC on March 3, 2022.

Net Cash (used in)/generated from Financing Activities

Net cash generated from financing activities was $650.0 million for the year ended December 31, 2021, compared to net cash used in financing activities of $82.8 million for the year ended December 31, 2022. The net change of $732.8 million was mainly attributable to net proceeds from issuances of shares of $685.4 million primarily from a private placement in April 2021 and our public offering on the SEHK. The net change was also attributable to an increase in purchases of ADSs of $20.8 million by a trustee for the settlement of equity awards of the Company which totaled $27.3 million for the year ended December 31, 2021 as compared to $48.1 million for the year ended December 31, 2022, as well as an increase in dividend paid to non-controlling shareholders of subsidiaries of $15.7 million from $9.9 million for the year ended December 31, 2021 to $25.6 million for the year ended December 31, 2022.

For a discussion of our net cash (used in)/generated from financing activities for the years ended December 31, 2021 and 2020, see Item 5.B. “Liquidity and Capital Resources” of our annual report on Form 20-F for the year ended December 31, 2021, filed with the SEC on March 3, 2022.

Contractual Obligations

The following table sets forth our contractual obligations as of December 31, 2022. For more information on bank borrowings and interest on bank borrowings, please see “—Loan Facilities.” Our purchase obligations relate to property, plant and equipment that are contracted for but not yet paid. Our lease obligations primarily comprise future aggregate minimum lease payments in respect of various factories, warehouse, offices and other assets under non-cancellable lease agreements. For more information on purchase obligations and lease obligations, please see “—Capital Expenditures.”

	Payment Due by Period				
	Total	Less Than 1 Year	1-2 Years	2-5 Years	More Than 5 Years
			($'000)		
Bank borrowings	18,104	—	—	2,278	15,826
Interest on bank borrowings	4,294	318	636	1,837	1,503
Purchase obligations	22,130	20,323	161	1,646	—
Lease obligations	10,122	4,498	3,431	2,078	115
Total	54,650	25,139	4,228	7,839	17,444

Shanghai Hutchison Pharmaceuticals

The following table sets forth the contractual obligations of our non-consolidated joint venture Shanghai Hutchison Pharmaceuticals as of December 31, 2022. Shanghai Hutchison Pharmaceuticals' purchase obligations comprise capital commitments for property, plant and equipment contracted for but not yet paid. Shanghai Hutchison Pharmaceuticals' lease obligations primarily comprise future aggregate minimum lease payments in respect of various offices under non-cancellable lease agreements.

	Payment Due by Period				
	Total	Less Than 1 Year	1-2 Years	2-5 Years	More Than 5 Years
			($'000)		
Purchase obligations	1,307	1,307	—	—	—
Lease obligations	2,243	826	757	660	—
Total	3,550	2,133	757	660	—

Loan Facilities

In May 2019, HUTCHMED Group (HK) Limited entered into a credit facility arrangement with HSBC for the provision of unsecured credit facilities in the aggregate amount of HK$400.0 million ($51.3 million). The 3-year credit facilities include (i) a HK$210.0 million ($26.9 million) term loan facility and (ii) a HK$190.0 million ($24.4 million) revolving loan facility, both with an interest rate at HIBOR plus 0.85% per annum. These credit facilities are guaranteed by us and include certain financial covenant requirements. In October 2019, we drew down HK$210.0 million ($26.9 million) from the term loan facility which was repaid in May 2022. The revolving loan facility also expired in May 2022.

In August 2020, HUTCHMED Group (HK) Limited entered into a 24-month revolving credit facility with Deutsche Bank AG in the amount of HK$117.0 million ($15.0 million) with an interest rate at HIBOR plus 4.5% per annum. This revolving facility is guaranteed by us and includes certain financial covenant requirements. The revolving loan facility expired in August 2022.

In October 2021, HUTCHMED Limited entered into a 10-year fixed asset loan facility agreement with Bank of China Limited for the provision of a secured credit facility of RMB754.9 million ($108.4 million) with an annual interest rate at the 5-year China Loan Prime Rate less 0.80% (which was supplemented in June 2022). This credit facility is guaranteed by HUTCHMED Limited's immediate holding company, HUTCHMED Investment (HK) Limited, and secured by the underlying leasehold land and buildings of HUTCHMED Limited, and includes certain financial covenant requirements. As of December 31, 2022, RMB126.1 million ($18.1 million) was utilized from the fixed asset loan facility.

In May 2022, HUTCHMED Group (HK) Limited entered into a 12-month revolving credit facility with HSBC in the amount of HK$390.0 million ($50.0 million) with an interest rate at HIBOR plus 0.5% per annum. This revolving facility is guaranteed by us. As of December 31, 2022, no amount was drawn from the revolving loan facility.

Our non-consolidated joint venture Shanghai Hutchison Pharmaceuticals had no bank borrowings outstanding as of December 31, 2022.

Gearing Ratio

The gearing ratio of our group, which was calculated by dividing total interest-bearing loans by total equity, was 2.8% as of December 31, 2022, an increase from 2.6% as of December 31, 2021. The increase was primarily attributable to the decrease in equity due to the increase in net loss during the year.

Capital Expenditures

We had capital expenditures of $19.6 million, $16.8 million and $36.7 million for the years ended December 31, 2020, 2021 and 2022, respectively. Our capital expenditures during these periods were primarily used for the purchases of leasehold land and property, plant and equipment for a new large-scale manufacturing facility for innovative drugs in Shanghai, China and to expand research facilities and our manufacturing facility in Suzhou, China. Our capital expenditures have been primarily funded by cash flows from operations, bank borrowings and proceeds from our initial public and follow-on offerings in Hong Kong and the United States and other equity offerings.

As of December 31, 2022, we had commitments for capital expenditures of approximately $22.1 million, primarily for the construction of the new manufacturing facility in Shanghai. We expect to fund these capital expenditures through cash flows from operations, bank borrowings and existing cash resources.

Our non-consolidated joint venture Shanghai Hutchison Pharmaceuticals had capital expenditures of $2.4 million, $3.4 million and $1.9 million for the years ended December 31, 2020, 2021 and 2022, respectively. These capital expenditures were primarily related to the renovation of new office and improvements to its production facilities in Shanghai. These capital expenditures were primarily funded through cash flows from operations of Shanghai Hutchison Pharmaceuticals.

C. Research and Development, Patents and Licenses, etc.

Full details of our research and development activities and expenditures are given in the "Business" and "Operating and Financial Review and Prospects" sections of this annual report above.

D. Trend Information.

Other than as described elsewhere in this annual report, we are not aware of any trends, uncertainties, demands, commitments or events that are reasonably likely to have a material adverse effect on our revenue, income, profitability, liquidity or capital resources, or that would cause our reported financial information not necessarily to be indicative of future operation results or financial condition.

E. Critical Accounting Estimates.

For information on our critical accounting estimates, please see "—Operating Results—Critical Accounting Policies and Significant Judgments and Estimates" section of this annual report above.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management.

Business Experience and Qualifications of our Directors and Senior Management

Below is a list of the names and ages of our directors and officers as of January 31, 2023, and a brief account of the business experience of each of them. The business address for our directors and officers is c/o HUTCHMED (China) Limited, Level 18, The Metropolis Tower, 10 Metropolis Drive, Hunghom, Kowloon, Hong Kong.

Name	Age	Position
TO Chi Keung, Simon	71	Executive Director and Chairman
Weiguo SU	65	Executive Director, Chief Executive Officer and Chief Scientific Officer
CHENG Chig Fung, Johnny	56	Executive Director and Chief Financial Officer
Edith SHIH	71	Non-executive Director and Company Secretary
Dan ELDAR	69	Non-executive Director
Lefei SUN	43	Non-executive Director
Paul Rutherford CARTER	62	Senior Independent Non-executive Director
Karen Jean FERRANTE	65	Independent Non-executive Director
Graeme Allan JACK	72	Independent Non-executive Director
MOK Shu Kam, Tony	62	Independent Non-executive Director
Michael Ming SHI	57	Executive Vice President, Head of R&D and Chief Medical Officer
Karen Jane ATKIN	57	Executive Vice President and Chief Operating Officer
Zhenping WU	63	Executive Vice President, Pharmaceutical Sciences
Mark Kin Hung LEE	45	Senior Vice President, Corporate Finance and Development
May Qingmei WANG	59	Senior Vice President, Business Development & Strategic Alliances
Hong CHEN	52	Senior Vice President and Chief Commercial Officer (China)
Charles George Rupert NIXON	53	Group General Counsel

To Chi Keung, Simon has been a director since 2000 and an executive director and chairman of our Company since 2006. He is also a member of our nomination committee, remuneration committee and technical committee. He is the managing director of Hutchison Whampoa (China) Limited ("Hutchison China") and has been with Hutchison China for over 40 years, building its business from a small trading company to a multi-billion dollar investment group. He has negotiated major transactions with multinational corporations such as Procter & Gamble, Lockheed, Pirelli, Beiersdorf, United Airlines, and British Airways. He is currently a non-executive director of Gama Aviation Plc and formerly served as independent non-executive director on the boards of China Southern Airlines Company Limited and Air China Limited. In addition, Mr. To is a director of certain substantial shareholders (within the meaning of the Securities and Futures Ordinance) of the Company and certain companies controlled by substantial shareholders of the Company. Mr. To's career in China spans more than 45 years. He is the original founder of the China healthcare business of Hutchison Whampoa Limited (currently a subsidiary of CK Hutchison) and has been instrumental in its acquisitions made to date. He received a Bachelor's degree in Mechanical Engineering from Imperial College, London and a Master in Business Administration from Stanford University's Graduate School of Business.

Weiguo Su has been an executive director since 2017 and chief executive officer of our Company since March 4, 2022. He is also our chief scientific officer since 2012. He is also a member of our technical committee. Dr. Su has headed all drug discovery and research since he joined our company, including master-minding our scientific strategy, being a key leader of our Oncology/Immunology operations, and responsible for the discovery of each and every small molecule drug candidate in our pipeline. Prior to joining our company in 2005, Dr. Su worked with the U.S. research and development department of Pfizer, Inc. In 2017, Dr. Su was granted the prestigious award by the China Pharmaceutical Innovation and Research Development Association (PhIRDA) as one of the Most Influential Drug R&D Leaders in China. Dr. Su received a bachelor of science degree in chemistry from Fudan University in Shanghai and completed a PhD and post-doctoral fellowship in chemistry at Harvard University under the guidance of Nobel Laureate Professor E. J. Corey.

Cheng Chig Fung, Johnny has been an executive director since 2011 and our chief financial officer since 2008. He is a member of our sustainability committee. Prior to joining our company, Mr. Cheng was vice president, finance of Bristol Myers Squibb in China and was a director of Sino-American Shanghai Squibb Pharmaceuticals Ltd. and Bristol-Myers Squibb (China) Investment Co. Ltd. in Shanghai between late 2006 and 2008. Mr. Cheng started his career as an auditor with Price Waterhouse (currently PricewaterhouseCoopers) in Australia and then KPMG in Beijing before spending eight years with Nestlé China where he was in charge of a number of finance and control functions in various operations. Mr. Cheng received a bachelor of economics, accounting major from the University of Adelaide and is a member of Chartered Accountants Australia and New Zealand.

Edith Shih has been a non-executive director since 2006, the company secretary of our company and the company secretary of group companies since 2000. She is also chairman of our sustainability committee. She has over 40 years of experience in legal, regulatory, corporate finance, compliance and corporate governance fields. She is also executive director and company secretary of CK Hutchison. She has been with the Cheung Kong (Holdings) Limited ("CKH") group since 1989 and with Hutchison Whampoa Limited ("HWL") since 1991. Both CKH and HWL were formerly listed on SEHK and became wholly-owned subsidiaries of CK Hutchison in 2015. She has acted in various capacities within the HWL group, including head group general counsel and company secretary of HWL as well as director and company secretary of HWL subsidiaries and associated companies. Ms. Shih is in addition a non-executive director of Hutchison Telecommunications Hong Kong Holdings Limited, Hutchison Port Holdings Management Pte. Limited as the trustee-manager of Hutchison Port Holdings Trust and a commissioner of PT Duta Intidaya Tbk. In addition, Ms. Shih is a director of certain substantial shareholders (within the meaning of the Securities and Futures Ordinance) of our company and certain companies controlled by certain substantial shareholders of our company. The aforementioned companies are either subsidiaries or associated companies of CK Hutchison of which Ms. Shih has oversight as a director of CK Hutchison. She is the past international president and current member of the council of The Chartered Governance Institute ("CGI") as well as a past president and current honorary advisor of The Hong Kong Chartered Governance Institute ("HKCGI") and current chairperson of its nomination committee. She is also chairman of the process review panel for the Accounting and Financial Reporting Council (formerly known as the Financial Reporting Council) and a member of the Securities and Futures Appeals Tribunal and of the Hong Kong-Europe Business Council. Ms. Shih is a solicitor qualified in England and Wales, Hong Kong and Victoria, Australia and a fellow of both the CGI and HKCGI, holding chartered secretary and chartered governance professional dual designations. She holds a bachelor of science degree and a master of arts degree from the University of the Philippines as well as a master of arts degree and a master of education degree from Columbia University, New York.

Dan Eldar has been a non-executive director of our company since 2016. He has more than 30 years of experience as a senior executive, leading global operations in telecommunications, water, biotech and healthcare. He is an executive director of Hutchison Water Israel Ltd which focuses on large scale projects including desalination, wastewater treatment and water reuse. He was formerly an independent non-executive director of Leumi Card Ltd., a subsidiary of Bank Leumi Le-Israel B.M., one of Israel's leading credit card companies. Dr. Eldar received a doctor of philosophy degree in government from Harvard University, master of arts degree in government from Harvard University, master of arts degree in political science and public administration from the Hebrew University of Jerusalem and a bachelor of arts degree in political science from the Hebrew University of Jerusalem.

Lefei Sun has been a non-executive director of our company since 2022. He is also a member of our technical committee. He has been the managing director and head of China healthcare for General Atlantic since 2018, in charge of private equity investment and portfolio management in healthcare and life sciences sectors. Before joining General Atlantic, Mr. Sun was the founding partner of Huatai Healthcare Investment Fund, successfully leading the investment in Mindray Medical, which is listed on Shenzhen Stock Exchange. Mr. Sun is also a director of Adagene Inc. and Genesis MedTech Group Inc. He was formerly a director of CANbridge Pharmaceuticals Inc. and Ocumension Therapeutics Inc. Mr. Sun holds a bachelor of science degree in mathematics and physics from Tsinghua University. He also holds a master of arts degree in neuroscience from the Johns Hopkins University.

Paul Rutherford Carter has been a senior independent non-executive director of our company since 2017. He is also chairman of our remuneration committee and a member of our audit committee and technical committee. He has more than 26 years of experience in the pharmaceutical industry. From 2006 to 2016, Mr. Carter served in various senior executive roles at Gilead Sciences, Inc. ("Gilead"), a research-based biopharmaceutical company, with the last position as executive vice president, commercial operations. In this role, Mr. Carter headed the worldwide commercial organization responsible for the launch and commercialization of all of the products of Gilead. He also worked as a senior executive at GlaxoSmithKline Plc. He is currently a director of Immatics N.V. and VectivBio Holding AG. He is the chairman of Evox Therapeutics and a retained advisor to several firms active in the life sciences sector. He was formerly a director of Alder Biopharmaceuticals, Inc and Mallinckrodt plc. Mr. Carter received a degree in business studies from the Ealing School of Business and Management (now merged into University of West London) and is a fellow of the Chartered Institute of Management Accountants in the United Kingdom.

Karen Jean Ferrante has been an independent non-executive director of our company since 2017. She is also chairman of our technical committee and a member of our audit committee. She has more than 26 years of experience in the pharmaceutical industry. She was the former chief medical officer and head of research and development of Tokai Pharmaceuticals, Inc., a biopharmaceutical company focused on developing and commercializing innovative therapies for prostate cancer and other hormonally driven diseases. Dr. Ferrante previously held senior positions at Millennium Pharmaceuticals, Inc. and its parent company, Takeda Pharmaceutical Company Limited, including chief medical officer and most recently as oncology therapeutic area and Cambridge USA site head. She had also held positions of increasing responsibility at Pfizer Inc. (“Pfizer”), with the last position as vice president, oncology development. Dr. Ferrante is currently a member of the board of directors of MacroGenics, Inc., and Cogent Biosciences, Inc. (formerly Unum Therapeutics Inc.). Dr. Ferrante was previously a director of Baxalta Incorporated until it was acquired by Shire plc in 2016 and a director of Progenics Pharmaceuticals, Inc., until it was acquired by Lantheus Holdings, Inc. in 2020. She was previously a member of the scientific advisory board of Trillium Therapeutics Inc. until it was acquired by Pfizer in November 2021. She was also a past member of the Scientific Advisory Board of Kazia Therapeutics Limited. Dr. Ferrante is an author of a number of papers in the field of oncology, an active participant in academic and professional associations and symposia and holder of several patents. Dr. Ferrante received a bachelor of science degree in chemistry and biology from Providence College and a doctor of medicine from Georgetown University.

Graeme Allan Jack has been an independent non-executive director of our company since 2017. He is also chairman of our audit committee and a member of our nomination committee and remuneration committee. He has more than 40 years of experience in finance and audit. He retired as partner of PricewaterhouseCoopers in 2006 after a distinguished career with the firm for over 33 years. He is currently an independent non-executive director of The Greenbrier Companies, Inc. (an international supplier of equipment and services to the freight rail transportation markets) and Hutchison Port Holdings Management Pte. Limited as the trustee-manager of Hutchison Port Holdings Trust (a developer and operator of deep water container terminals). He was formerly a director of COSCO SHIPPING Development Co., Ltd. (formerly known as “China Shipping Container Lines Company Limited”, an integrated financial services platform principally engaged in vessel and container leasing). Mr. Jack received a bachelor of commerce degree from University of New South Wales, Australia and is a fellow of the Hong Kong Institute of Certified Public Accountants and an associate of Chartered Accountants Australia and New Zealand.

Mok Shu Kam, Tony has been an independent non-executive director of our company since 2017. He is also chairman of our nomination committee and a member of our sustainability committee and technical committee. Professor Mok has more than 31 years of experience in clinical oncology with his main research interest focusing on biomarker and molecular targeted therapy in lung cancer. He is currently Li Shu Fan Medical Foundation named professor and chairman of department of clinical oncology at The Chinese University of Hong Kong. Professor Mok has contributed to over 250 articles in international peer-reviewed journals, as well as multiple editorials and textbooks. In October 2018, Professor Mok was the first Chinese to be bestowed with the European Society for Medical Oncology (ESMO) Lifetime Achievement Award, one of the most prestigious international honors and recognitions given to cancer researchers, for his contribution to and leadership in lung cancer research worldwide. Professor Mok is a non-executive director of AstraZeneca PLC, a non-executive independent director of Lunit USA Inc and a member of the scientific advisory board of Prenetics Global Limited (“Prenetics”). He is co-founder of Sanomics Limited (acquired by ACT Genomics Holdings Ltd. in November 2021) and Aurora Tele-Oncology Limited. He was formerly a board director of the American Society of Clinical Oncology (“ASCO”), a steering committee member of the Chinese Society of Clinical Oncology, past president of the International Association for the Study of Lung Cancer, and the chairman of the board of ACT Genomics Holdings Ltd. until it was acquired by Prenetics in December 2022. Professor Mok is also closely affiliated with the oncology community in China and has been awarded an Honorary Professorship at Guangdong Province People’s Hospital, Guest Professorship at Peking Union Medical College Hospital and Visiting Professorship at Shanghai Jiao Tong University. He received his bachelor of medical science degree and a doctor of medicine from University of Alberta, Canada. He is also a fellow of the Royal College of Physicians and Surgeons of Canada, Hong Kong College of Physicians, Hong Kong Academy of Medicine, Royal College of Physicians of Edinburgh and ASCO.

Michael Ming Shi is our executive vice president, head of R&D and chief medical officer, oversees the drug discovery and development of our Company from strategy to execution. Prior to joining our company in 2022, Dr. Shi was the global head of R&D and chief medical officer at Transcenta Holding Limited where he helped building a strong global research and development organization across China and the U.S. and advanced seven programs into clinical development and multiple preclinical candidate nominations. Before that, Dr. Shi worked at Novartis for over 15 years, where he held various senior leadership positions including global program clinical head in clinical development. He played key leadership roles in the clinical development of multiple novel oncology/hematology products from clinical proof-of-concept to successful execution of global pivotal trials, product registration and life-cycle management. Dr. Shi is a member of American Society of Clinical Oncology, European Society of Clinical Oncology, American Society of Hematology, American Association for Cancer Research, Sino-American Pharmaceutical Association and an executive committee member of the US-China Anticancer Association (USCACA). Dr. Shi also worked as the program director of Genetics Variation at National Institution of Health ("NIH") under the direct supervision of NIH director Dr. Francis Collins and was an adjunct assistant professor at the University of Michigan Medical School. Dr. Shi holds a Ph.D. in Molecular Pharmacology and Toxicology from the University of Southern California, and conducted postdoctoral research at the Harvard Medical School. He received his medical education from Peking Union Medical College.

Karen Jane Atkin is our executive vice president and chief operating officer. Prior to joining our company in 2021, Dr. Atkin spent 24 years at AstraZeneca in senior medical, regulatory, pharmacovigilance, R&D and commercial leadership roles, including as senior vice president of medical for biopharmaceuticals, vice president of the global infection, neuroscience and autoimmunity therapy area and the established branch business, country president of Indonesia and led China R&D for over four years. Dr. Atkin is also a registered physician with advanced level qualifications in internal medicine and pharmaceutical medicine. Dr. Atkin holds three bachelor's degrees in physiology, medicine and surgery, respectively, from University College London. She graduated with a first class honors degree in medicine, holds an MBA from the Open University, and is a Member of the Royal College of Physicians and a fellow of the Faculty of Pharmaceutical Medicine in the UK.

Zhenping Wu joined our company in 2008 and is our executive vice president of pharmaceutical sciences. Dr. Wu has over 29 years of experience in drug discovery and development. His past positions include senior director of pharmaceutical sciences at Phenomix Corporation, a U.S.-based biotechnology company, director of pharmaceutical development at Pfizer Global Research & Development in California (formerly Agouron Pharmaceuticals) and a group leader at Roche at its Palo Alto site. He is a past chairman and president of the board of the Sino-American Biotechnology and Pharmaceutical Association. Dr. Wu received a Ph.D. from the University of Hong Kong and a master in business administration from the University of California at Irvine.

Mark Kin Hung Lee is our senior vice president of corporate finance and development and joined our company in 2009. He began working in healthcare investment banking in the United States and Europe in 1998. Based in the New York and London offices of Credit Suisse, Mr. Lee was involved in the execution and origination of mergers, acquisitions, public and private financings and corporate strategy for life science companies such as AstraZeneca, Bristol-Myers Squibb and Genzyme, as well as other medical product and service companies. Mr. Lee received his bachelor's degree in biochemical engineering with first class honors from University College London, where he was awarded a Dean's Commendation. He also received a master of business administration from the Massachusetts Institute of Technology's Sloan School of Management.

May Qingmei Wang is our senior vice president of business development & strategic alliances. Prior to joining our company in 2010, Dr. Wang spent 16 years with Eli Lilly where she was the head of Eli Lilly's Asian Biology Research and responsible for establishing and managing research collaborations in China and across Asia. Dr. Wang holds numerous patents, has published more than 50 peer-reviewed articles and has given dozens of seminars and plenary lectures. Dr. Wang received a Ph.D. in biochemistry from Purdue University.

Hong Chen is our senior vice president and chief commercial officer (China). Prior to joining our company in 2011, Mr. Chen spent 12 years with Bristol-Myers Squibb and was last serving as its national sales & marketing director in China. Mr. Chen received a bachelor's degree in medicine from Nanjing Medical University and an EMBA from Cheung Kong Graduate School of Business.

Charles George Rupert Nixon has been our group general counsel since 2015 and has worked with us since 2006. Prior to joining us, Mr. Nixon was group senior legal counsel for Hutchison Whampoa Limited (previously a listed company in Hong Kong and after a restructuring, a subsidiary of CK Hutchison) in both Hong Kong and London and prior to that senior legal counsel for Three UK, a mobile phone operator. Mr. Nixon has been with the CK Hutchison Group since 2001. Mr. Nixon received an LL.B (Hons) from Middlesex University and is a qualified solicitor in England & Wales with over 30 years of experience.

Board Diversity

On August 6, 2021, the SEC approved the Nasdaq Stock Market's proposal to amend its listing standards to encourage greater board diversity and to require board diversity disclosures for Nasdaq-listed companies. Pursuant to the amended listing standards, HUTCHMED, as a foreign private issuer, is required to have at least two diverse board members or explain the reasons for not meeting this objective by 2025. Furthermore, a board diversity matrix is required to be included in the annual report on Form 20-F, containing certain demographic and other information regarding members of our board of directors. HUTCHMED currently complies with the diversity requirement, as we currently have two female and eight male members on our board of directors. The board diversity matrix is set out below.

Board Diversity Matrix (As of February 28, 2023)	
Place of Principal Executive Offices	Hong Kong
Foreign Private Issuer	Yes
Disclosure Prohibited under Home Country Law	No
Total Number of Directors	10

	Female	Male	Non-Binary	Did Not Disclose Gender
Part I: Gender Identity				
Directors	2	8	—	—
Part II: Demographic Background				
Underrepresented Individual in Place of Principal Executive Offices	—	—	—	—
LGBTQ+	—	—	—	—
Did Not Disclose Demographic Background	—	—	—	—

B. Compensation.

Executive Officer Compensation

Summary Compensation Table

The following table sets forth the non-equity compensation paid or accrued during the year ended December 31, 2022 to our chief executive officer and chief scientific officer, chief financial officer and other executive officers on an aggregate basis.

Name and Principal Position	Salary and fees ($)	Bonus(3) ($)	Taxable benefits ($)	Non-taxable benefits ($)	Pension contributions ($)	Total ($)
Weiguo SU	774,940 (1)	1,126,563	—	6,548	64,217	1,972,268
CHENG Chig Fung, Johnny	404,415 (2)	443,077	—	10,577	29,018	887,087
Other Executive Officers in the Aggregate	3,082,493	3,748,868	26,646	101,846	183,020	7,142,873

Notes:

(1) Amount includes director's fees of $75,000.

(2) Amount includes director's fees of $75,000.

(3) In December 2013 and March 2014, we awarded cash retention bonuses to certain of our executive officers in the aggregate amount of $2,977,751. Each such executive officer receives portions of his or her retention bonus upon certain dates in the future depending on when the bonus was granted and, in each case, assuming he or she remains employed by our company on such future dates. In 2022, we awarded $322,188 of such cash retention bonuses.

Employment Arrangements with our Executive Officers

Employment Agreements with Executive Officers at HUTCHMED Group (HK) Limited and HUTCHMED Holdings (HK) Limited

We have entered into employment agreements with each of our executive officers who are directly employed by HUTCHMED Group (HK) Limited or HUTCHMED Holdings (HK) Limited, namely Mr. Cheng Chig Fung, Johnny, Ms. Karen Jane Atkin, Mr. Mark Kin Hung Lee and Mr. Charles George Rupert Nixon. Under these employment agreements, our executives receive compensation in the form of salaries, discretionary bonuses, participation in the Hutchison Provident Fund retirement scheme, medical coverage under the CK Hutchison Group Medical Scheme, personal accident insurance and annual leave. None of the employment arrangements provide benefits to our executive officers upon termination. We may terminate employment by giving the executive officers three months' prior written notice. The executive officer may also voluntarily terminate his/her employment with us upon not less than three months' prior written notice to us.

Each executive officer has agreed, for the term of employment with us and thereafter, not to disclose or use for his/her own purposes any of our and our associated companies' confidential information that the executive officer may develop or learn in the course of employment with us. Moreover, each of our executive officers has agreed, for the term of employment with us and for a period of twelve months thereafter, (i) not to undertake or be employed or interested directly or indirectly anywhere in Hong Kong in any activity which is similar to and competitive with our company or associated companies in which the executive officer had been involved in the period of 12 months prior to such termination and (ii) not to solicit for any employees of our company or our joint ventures or orders from any person, firm or company which was at any time during the 12 months prior to termination of such employment a customer or supplier of our company or associated companies.

Employment Agreements with Executive Officers at HUTCHMED Limited

We have entered into employment agreements with each of our executive officers who are employed directly by HUTCHMED Limited, namely Dr. Weiguo Su, Dr. Michael Ming Shi, Dr. May Qingmei Wang and Dr. Zhenping Wu. Under these employment agreements, we engage the executive officer on either an open-ended or a fixed term. Our executive officers receive compensation in the form of salaries, discretionary bonuses, annual leave, statutory maternity leave and nursing leave.

Under the terms of these agreements, we provide labor protection and work conditions that comply with the safety and sanitation requirements stipulated by the relevant PRC laws. The employment agreements prohibit the executive officers from engaging in any conduct and business activities which may compete with the business or interests of HUTCHMED Limited during the term of the executive officer's employment. These executive officers also enjoy the Hutchison Provident Fund retirement scheme, medical coverage under the CK Hutchison Group Medical Scheme and personal accident insurance.

We may terminate an executive officer's employment for cause at any time without notice. Termination for cause may include a serious breach of our internal rules and policies, serious negligence in the executive officer's performance of his or her duties, an accusation or conviction of a criminal offence, acquisition of another job which materially affects the executive officer's ability to perform his or her duties for our company and other circumstances stipulated by applicable PRC laws. We may terminate an executive officer's employment with three months' prior notice if the executive officer is unable to perform his or her duties (after the expiration of the prescribed medical treatment period) because of an illness or non-work-related injury or the executive officer is incompetent and remains incompetent after training or adjustment of his or her position.

The executive officer may voluntarily terminate his or her contract without cause with three months' prior notice. The executive officer may also terminate the employment agreement immediately for cause, which includes a failure by us to provide labor protection and the work conditions as specified under the employment agreement. In case of termination for any reason, we agree to make any mandatory severance payments required by the relevant PRC labor laws.

Employment Agreement with Executive Officer at Hutchison Sinopharm

We have entered into an employment agreement with Mr. Hong Chen, one of our executive officers, who is directly employed by Hutchison Sinopharm. Under his employment agreement with Hutchison Sinopharm, Mr. Chen's employment is for a fixed term, and he receives compensation in the form of salaries, discretionary bonuses, annual leave, statutory maternity leave and nursing leave.

Under the terms of this agreement, we provide labor protection and work conditions that comply with the safety and sanitation requirements stipulated by the relevant PRC laws. The employment agreement prohibits any conduct directly or indirectly which is harmful to Hutchison Sinopharm during the term of the employment.

We may terminate Mr. Chen’s employment for cause at any time without notice. We may also terminate the employment with prior notice and termination compensation if Mr. Chen is unable to perform his duties because of an illness or non-work-related injury or he is incompetent and remains incompetent after training or adjustment of his position. Mr. Chen may voluntarily terminate his employment agreement without cause with one month’s prior notice and immediately for cause.

Share Options

The following table sets forth information concerning the outstanding equity awards held by our chief executive officer and chief scientific officer, chief financial officer and other executive officers on an aggregate basis as of December 31, 2022.

Name and Principal Position	Date of grant of share options[(1)]	Number of unexercised shares which are vested	Number of unexercised shares which are unvested	Exercise price		Number of shares issued upon exercise in 2022	Number of options lapsed/ cancelled in 2022	Option expiration date
Weiguo SU	Jun 15, 2016	3,000,000	—	£	1.970	—	—	Dec 19, 2023
Weiguo SU	Mar 27, 2017	1,000,000	—	£	3.105	—	—	Mar 26, 2027
Weiguo SU	Mar 19, 2018	1,000,000	—	£	4.974	—	—	Mar 18, 2028
Weiguo SU	Apr 28, 2020	394,850 (= 78,970 ADSs)	394,850 (= 78,970 ADSs)	$	22.090	—	—	Apr 27, 2030
Weiguo SU	Dec 14, 2020	9,480 (= 1,896 ADSs)	9,480 (= 1,896 ADSs)	$	29.000	—	—	Dec 13, 2030
Weiguo SU	Mar 26, 2021	70,600 (= 14,120 ADSs)	211,800 (= 42,360 ADSs)	$	27.940	—	—	Mar 25, 2031
Weiguo SU	Dec 14, 2021	6,230 (= 1,246 ADSs)	18,700 (= 3,740 ADSs)	$	35.210	—	—	Dec 13, 2031
Weiguo SU	May 23, 2022	—	861,220 (= 172,244 ADSs)	$	10.750	—	—	May 22, 2032
CHENG Chig Fung, Johnny	Apr 28, 2020	200,950 (= 40,190 ADSs)	200,950 (= 40,190 ADSs)	$	22.090	—	—	Apr 27, 2030
CHENG Chig Fung, Johnny	Mar 26, 2021	60,125 (= 12,025 ADSs)	180,375 (= 36,075 ADSs)	$	27.940	—	—	Mar 25, 2031
CHENG Chig Fung, Johnny	May 23, 2022	—	446,600 (= 89,320 ADSs)	$	10.750	—	—	May 22, 2032
Other Executive Officers in the Aggregate	Jun 15, 2016	2,736,860	—	£	1.970	200,000	—	Dec 19, 2023
Other Executive Officers in the Aggregate	Apr 20, 2018	701,100	—	£	4.645	—	—	Apr 19, 2028
Other Executive Officers in the Aggregate	Aug 6, 2018	375,000	—	£	4.860	—	—	Aug 5, 2028
Other Executive Officers in the Aggregate	Dec 11, 2019	300,000	100,000	£	3.592	—	—	Dec 10, 2029
Other Executive Officers in the Aggregate	Apr 28, 2020	879,200 (= 175,840 ADSs)	879,200 (= 175,840 ADSs)	$	22.090	—	—	Apr 27, 2030
Other Executive Officers in the Aggregate	Dec 14, 2020	154,930 (= 30,986 ADSs)	154,960 (= 30,992 ADSs)	$	29.000	—	—	Dec 13, 2030
Other Executive Officers in the Aggregate	Mar 26, 2021	257,775 (= 51,555 ADSs)	773,325 (= 154,665 ADSs)	$	27.940	—	—	Mar 25, 2031
Other Executive Officers in the Aggregate	Dec 14, 2021	89,225 (= 17,845 ADSs)	267,730 (= 53,546 ADSs)	$	35.210	—	—	Dec 13, 2031
Other Executive Officers in the Aggregate	May 23, 2022	—	1,015,800 (= 203,160 ADSs)	$	10.750	—	—	May 22, 2032
Other Executive Officers in the Aggregate	Sep 13, 2022	—	1,500,000 (= 300,000 ADSs)	$	13.140	—	—	Sep 12, 2032

Notes:

(1) The share options granted on or after April 28, 2020 were in the form of ADSs and the relevant exercise prices were stated in U.S. dollars per ADS. For purposes of this table, these share options are presented in the form of ordinary shares (with the corresponding number of ADSs where appropriate). Each ADS represents five ordinary shares.

Long-Term Incentive Compensation

The following table sets forth information regarding performance based LTIP awards granted to our chief executive officer and chief scientific officer, chief financial officer and other executive officers on an aggregate basis in the year ended December 31, 2022.

Name and Principal Position	Maximum Aggregate Value of LTIP awards(1) (2)(3)
Weiguo SU, Chief Executive Officer and Chief Scientific Officer	$ 3,232,845
CHENG Chig Fung, Johnny, Chief Financial Officer	$ 680,242
Other Executive Officers in the Aggregate	$ 3,410,498

Notes:

(1) The amounts reflected in the table above represent the maximum aggregate value of all LTIP awards outstanding as of December 31, 2022. The LTIP awards are conditional upon the achievement of annual performance targets for the fiscal year 2022. The amounts reflected in the table above assume the maximum amount that may be paid under these contingent LTIP awards. The LTIP awards will be settled in a variable number of shares based on a fixed monetary amount awarded upon achievement of performance targets. An independent third-party trustee who administers the LTIP purchased shares of our company on either the AIM or Nasdaq market which will be used to settle the LTIP awards. See "Outstanding Awards" for more details.

(2) Vesting will occur two business days after the date of the announcement of our annual results for the financial year 2024.

(3) Excluding performance based LTIP awards abovementioned, a non-performance based LTIP award granted to an Executive Officer in an amount of US$1,500,000, for which 111,731 ADSs were allocated on September 13, 2022. 25% of the shares will be vested on September 13, 2023, September 13, 2024, September 13, 2025 and September 13, 2026 respectively.

Director Compensation

The following table sets forth a summary of the compensation we paid to our directors other than Weiguo Su and Cheng Chig Fung, Johnny during 2022.

Name of Director	Fees Earned or Paid in Cash	Maximum Value of Non-Performance Based LTIP Awards Granted
TO Chi Keung, Simon	$ 85,000 (1)	—
Dan ELDAR	—	—
Edith SHIH	— (2)	—
Lefei SUN	—	—
Paul Rutherford CARTER	$ 117,000	—
Karen Jean FERRANTE	$ 102,500	—
Graeme Allan JACK	$ 111,000	—
MOK Shu Kam, Tony	$ 103,000	—

Notes:

(1) Such director's fees were paid to Hutchison Whampoa (China) Limited, a wholly owned subsidiary of CK Hutchison. Director's fees received from our subsidiaries during the period he served as director that were paid to an intermediate holding company of our company are not included in the amounts above.

(2) Director's fees received from our subsidiaries during the period she served as director that were paid to a subsidiary of CK Hutchison are not included.

Equity Compensation Schemes and Other Benefit Plans

We have two share option schemes. We refer to these collectively as the Option Schemes. Our shareholder adopted the first option scheme, or the 2005 Option Scheme, in June 2005, and it was subsequently approved by the shareholders of Hutchison Whampoa Limited, our then majority shareholder, in May 2006 and later amended by our board of directors in March 2007. This share option scheme expired in 2016. In April 2015, our shareholders adopted the second option scheme, or the 2015 Option Scheme, which was later approved by the shareholders of CK Hutchison, the ultimate parent of our then majority shareholder, in May 2016. The 2015 Option Scheme was subsequently amended in April 2020.

We also have a long-term incentive scheme which was adopted by our shareholders in April 2015. We refer to this as our LTIP.

Our Option Schemes and LTIP each terminates on the tenth anniversary of their adoption. Each may also be terminated by its board of directors at any time. Any termination of a scheme is without prejudice to the awards outstanding at such time. Options are no longer being granted under the 2005 Option Scheme, but outstanding awards under the 2005 Option Scheme continue to be governed by the terms thereof.

The following describes the material terms of our Option Schemes and LTIP, or collectively the Schemes.

Awards and Eligible Grantees. The Option Schemes provide for the award of share options exercisable for ordinary shares or ADSs of our company to Eligible Employees (as defined in the Option Schemes) or non-executive directors (excluding any independent non-executive directors under the Option Schemes).

Under our LTIP, awards in the form of contingent rights to receive either shares purchased from the market by the scheme trustee or cash payments may be granted to the directors of our company, directors of our subsidiaries and employees of our company, subsidiaries, affiliates or such other companies as determined by our board of directors in its absolute discretion.

Scheme Administration. Our board of directors has delegated its authority for administering our Option Schemes and our LTIP to our remuneration committee. Each such plan administrator has the authority to, among other things, select participants and determine the amount and terms and conditions of the awards under the applicable Schemes as it deems necessary and proper, subject to the restrictions described in "—Restrictions on Grants" below.

Restrictions on Grants. Under the Option Schemes, grants may not be made to independent non-executive directors. Furthermore, those grants may not be made to any of our employees or directors if such person is also a director, chief executive or substantial shareholder of any of our direct or indirect parent companies which is listed on a stock exchange or any of its associates without approval by the independent non-executive directors of such parent company (excluding any independent non-executive director who is a proposed grantee). In addition, approval by our shareholders and the shareholders of such listed parent company is required if an option grant under our Option Schemes is to be made to a substantial shareholder or independent non-executive director of a listed parent company or any of its associates and, upon exercise of such grant and any other grants made during the prior 12-month period to that shareholder, that individual would receive an amount of our ordinary shares equal or greater than 0.1% of our total outstanding shares or with an aggregate value in excess of HK$5 million (equivalent to $0.6 million as of December 31, 2022).

In addition, options under our Option Schemes may not be granted to any individual if, upon the exercise of such options, the individual would receive an amount of shares when aggregated with all other options granted to such individual under the applicable Scheme in the 12-month period up to and including the grant date, that exceeds 1% of the total shares outstanding of the company granting the award on such date. There are no individual limits under our LTIP.

Under our LTIP, no grant to any director, chief executive or substantial shareholder of our company may be made without the prior approval of our independent non-executive directors (excluding an independent non-executive director who is a proposed grantee).

Vesting. Vesting conditions of options granted under the Schemes are determined by the respective board of directors at the time of grant.

Under our Option Schemes, if a participant has committed any misconduct or any conduct making such participant's service terminable for cause, all options (whether vested or unvested) lapse unless the respective board of directors otherwise determines in its absolute discretion. Options may be exercised to the extent vested where a participant's service ceases due to the participant's death, serious illness, injury, disability, retirement at the applicable retirement age, or earlier if determined by the participant's employer, or if a participant's service ceases for any other reason other than for cause.

Under our LTIP, if a participant's employment or service with our company or its subsidiaries is terminated for cause or if the participant breaches certain provisions in our LTIP restricting the transfer of awards by grantees and imposing non-competition obligations on grantees, all unvested awards are automatically cancelled. Where a participant's employment or service ceases for any reason other than the reasons listed above (including due to the participant's resignation, retirement, death or disability or upon the non-renewal of such participant's employment or service agreement other than for cause), our board of directors may determine at its discretion whether unvested awards shall be deemed vested.

Exercise Price. The exercise price for each share pursuant to the initial options granted under the 2005 Option Scheme was a price determined by our board of directors at the date of grant, and for grants made thereafter, the exercise price was the Market Value of a share at the date of grant (as defined in our Option Schemes).

The exercise price for each share pursuant to the options granted under the 2015 Option Scheme must be the Market Value of a share at the date of grant (as defined in our Option Schemes).

Non-transferability of Awards. Awards may not be transferred except in the case of a participant's death by the terms of each Scheme.

Takeover or Scheme of Arrangement. In the event of a general or partial offer for the shares of our company under our Option Schemes, whether by way of takeover, offer, share repurchase offer, or scheme of arrangement, the affected company is required to use all reasonable endeavors to procure that such offer is extended to all holders of options granted by such company on the same terms as those applying to shareholders. Both vested and unvested options may be exercised up until (i) the closing date of any such offer and (ii) the record date for entitlements under a scheme of arrangement, and will lapse thereafter. Certain options may also be exercised on a voluntary winding up of our company.

Under our LTIP, in the event of a general offer for all the shares of our company, whether by way of takeover or scheme of arrangement, or if our company is to be voluntarily wound up, our board of directors shall determine in its discretion whether outstanding unvested awards will vest and the period within which such awards will vest.

Amendment. Our Option Schemes require that amendments of a material nature only be made with the approval of our shareholders.

Our board of directors may alter the terms of our LTIP, but amendments which are of a material nature cannot take effect without shareholders' approval, unless the changes take effect automatically under the terms of our LTIP.

Authorized Shares. Under our 2015 Option Scheme, our board of directors may "refresh" the scheme limit from time to time provided that the total number of shares which may be issued upon exercise of all options to be granted under our Option Schemes shall not exceed 10% of our total shares outstanding on such date. In addition, the limit on the number of shares which may be issued upon exercise of all outstanding options granted and not yet exercised under the 2015 Option Scheme and any options granted and not yet exercised under any other schemes must not exceed 10% of the outstanding shares of the company in issue from time to time. In April 2020, our shareholders approved a refresh of the 2015 Option Scheme.

Following the 2015 Option Scheme refresh discussed above, subject to certain adjustments for share splits, share consolidations and other changes in capitalization, the maximum number of shares that may be issued upon exercise of all options granted may not in the aggregate exceed 5% of our shares outstanding on April 27, 2020. Share awards under our LTIP may not exceed 5% of our shares outstanding on the adoption date of our LTIP.

Outstanding Awards and Grants of Awards

Share options outstanding under the 2005 Option Scheme

The 2005 Option Scheme expired in 2016, and no further share options can be granted under it. As of December 31, 2022, options to purchase an aggregate of 660,570 ordinary shares, representing approximately 0.1% of our outstanding share capital, with an exercise price of £0.61 ($0.74) per ordinary share and an expiration date of December 19, 2023 remained outstanding under the 2005 Option Scheme.

Share options outstanding and grants made in 2022 under the 2015 Option Scheme

As of December 31, 2022, options to purchase an aggregate of 38,860,825 ordinary shares, representing approximately 4.5% of our outstanding share capital, at a weighted average exercise price of £3.48 ($4.21) per ordinary share and an expiration date of 10 years from the respective date of grant except for the grant on June 15, 2016 of which the expiration date is December 19, 2023 remained outstanding under the 2015 Option Scheme. In the year ended December 31, 2022, we granted options to purchase an aggregate of 7,680,820 ordinary shares, representing approximately 0.9% of our outstanding share capital, at a weighted average exercise price of £1.87 ($2.26) per share under the 2015 Option Scheme. For the share options granted to Weiguo Su in 2022, the exercise of the share options is conditional upon the fulfilment of certain performance targets relating to the Group over the financial year of 2022 to 2024. Vesting will occur two business days after the date of announcement of the annual results of the Company for the financial year ending December 31, 2024. The other options vest in equal instalments of 25% over a four-year period.

Grants and vesting of LTIPs

In the year ended December 31, 2022, we granted performance based awards under our LTIP to two of our executive directors and 976 employees, giving them a conditional right to receive ordinary shares to be purchased by the third-party trustee up to an aggregate maximum cash amount of $64,186,839. These awards are related to the achievement of performance targets and will vest two business days after the date of the announcement of our annual results for the financial year 2024. For additional information on LTIP awards held by our executive officers, please see “B. Compensation—Executive Officer Compensation—Long-Term Incentive Compensation.”

In the year ended December 31, 2022, we also granted non-performance based awards under our LTIP to two employees, giving them a conditional right to receive ordinary shares to be purchased by the third-party trustee up to an aggregate maximum cash amount of $1,730,000. The LTIP awards vest in equal installments of 25% over four years. For additional information on LTIP awards to our directors, please see “B. Compensation—Director Compensation.”

Vesting of our LTIP awards will also depend upon the award holder’s continued employment or continued service on our board, as the case may be.

In the year ended December 31, 2022, an aggregate of 55,904 ADSs were given to award holders upon the vesting of performance based LTIP awards, and 457,349 ADSs were given to award holders upon the vesting of non-performance based LTIP awards.

C. Board Practices.

Our board of directors consists of ten directors including three executive directors, three non-executive directors and four independent non-executive directors. Pursuant to a relationship agreement dated April 21, 2006, and amended and restated on June 13, 2019, by and between our company and Hutchison Whampoa (China) Limited, a parent company of Hutchison Healthcare Holdings Limited, or the Relationship Agreement, our board of directors must consist of at least one director who is independent of the CK Hutchison group if Hutchison Whampoa (China) Limited is entitled to cast at least 50% votes eligible to be cast on a poll vote at a general meeting of our company. The Relationship Agreement will continue in effect until our ordinary shares cease to be traded on the AIM market or the CK Hutchison group individually or collectively ceases to hold at least 30% of our shares.

Our directors are subject to a three-year term of office and hold office until such time as they wish to retire and not offer themselves up for re-election, are not re-elected by the shareholders, or are removed from office by ordinary resolution at an annual general meeting of the shareholders. Under our Articles of Association, a director will be vacated if, among other things, the director (i) becomes bankrupt or has a receiving order made against him or suspends payment or compounds with his creditors; or (ii) becomes of unsound mind. For information regarding the period during which our officers and directors have served in their respective positions, please see Item 6.A. "Directors and Senior Management."

Board Committees

Our board of directors has established an audit committee, remuneration committee, technical committee, nomination committee and sustainability committee.

Audit Committee

Our audit committee consists of Graeme Allan Jack, Paul Rutherford Carter and Karen Jean Ferrante, with Graeme Allan Jack serving as chairman of the committee. Graeme Allan Jack, Paul Rutherford Carter and Karen Jean Ferrante each meets the independence requirements under the rules of the Nasdaq Stock Market and under Rule 10A-3 under the Exchange Act. We have determined that Graeme Allan Jack is an "audit committee financial expert" within the meaning of Item 407 of Regulation S-K. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq Stock Market.

Although we are a foreign private issuer, we are required to comply with Rule 10A-3 of the Exchange Act, relating to audit committee composition and responsibilities. Rule 10A-3 provides that the audit committee must have direct responsibility for the nomination, compensation and choice of our auditor, as well as control over the performance of their duties, management of complaints made, and selection of consultants. Under Rule 10A-3, if the governing law or documents of a listed issuer require that any such matter be approved by the board of directors or the shareholders of the company, the audit committee's responsibilities or powers with respect to such matter may instead be advisory. Our Articles of Association provide that the appointment of our auditor must be decided by our shareholders at our annual general meeting or at a subsequent extraordinary general meeting in each year.

The audit committee formally meets at least twice a year and otherwise as required. The audit committee's purpose is to oversee our accounting and financial reporting process and the audit of our financial statements. Our audit committee's primary duties and responsibilities are to:

- monitor the integrity of our financial statements, our annual and half-year reports and accounts and our announcements of interim or final results;
- provide advice, where requested by the board of directors, on whether the annual report and accounts, taken as a whole, are fair, balanced and understandable, and provide the information necessary for shareholders to assess our company's position and performance, business model and strategy;
- review significant financial reporting issues and the judgments which they contain;
- review, whenever practicable without being inconsistent with any requirement for prompt reporting under applicable listing rules, other statements containing financial information such as significant financial returns to regulators and release of price sensitive information first where board of director approval is required; and
- review and challenge where necessary:
  - the consistency of, and any changes to, accounting policies both on a year-on-year basis and across our company;
  - the methods used to account for significant or unusual transactions where different approaches are possible;
  - whether our company has followed appropriate accounting standards and made appropriate estimates and judgments, taking into account the views of the external auditor;

- the clarity of the disclosure in our financial reports and the context in which statements are made; and
- all material information presented with the financial statements, such as any operations and financial review and any corporate governance statements (insofar as it relates to the audit and risk management).

In relation to our internal controls and risk management systems, our audit committee, among other things:

- reviews the effectiveness of our internal control and risk management systems;
- reviews the policies and procedures for the identification, assessment and reporting of financial and non-financial risks and our management of those risks in accordance with the requirements of the Sarbanes-Oxley Act and other applicable laws, rules and regulations and the applicable requirements of any stock exchange;
- approves the appointment and removal of the head of the internal audit function;
- ensures our internal audit function has adequate standing and resources and is free from management or other restrictions;
- reviews and monitors our executive management's responsiveness to the findings and recommendations of the internal audit function; and
- reviews with management and our independent auditors the adequacy and effectiveness of our internal control over financial reporting and disclosure controls and procedures.

In relation to our external auditor, our audit committee, among other things:

- recommends the appointment, reappointment or removal of the external auditor and considers any issues relating to their resignation, dismissal, remuneration or terms of engagement, subject to approval by the shareholders;
- considers and monitors the external auditor's independence, objectivity and effectiveness;
- reviews and monitors the effectiveness of the audit process, considering relevant ethical or professional requirements;
- develops and implements policy on the engagement of the external auditor to provide non-audit services, taking into any relevant ethical guidance; and
- pre-approves the external auditors' annual audit fees and the nature and scope of proposed audit coverage, subject to approval by our shareholders.

The audit committee is authorized to obtain, at our company's expense, reasonable outside legal or other professional advice on any matters within the scope of its responsibilities.

Remuneration Committee

Our remuneration committee consists of Paul Rutherford Carter, Graeme Allan Jack and To Chi Keung, Simon, with Paul Rutherford Carter serving as chairman of the committee. The remuneration committee is responsible for considering all material elements of remuneration policy and remuneration and incentives of our executive directors and key employees with reference to independent remuneration research and professional advice. The remuneration committee meets formally at least once each year and otherwise as required and make recommendations to our board of directors on the framework for executive remuneration and on proposals for the granting of share options and other equity incentives. Our board of directors is responsible for implementing these recommendations and agreeing the remuneration packages of individual directors. No director is permitted to participate in discussions or decisions concerning his or her own remuneration.

Technical Committee

Our technical committee consists of Karen Jean Ferrante, Paul Rutherford Carter, To Chi Keung, Simon, Weiguo Su, Mok Shu Kam, Tony and Lefei Sun, with Karen Jean Ferrante serving as chairman of the committee. The technical committee's responsibility is to consider, from time to time, matters relating to the technical aspects of the research and development activities of our Oncology/Immunology operations. It invites such executives as it deems appropriate to participate in meetings from time to time.

Nomination Committee

Our nomination committee consists of Mok Shu Kam, Tony, Graeme Allan Jack and To Chi Keung, Simon, with Mok Shu Kam, Tony serving as chairman of the committee. Our nomination committee reviews the structure, size, diversity profile and skills set of the board against its needs and makes recommendations on the composition of the board to achieve our corporate strategy as well as promote shareholder value. It facilitates the board in the conduct of the selection and nomination of directors, makes recommendations to the board on the appointment or reappointment of directors and succession planning for directors. It also assesses director independence having regard to the criteria under the applicable corporate governance code, SEC or stock exchange rules.

Sustainability Committee

Our sustainability committee consists of Edith Shih, Cheng Chig Fung, Johnny and Mok Shu Kam, Tony, with Edith Shih serving as chairman of the committee. The sustainability committee is responsible for strengthening our corporate governance and reporting framework. It advises our board of directors and management on and oversees the development and implementation of our corporate social responsibility and sustainability initiatives, including reviewing related policies and practices as well as assessing and making recommendations on matters pertaining to our sustainability governance, strategies, planning and risk management.

Hong Kong Corporate Governance Code

Following the listing on the SEHK on June 30, 2021, our board of directors has adopted the Corporate Governance Code ("Hong Kong Corporate Governance Code") contained in Appendix 14 of the Rules Governing the Listing of Securities on SEHK in replacement of the U.K. Corporate Governance Code 2018 and is in compliance with all code provisions of the Hong Kong Corporate Governance Code.

Code of Ethics

Our board of directors has adopted a code of ethics to set standards for our directors, officers and employees as are reasonably necessary to promote (i) honest and ethical conduct, including the ethical handling of actual or apparent conflicts of interest between personal and professional relationships; (ii) full, fair, accurate, timely and understandable disclosure in the reports and documents that we file or submit to the applicable stock exchanges, and in any other public communications; (iii) compliance with applicable governmental and regulatory laws, rules, codes and regulations; (iv) prompt internal reporting of any violations of the code of ethics; and (v) accountability for adherence to the code of ethics.

Code of Ethics for Business Partners

Our board of directors has adopted a code of ethics for our business partners, including our suppliers, vendors, customers, agents, contractors, joint venture partners and representatives. This code of ethics contains general guidelines to promote the standards outlined in our internal code of ethics as described above.

Complaints Procedures / Whistleblowing Policy

Our board of directors has adopted procedures for the confidential receipt, retention, and treatment of complaints from, or concerns raised by, employees regarding accounting, internal accounting controls and auditing matters as well as illegal or unethical matters. The complaint procedures are reviewed by the audit committee from time to time as warranted to ensure their continuing compliance with applicable laws and listing standards as well as their effectiveness.

Policy on Personal Information Governance

Our board of directors has adopted a policy on personal information governance which sets out our governance framework for the safeguard of personal information of employees, customers and other relevant personal information subjects. The senior management of each group company is accountable for the effective implementation of this policy.

Information Security Policy

Our board of directors has adopted an information security policy to define and help communicate the common policies for information confidentiality, integrity and availability to be applied to us and our joint ventures. The purpose of the information security policy is to ensure business continuity by preventing and minimizing the impact of security risks within our company and our joint ventures. Our information security policy applies to all of our and our joint ventures' business entities across all countries. It applies to the creation, communication, storage, transmission and destruction of all different types of information. It applies to all forms of information, including but not limited to electronic copies, hardcopy, and verbal disclosures whether in person, over the telephone, or by other means.

Code on Dealings in Shares

Our board of directors has adopted a policy on the handling of material inside information, consisting of information which is either "inside information" under the EU Market Abuse Regulation (Regulation (EU) 596/2014), or MAR, or "material non-public information" under U.S. law. This policy, among other things, prohibits any employees, directors, other persons discharging managerial responsibilities or their connected persons dealing in our securities or their derivatives, or those of our collaborators, business partners, suppliers and customers, while in possession of material inside information. Certain members of our senior management or staff, including persons discharging managerial responsibilities, and their connected persons are subject to additional compliance requirements which are outlined in the code (including but not limited to obtaining written pre-clearance from designated members of management prior to any dealing in any such securities is allowed).

Board Diversity Policy

Our board of directors has established a board diversity policy as our board of directors recognizes the benefits of a board of directors that possesses a balance of skills, experience, expertise, independence and knowledge and diversity of perspectives appropriate to the requirements of our businesses.

We maintain that appointment to our board of directors should be based on merit that complements and expands the skills, experience, expertise, independence and knowledge of the board of directors as a whole, taking into account gender, age, professional experience and qualifications, cultural and educational background, and any other factors that our board of directors might consider relevant and applicable from time to time towards achieving a diverse board of directors. See also"—Directors and Senior Management—Board Diversity."

D. Employees.

As of December 31, 2020, 2021 and 2022, we had 1,280, 1,759 and 2,025 full-time employees, respectively. None of our employees are represented by labor unions or covered by collective bargaining agreements. The number of employees by function as of the end of the period for our fiscal years ended December 31, 2020, 2021 and 2022 was as follows:

	2022	2021	2020
By Function:			
Oncology/Immunology	1,022	891	643
Other Ventures	960	820	594
Corporate Head Office	43	48	43
Total	2,025	1,759	1,280

As of December 31, 2022, a total of 149 employees on our Oncology/Immunology research and development team have M.D. or Ph.D. degrees. Additionally, our Other Ventures joint venture Shanghai Hutchison Pharmaceuticals employed a total of 2,986 full time employees as of December 31, 2022, and such employees are represented by labor unions and covered by collective bargaining agreements. To date, we have not experienced any strikes, labor disputes or industrial actions which had or would have a material effect on our business, and consider our relations with the union and employees to be good.

We recognize the importance of high-quality human resources in sustaining market leadership. Salary and benefits are kept at competitive levels, while individual performance is rewarded within the general framework of the salary, bonus and incentive system of our company, which is reviewed annually. Employees are provided with a wide range of benefits that include medical coverage, provident funds and retirement plans and long service awards. We stress the importance of staff development and provides training programs on an ongoing basis. Employees are also encouraged to play an active role in community care activities.

E. Share Ownership.

See Item 6.B. “Compensation” and Item 7 “Major Shareholders and Related Party Transactions.”

F. Disclosure of a Registrant’s Action to Recover Erroneously Awarded Compensation.

Not applicable.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders.

We had 864,775,340 ordinary shares outstanding as of February 15, 2023. The following table and accompanying footnotes set forth information relating to the beneficial ownership of our ordinary shares as of February 15, 2023 by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding ordinary shares;
- each of our directors; and
- each of our named executive officers.

Our major shareholders do not have voting rights that are different from our shareholders in general. Beneficial ownership is determined in accordance with the rules and regulations of the SEC. In computing the number of shares beneficially owned by a person and the percentage ownership of that person, we have included shares that the person has the right to acquire within 60 days of February 15, 2023, including through the exercise of any option, warrant, or other right or the conversion of any other security. These shares, however, are not included in the computation of the percentage ownership of any other person.

Name of beneficial owner	Number of Ordinary Share held	Number of American Depositary Share held	Percent of Issued Share Capital**
Executive Officers and Directors:			
Weiguo SU	*	*	*
CHENG Chig Fung, Johnny	*	*	*
TO Chi Keung, Simon	*	*	*
Edith SHIH	*	*	*
Dan ELDAR	*	*	*
Lefei SUN	—	—	—
MOK Shu Kam, Tony	—	*	*
Michael Ming SHI	—	*	*
Paul Rutherford CARTER	*	*	*
Karen Jean FERRANTE	—	*	*
Graeme Allan JACK	—	*	*
Karen Jane ATKIN	—	*	*
Zhenping WU	*	*	*
Mark Kin Hung LEE	*	*	*
May Qingmei WANG	*	*	*
Hong CHEN	*	*	*
Charles George Rupert NIXON	*	*	*
All Executive Officers and Directors as a Group	14,035,014	1,003,390	2.2 %
Principal Shareholders:			
Hutchison Healthcare Holdings Limited(1)	332,478,770	—	38.5 %

* Less than 1% of our total outstanding ordinary shares.

** For each person and group included in this table, percentage ownership is calculated by dividing the number of shares beneficially owned by such person or group by the sum of (i) 864,775,340 ordinary shares outstanding as of February 15, 2023, and (ii) the number of ordinary shares or ADSs underlying share options held by such person or group that are exercisable within 60 days of February 15, 2023.

(1) Hutchison Healthcare Holdings Limited, a British Virgin Islands company, is an indirect wholly owned subsidiary of CK Hutchison, a company incorporated in the Cayman Islands and listed on The Hong Kong Stock Exchange. The registered address of Hutchison Healthcare Holdings Limited is Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola VG1110, British Virgin Islands.

As of February 15, 2023, based on public filings with the SEC, AIM and SEHK, there are no other major shareholders holding 5% or more of our ordinary shares or ADSs representing ordinary shares except as described above. As of February 15, 2023, there were three ordinary shareholders of record with an address in the United States. Deutsche Bank Trust Company America, as depositary of our ADS program, held 158,779,205 ordinary shares as of that date in the name of DB London (Investors Services) Nominees Limited.

To our knowledge, except as disclosed above, we are not owned or controlled, directly or indirectly, by another corporation, by any foreign government or by any other natural or legal person or persons, severally or jointly. To our knowledge, there are no arrangements or operations of which may at a subsequent date result in us undergoing a change in control. Our major shareholders do not have different voting rights than any of our other shareholders.

B. Related Party Transactions.

Relationship with CK Hutchison

Letters of awareness with respect to loans

CK Hutchison has provided letters of awareness to certain of our lenders stating that it is aware that loan facilities have been provided to us and that its current intention is that for so long as amounts are outstanding under such loan facilities, it will not reduce its direct or indirect shareholding as to result in it ceasing to be the single largest indirect shareholder of our company.

Relationship Agreement with the CK Hutchison group

We entered into a relationship agreement dated April 21, 2006, which was amended and restated on June 13, 2019 with effect from June 3, 2015, with Hutchison Whampoa (China) Limited, which is an indirect wholly owned subsidiary of CK Hutchison, with a view to ensuring that our company is capable of carrying on its business independent of the CK Hutchison group. We refer to this agreement as the Relationship Agreement. The Relationship Agreement provides, among other things, that all transactions between any of us or our joint ventures, on the one hand, and the CK Hutchison group, on the other, will be on an arm's length basis, on normal commercial terms and in a manner consistent with the AIM Rules. The Relationship Agreement further provides that the approval of our board of directors shall be required for any transaction between any of us or our joint ventures, on one hand, and the CK Hutchison group, on the other hand and that in approving any such transaction, our board of directors must consist of at least one director who is independent of CK Hutchison. Our board of directors must consist of at least one director who is independent of the CK Hutchison group if Hutchison Whampoa (China) Limited is entitled to cast at least 50% votes eligible to be cast on a poll vote at a general meeting of our company, see Item 6.C. "Directors, Senior Management and Employees—Board Practices." Hutchison Whampoa (China) Limited has also agreed to procure that each member of the Hutchison Whampoa (China) Limited group will not exercise its voting rights and powers so as to amend our Memorandum or Articles of Association in a manner which is inconsistent with the Relationship Agreement. The Relationship Agreement will continue to be effective until the first to occur of: (i) our shares ceasing to be traded on the AIM market or; (ii) the CK Hutchison group individually or collectively cease to hold or control the exercise of at least 30% or more of the rights to vote at our general meetings.

Products sold to group companies of CK Hutchison

We have entered into agreements with members of the CK Hutchison group, including the retail grocery and pharmacy chains PARKnSHOP and Watsons which are owned and operated by the A.S. Watson Group, an indirect subsidiary of CK Hutchison, in respect of the distribution of certain of our consumer health products. For the year ended December 31, 2022, sales of our products to members of the CK Hutchison group amounted to $3.6 million. In addition, for the year ended December 31, 2022, we paid approximately $0.2 million to members of the CK Hutchison group for the provision of marketing services associated with these products. Our sales to CK Hutchison group companies are made pursuant to purchase orders issued by each purchaser periodically, the terms of which are on an arm's length basis on normal commercial terms.

See Item 3.D. "Risk Factors—Risks Relating to Our Dependence on Third Parties—There is no assurance that the benefits currently enjoyed by virtue of our association with CK Hutchison will continue to be available" for more information on the risks associated with our relationship with CK Hutchison's group companies.

Intellectual property licensed by the CK Hutchison group

We conduct our business using trademarks with various forms of the "Hutchison", "Chi-Med", "Hutchison China MediTech", "HUTCHMED", "Elunate" and "Sulanda" brands, the logos used by HUTCHMED Limited, as well as domain names incorporating some or all of these trademarks. We have entered into a brand license agreement dated April 21, 2006 (as amended and restated on June 13, 2019 with effect from June 3, 2015 and as further amended and restated on June 15, 2021 with effect from March 4, 2021) with Hutchison Whampoa Enterprises Limited, which is an indirect wholly owned subsidiary of CK Hutchison, pursuant to which we have been granted a non-exclusive, non-transferrable, royalty-free right to use the "Hutchison," "Hutchison China MediTech", "Chi-Med", "HUTCHMED" trademarks, domain names and other intellectual property rights owned by the CK Hutchison group in connection with the operation of our business worldwide. We refer to this amended and restated agreement as the Brand License Agreement. We are also permitted to sub-license such intellectual property rights to our affiliates.

The Brand License Agreement contains provisions on quality control pursuant to which we are obliged to use the brands and related materials in compliance with the brand guidelines, industry best practice and other quality directives issued by Hutchison Whampoa Enterprises Limited from time to time. Under this agreement, we assign all intellectual property rights, including future copyrights in any works incorporating brand-related material or translations thereof, to Hutchison Whampoa Enterprises Limited (subject to any third-party rights).

Hutchison Whampoa Enterprises Limited may terminate the Brand License Agreement (or any sub-license) if, among other things, we commit a material breach of the agreement, or within any twelve-month period aggregate direct or indirect shareholding in our company held by CK Hutchison , our indirect shareholder, is reduced to less than 35%, 30% or 20%. On termination of the Brand License Agreement, we (and any sub-licensees) must immediately cease using the brands and are obliged to withdraw from the sale of any products bearing the brands; provided that if the agreement is terminated following a change in CK Hutchison's aggregate direct or indirect shareholding in our company, we will have a six-month transitional period during which we can continue to use the licensed rights.

On June 15, 2021, we entered into a brand license royalty agreement with Hutchison Whampoa Enterprises Limited, pursuant to which we will pay an annual fee of HK$12 million (up to an aggregate royalty payable of no more than HK$120 million) in consideration of the grant of the royalty-free right to use the trademarks owned by Hutchison Whampoa Enterprises Limited to Hutchison Baiyunshan and HBYS JV companies upon the completion of the disposal of shareholding interest in Hutchison Baiyunshan.

Sharing of services with the CK Hutchison group

Pursuant to an amended and restated services agreement dated January 1, 2016 between us and Hutchison Whampoa (China) Limited, an indirect wholly owned subsidiary of CK Hutchison, we share certain services with and receive operational support from the CK Hutchison group including, among others, legal and regulatory services, company secretarial support services, tax and internal audit services, shared use of accounting software system and related services, participation in the CK Hutchison group's pension, medical and insurance plans, participation in the CK Hutchison group's procurement projects with third-party vendors/suppliers, other staff benefits and staff training services, company functions and activities and operation advisory and support services. We refer to this amended and restated agreement as the Services Agreement. The Services Agreement replaces our prior services agreement with Hutchison Whampoa (China) Limited, dated April 21, 2006, which had substantially similar terms. We pay a management fee to Hutchison Whampoa (China) Limited for the provision of such services. In addition, we make payments under the Services Agreement to Hutchison Whampoa (China) Limited for our executive offices in Hong Kong. Furthermore, pursuant to the terms of the Services Agreement, Hutchison Whampoa (China) Limited charges us management fees and other costs through Hutchison Healthcare Holdings Limited, its wholly owned subsidiary.

The Services Agreement may be terminated by either party by giving three months' written notice. Hutchison Whampoa (China) Limited may also immediately terminate if its shareholding in our company falls below 30%. The services provided under the Services Agreement are provided on an arm's length basis, on normal commercial terms.

Any amount unpaid after 30 days accrues interest at the rate of 1.5% per annum. In the year ended December 31, 2022, we paid a management fee of approximately $1.0 million under the Services Agreement. As of December 31, 2022, we had $0.4 million in unpaid fees outstanding to Hutchison Whampoa (China) Limited.

Agreements with Our Directors and Executive Officers

Director and Executive Officer Compensation

See Item 6.B. "Compensation—Executive Officer Compensation" and "Compensation—Director Compensation" for a discussion of our compensation of directors and executive officers.

Equity Compensation

See Item 6.B. "Compensation—Equity Compensation Schemes and Other Benefit Plans."

Employment Agreements

We have entered into employment agreements with our executive officers. For more information regarding these agreements, see Item 6.B. "Compensation—Executive Officer Compensation—Employment Arrangements with our Executive Officers." No director has a service contract with us not terminable by us within one year without payment of compensation (other than statutory compensation).

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. We also maintain a general liability insurance policy which covers certain liabilities of our directors and executive officers arising out of claims based on acts or omissions in their capabilities as directors or officers.

C. Interests of Experts and Counsel.

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated Financial Statements and Other Financial Information.

See Item 18 "Financial Statements."

A.7 Legal Proceedings.

There are no material legal proceedings pending or, to our knowledge, threatened against us. We are also not aware of any incidents of non-compliance with laws and regulations that may have a significant impact on us which would have a material adverse effect on our financial condition or results of operations. From time to time we become subject to legal proceedings and claims in the ordinary course of our business, including claims of alleged infringement of patents and other intellectual property rights. Such legal proceedings or claims, even if not meritorious, could result in the expenditure of significant financial and management resources.

A.8 Dividend Policy.

We have never declared or paid dividends on our ordinary shares. We currently expect to retain all future earnings for use in the operation and expansion of our business and do not have any present plan to pay any dividends. The declaration and payment of any dividends in the future will be determined by our board of directors in its discretion, and will depend on a number of factors, including our earnings, capital requirements, overall financial condition, and contractual restrictions.

B. Significant Changes.

We have not experienced any significant changes since the date of our audited consolidated financial statements included in this annual report.

ITEM 9. THE OFFER AND LISTING

Not applicable except for Item 9.A.4 and Item 9.C.

Our ADSs are listed on the Nasdaq Global Select and our ordinary shares are admitted to trading on the AIM market under the symbol "HCM." In addition, our ordinary shares are listed on the SEHK under stock code "0013."

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital.

Not applicable.

B. Memorandum and Articles of Association.

On May 29, 2019, we conditionally adopted an amended and restated memorandum and articles of association by special resolution and effective on the date on which our shares are listed on the SEHK (the "Amended and Restated Articles"). On June 30, 2021, the listing date of our shares on the SEHK, the Amended and Restated Articles replaced the then existing articles of association of our company adopted by at the annual general meeting held on April 27, 2020.

C. Material Contracts.

Except as otherwise disclosed in this annual report (including the exhibits hereto), we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of our business.

D. Exchange Controls.

Foreign currency exchange in the PRC is primarily governed by the Foreign Exchange Administration Rules issued by the State Council on January 29, 1996 and effective as of April 1, 1996 (and amended on January 14, 1997 and August 5, 2008) and the Regulations of Settlement, Sale and Payment of Foreign Exchange which came into effect on July 1, 1996.

Under the Foreign Exchange Administration Rules, renminbi is freely convertible for current account items, including the distribution of dividends payments, interest payments, and trade and service-related foreign exchange transactions. Conversion of renminbi for capital account items, such as direct investment, loans, securities investment and repatriation of investment, however, is still generally subject to the approval or verification of the SAFE.

Under the Regulations of Settlement, Sale and Payment of Foreign Exchange, foreign invested enterprises including wholly foreign owned enterprises, may buy, sell or remit foreign currencies only at those banks that are authorized to conduct foreign exchange business after providing such banks with valid commercial supporting documents and, in the case of capital account item transactions, after obtaining approvals from the SAFE. Capital investments by foreign invested enterprises outside the PRC are also subject to limitations, which include approvals by the MOFCOM, the SAFE and the NDRC.

In March 2015, the SAFE released the Circular on Reforming the Management Approach regarding the Foreign Exchange Capital Settlement of Foreign-invested Enterprises, or FIEs, or the Foreign Exchange Capital Settlement Circular, which became effective from June 1, 2015. This circular replaced the SAFE's previous related circulars, including the Circular on Issues Relating to the Improvement of Business Operation with Respect to the Administration of Foreign Exchange Capital Payment and Settlement of Foreign Invested Enterprises. The Foreign Exchange Capital Settlement Circular clarifies that FIEs may settle a specified proportion of their foreign exchange capital in banks at their discretion, and may choose the timing for such settlement. The proportion of foreign exchange capital to be settled at FIEs' discretion for the time being is 100% and the SAFE may adjust the proportion in due time based on the situation of international balance of payments. The circular also stipulates that FIEs' usage of capital and settled foreign exchange capital shall comply with relevant provisions concerning foreign exchange control and be subject to the management of a negative list. The Notice of the SAFE on Policies for Reforming and Regulating Control over Foreign Exchange Settlement under the Capital Account, which became effective from June 9, 2016 and supplements the Foreign Exchange Capital Settlement Circular, stipulates that the FIEs' capital and Renminbi capital gained from the settlement of foreign exchange capital may not be directly or indirectly used for expenditure beyond the business scope of the FIEs or as prohibited by laws and regulations of the PRC. Such capital also may not be directly or indirectly used for granting loans to non-affiliated enterprises except as permitted by the business scope of the FIE or for construction or purchase of real estate other than self-use (exceptions only apply for real estate enterprises).

In addition, the payment of dividends by entities established in the PRC is subject to limitations. Regulations in the PRC currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in the PRC. Each of our PRC subsidiaries that is a domestic company is also required to set aside at least 10.0% of its after-tax profit based on PRC accounting standards each year to its general reserves or statutory capital reserve fund until the accumulative amount of such reserves reach 50.0% of its respective registered capital. These restricted reserves are not distributable as cash dividends. In addition, if any of our PRC subsidiaries or joint ventures incurs debt on its own behalf in the future, the instruments governing the debt may restrict its ability to pay dividends or make other distributions to us.

For more information about foreign exchange control, see Item 3.D. "Risk Factors—Other Risks and Risks Relating to Doing Business in China—Restrictions on currency exchange may limit our ability to receive and use our revenue effectively."

E. Taxation.

The following is a general summary of certain PRC, Hong Kong, Cayman Islands and U.S. federal income tax consequences relevant to the acquisition, ownership and disposition of our ADSs. The discussion is not intended to be, nor should it be construed as, legal or tax advice to any particular individual. The discussion is based on laws and relevant interpretations thereof in effect as of February 27, 2023, all of which are subject to change or different interpretations, possibly with retroactive effect. The discussion does not address U.S. state or local tax laws, or tax laws of jurisdictions other than the PRC, Hong Kong, the Cayman Islands and the United States. You should consult your own tax advisors with respect to the consequences of acquisition, ownership and disposition of our ADSs and ordinary shares.

Taxation in the PRC

PRC Enterprise Income Tax

Under the EIT Law, which was promulgated on March 16, 2007 and subsequently amended on February 24, 2017 and December 29, 2018, and its implementation rules which became effective on January 1, 2008 and subsequently amended on April 23, 2019, the standard tax rate of 25% applies to all enterprises (including FIEs) with exceptions in special situations if relevant criteria are met and subject to the approval of the PRC tax authorities.

An enterprise incorporated outside of the PRC whose "de facto management bodies" are located in the PRC is considered a "resident enterprise" and will be subject to a uniform EIT rate of 25% on its global income. In April 2009, the SAT, in Circular 82, specified certain criteria for the determination of what constitutes "de facto management bodies." If all of these criteria are met, the relevant foreign enterprise will be deemed to have its "de facto management bodies" located in the PRC and therefore be considered a resident enterprise in the PRC. These criteria include: (a) the enterprise's day-to-day operational management is primarily exercised in the PRC; (b) decisions relating to the enterprise's financial and human resource matters are made or subject to approval by organizations or personnel in the PRC; (c) the enterprise's primary assets, accounting books and records, company seals, and board and shareholders' meeting minutes are located or maintained in the PRC; and (d) 50% or more of voting board members or senior executives of the enterprise habitually reside in the PRC. Although Circular 82 only applies to foreign enterprises that are majority-owned and controlled by PRC enterprises, not those owned and controlled by foreign enterprises or individuals, the determining criteria set forth in Circular 82 may be adopted by the PRC tax authorities as the test for determining whether the enterprises are PRC tax residents, regardless of whether they are majority-owned and controlled by PRC enterprises. However, it is not entirely clear how the PRC tax authorities will determine whether a non-PRC entity (that has not already been notified of its status for EIT purposes) will be classified as a "resident enterprise" in practice.

Except for our PRC subsidiaries and joint ventures incorporated in China, we believe that none of our entities incorporated outside of China is a PRC resident enterprise for PRC tax purposes. However, the tax resident status of an enterprise is subject to determination by the PRC tax authorities, and uncertainties remain with respect to the interpretation of the term "de facto management body."

If a non-PRC enterprise is classified as a "resident enterprise" for EIT purposes, any dividends to be distributed by that enterprise to non-PRC resident shareholders or ADS holders or any gains realized by such investors from the transfer of shares or ADSs may be subject to PRC tax. If the PRC tax authorities determine that we should be considered a PRC resident enterprise for EIT purposes, any dividends payable by us to our non-PRC resident enterprise shareholders or ADS holders with no office or premises established in China, or with an office or premises established in China but whose income (i.e. dividends received) has no de facto relationship with said office or premises, as well as gains realized by such investors from the transfer of our shares or ADSs may be subject to a 10% withholding tax. Furthermore, if we are considered a PRC resident enterprise for EIT purposes, it is unclear whether our non-PRC individual shareholders (including our ADS holders) would be subject to any PRC tax on dividends or gains obtained by such non-PRC individual shareholders. If any PRC tax were to apply to dividends realized by non-PRC individuals, it would generally apply at a rate of up to 20% (which in the case of dividends may be withheld at source). The foregoing rates may be reduced by an applicable tax treaty, but it is unclear if a non-PRC resident shareholder or ADS holder would be able to obtain in practice the benefits of any tax treaties between their country of tax residence and the PRC in the event that we are treated as a PRC resident enterprise.

According to the EIT Law, dividends declared after January 1, 2008 and paid by PRC FIEs to their non-PRC parent companies will be subject to PRC withholding tax at 10% unless there is a tax treaty between the PRC and the jurisdiction in which the overseas parent company is a tax resident and which specifically exempts or reduces such withholding tax, and such tax exemption or reduction is approved by the relevant PRC tax authorities. Pursuant to the Arrangement, if the non-PRC immediate holding company is a Hong Kong tax resident and directly holds a 25% or more equity interest in the PRC enterprise and is considered to be the beneficial owner of dividends paid by the PRC enterprise, such withholding tax rate may be lowered to 5%, subject to approval by the relevant PRC tax authorities in accordance with relevant tax regulations upon the assessment of beneficial ownership.

Overview of Tax Implications of Various Other Jurisdictions

Cayman Islands Taxation

According to our Cayman Islands counsel, Conyers Dill & Pearman, the Cayman Islands currently levies no taxes on individuals or corporations based upon profits, income, gains or appreciation and there is no taxation in the nature of inheritance tax or estate duty. There are no other taxes likely to be material to us levied by the government of the Cayman Islands except for stamp duties which may be applicable on instruments executed in, or brought within the jurisdiction of the Cayman Islands. The Cayman Islands is a party to a double tax treaty entered into with the United Kingdom in 2010 but it is otherwise not a party to any double tax treaties that are applicable to any payments made to or by our company. There are no exchange control regulations or currency restrictions in the Cayman Islands.

Pursuant to the Tax Concessions Act of the Cayman Islands, HUTCHMED (China) Limited has obtained an undertaking: (a) that no law which is enacted in the Cayman Islands imposing any tax to be levied on profits or income or gains or appreciations shall apply to us or our operations; and (b) that the aforesaid tax or any tax in the nature of estate duty or inheritance tax shall not be payable (i) on its shares, debentures or other obligations or (ii) by way of the withholding in whole or in part of any relevant payment as defined in the Tax Concessions Act.

The undertaking is for a period of twenty years from December 31, 2020.

Hong Kong Taxation

Profits Tax

HUTCHMED (China) Limited is a Hong Kong tax resident. Hong Kong tax residents are subject to Hong Kong Profits Tax in respect of profits arising in or derived from Hong Kong at the current rate of 16.5% (except portions eligible for the two-tiered profits tax as discussed above). Dividend income earned by a Hong Kong tax resident is generally not subject to Hong Kong Profits Tax. The Inland Revenue (Amendment) (Taxation on Specified Foreign-sourced Income) Bill 2022 (the Amendment Bill) was gazetted on 28 October 2022 to provide a new framework for Hong Kong's Foreign Source Income Exemption regime with a view to bringing the regime into force from 1 January 2023. The Amendment Bill aims to amend the Inland Revenue Ordinance (Cap. 112) to regard certain foreign-sourced income as arising in or derived from Hong Kong and to provide for relief against double taxation in respect of certain foreign-sourced income. Covered income includes interest, dividend, disposal gain from the sale of equity interests in an entity and intellectual property income.

Hong Kong tax on shareholders and ADS holders

No tax is payable in Hong Kong in respect of dividends paid by a Hong Kong tax resident to their shareholders, including our ADS holders.

Hong Kong Profits Tax will not be payable by our shareholders, including our ADS holders (other than shareholders / ADS holders carrying on a trade, profession or business in Hong Kong and holding the shares / ADSs for trading purposes), on any capital gains made on the sale or other disposal of the shares or ADSs. Shareholders, including our ADS holders, should take advice from their own professional advisors as to their particular tax position.

U.S. Taxation

Corporate Tax

Our subsidiaries in the United States, HUTCHMED International Corporation and HUTCHMED US Corporation, are subject to a federal corporate tax of 21%.

Material U.S. Federal Income Tax Considerations with Respect to Ordinary Shares and ADSs

The following summary, subject to the limitations set forth below, describes the material U.S. federal income tax consequences for a U.S. Holder (as defined below) of the ownership and disposition of ordinary shares and ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's ownership of our securities. This discussion is limited to U.S. Holders that hold such ordinary shares or ADSs as capital assets within the meaning of Section 1221 of the Internal Revenue Code of 1986, as amended, or the Code (generally, property held for investment). For the purposes of this summary, a "U.S. Holder" is a person that is, for U.S. federal income tax purposes, a beneficial owner of an ordinary share or ADS and:

- a citizen or individual resident of the United States;
- a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) organized in or under the laws of the United States or any state thereof, or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (i) it has a valid election in effect to be treated as a U.S. person for U.S. federal income tax purposes or (ii) a U.S. court can exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of its substantial decisions.

This summary does not purport to consider all aspects of U.S. federal income taxation that may be relevant to U.S. Holders in light of their particular circumstances, including the possible effect of the special tax accounting rules under Section 451 of the Code, or alternative minimum or Medicare contribution tax consequences. In addition, it does not address aspects of U.S. federal income taxation that may be applicable to U.S. Holders subject to special rules, including:

- banks or other financial institutions;
- insurance companies;
- real estate investment trusts;
- regulated investment companies;
- grantor trusts;
- tax-exempt organizations, "individual retirement accounts or "Roth IRAs";
- partnerships (or other entities or ararngments treated as partnerships for U.S. federal income tax purposes) or S corporations holding our ordinary shares or ADSs, and their partners or shareholders;
- dealers or electing traders in securities that use a mark-to-market method of tax accounting;
- persons whose functional currency is not the U.S. dollar;
- persons that acquired ordinary shares or ADSs as compensation;
- persons holding ordinary shares or ADSs in connection with a trade or business conducted outside of the United States.

- persons holding our ordinary shares or ADSs as part of a straddle, integrated or similar transaction for U.S. federal income tax purposes; or

- direct, indirect or constructive owners of 10% or more of our equity (by vote or value).

If an entity or arrangement treated as a partnership for U.S. federal income tax purposes owns our ordinary shares or ADSs, the tax treatment of the partnership and a partner in such partnership generally will depend on the status of the partner and the activities of the partnership. Such partnerships and partners should consult their tax advisors as to the U.S. federal income tax consequences of acquiring, owning and disposing of our ordinary shares or ADSs.

This discussion does not address the effects of any state, local or non-U.S. tax law or any U.S. federal taxes other than income taxes (such as U.S. federal estate or gift tax consequences). We have not received nor do we expect to seek a ruling from the U.S. Internal Revenue Service, or the IRS, regarding any matter discussed herein. No assurance can be given that the IRS would not assert, or that a court would not sustain, a position contrary to any of those set forth below. Each investor should consult its tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning and disposing of our ordinary shares and ADSs.

This discussion is based on the Code, final and proposed U.S. Treasury Regulations promulgated thereunder and administrative and judicial interpretations thereof, and the income tax treaty between the PRC and the United States, or the U.S.- PRC Tax Treaty, each as of the date hereof, all of which are subject to change or differing interpretations, possibly with retroactive effect, which could affect the tax consequences described herein. In addition, this summary assumes that the deposit agreement, and all other related agreements, will be performed in accordance with their terms.

INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH REGARD TO THE PARTICULAR TAX CONSEQUENCES APPLICABLE TO THEIR SITUATIONS AS WELL AS THE APPLICATION OF ANY U.S. FEDERAL, STATE, LOCAL, NON-U.S. OR OTHER TAX LAWS, INCLUDING GIFT AND ESTATE TAX LAWS.

ADSs

A U.S. Holder of ADSs will generally be treated, for U.S. federal income tax purposes, as the owner of the underlying ordinary shares that such ADSs represent. Accordingly, no gain or loss will be recognized if a U.S. Holder exchanges ADSs for the underlying shares represented by those ADSs.

Taxation of Dividends

The following is subject to the discussion under "—*Passive Foreign Investment Company Considerations*" below.

As described in Item 8. "Financial Information—A.8 Dividend Policy" above, we do not currently anticipate paying any distributions on our ordinary shares or ADSs in the foreseeable future. However, to the extent there are any distributions made with respect to our ordinary shares or ADSs, the gross amount of any such distribution (including withheld taxes, if any) made out of our current or accumulated earnings and profits (as determined for U.S. federal income tax purposes) will generally be taxable to a U.S. Holder as ordinary dividend income on the date such distribution is actually or constructively received. Distributions in excess of our current and accumulated earnings and profits will be treated as a non-taxable return of capital to the extent of the U.S. Holder's adjusted tax basis in the ordinary shares or ADSs, as applicable, and thereafter as capital gain. However, because we do not maintain calculations of our earnings and profits in accordance with U.S. federal income tax accounting principles, U.S. Holders should expect to treat distributions paid with respect to our ordinary shares and ADSs as dividends. Dividends paid to corporate U.S. Holders will not qualify for the dividends received deduction that may otherwise be allowed under the Code.

The amount of income from dividends paid in a non-U.S. currency will be the U.S. dollar amount of the dividend calculated by reference to the exchange rate in effect on the date of receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder generally should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss, taxable as ordinary income or loss, if the dividend is converted into U.S. dollars after the date of receipt. Foreign currency gain or loss generally will be treated as U.S.-source gain or loss.

Dividends paid to a non-corporate U.S. Holder by a "qualified foreign corporation" may be subject to reduced rates of U.S. federal income taxation if certain holding period and other requirements are met. A qualified foreign corporation generally includes a foreign corporation (other than a PFIC) if (1) its ordinary shares (or ADSs backed by ordinary shares) are readily tradable on an established securities market in the United States or (2) it is eligible for benefits under a comprehensive U.S. income tax treaty that includes an exchange of information program and which the U.S. Treasury Department has determined is satisfactory for these purposes. We are not eligible for the benefits of any U.S. income tax treaty. However, because our ADSs are listed on the Nasdaq, a non-corporate U.S. Holder of ADSs may be eligible for the preferential tax rates on dividends, subject to applicable limitations (including a minimum holding period and other requirements) and provided that we are not a PFIC (and are not treated as a PFIC with respect to the U.S. Holder) for the taxable year of distribution of the precedeing taxable year.

For purposes of the foreign tax credit rules, dividends will be treated as foreign-source income. As described in "—Taxation in the PRC" above, if we are deemed to be a "resident enterprise" under PRC tax law, U.S. Holders may be subject to PRC withholding taxes on dividends paid by us. In that case, subject to certain conditions and limitations and the discussion below regarding the impact of certain Treasury regulations, such PRC taxes withheld from dividend payments (at a rate not exceeding the applicable rate provided in the U.S.-PRC Tax Treaty for U.S. Holders eligible for the benefits of the U.S.-PRC Tax Treaty) generally will be eligible for credit against a U.S. Holder's U.S. federal income tax liability under the U.S. foreign tax credit rules. The U.S. foreign tax credit rules are complex. For example, under Treasury regulations, in the absence of an election to apply the benefits of an applicable income tax treaty, in order to be creditable, non-U.S. income tax rules must be consistent with certain U.S. federal income tax principles, and we have not determined whether the PRC income tax system meets these requirements. A U.S. Holder that is not entitled, or does not elect, to claim a foreign tax credit for PRC tax withheld may instead be eligible to claim a deduction in respect of such withholding, but only for a year in which such U.S. Holder elects to do so for all creditable foreign income taxes and subject to other applicable limitations. U.S. Holders should consult their tax advisors regarding the foreign tax credit and deduction rules in light of their particular circumstances.

Taxation of Capital Gains

The following is subject to the discussion under "—*Passive Foreign Investment Company Considerations" below*.

Upon the sale, exchange, or other taxable disposition of our ordinary shares or ADSs, a U.S. Holder generally will recognize gain or loss in an amount equal to the difference between the amount realized on such sale or exchange and the U.S. Holder's adjusted tax basis in such ordinary shares or ADSs, in each case determined in U.S. dollars. A U.S. Holder's initial tax basis will be the U.S. Holder's U.S. dollar purchase price for such ordinary shares or ADSs.

Such gain or loss generally will be capital gain or loss, and will be long-term capital gain or loss if a U.S. Holder held the ordinary share or ADS for more than one year. Long-term capital gains of non-corporate U.S. Holders are taxed at a preferential tax rate. The deductibility of capital losses is subject to limitations.

As described in "—Taxation in the PRC" above, if we are deemed to be a "resident enterprise" under PRC tax law, any gain on the sale of ordinary shares or ADSs may be subject to PRC taxes. Under the Code, capital gains of U.S. persons generally are treated as U.S.-source income. However, if a U.S. Holder is eligible for the benefits of the U.S.-PRC Tax Treaty, the holder may be able to elect to treat such disposition gain as PRC-source gain under the U.S.-PRC Tax Treaty for U.S. foreign tax credit purposes and claim a foreign tax credit in respect of PRC taxes on such gains. A U.S. Holder will be eligible for U.S.-PRC Tax Treaty benefits if (for the purposes of the treaty) such holder is a resident of the United States and satisfies the "limitations of benefits" requirements specified in the U.S.-PRC Tax Treaty. Because the determination of treaty benefit eligibility is fact-intensive and depends upon a U.S. Holder's particular circumstances, U.S. Holders should consult their tax advisors regarding their eligibility for the U.S.-PRC Tax Treaty benefits. Treasury regulations generally preclude a U.S. Holder from claiming a foreign tax credit with respect to PRC income taxes on gains from dispositions of ordinary shares or ADSs if a U.S. Holder is not eligible for, or does not elect to apply the benefits of, the U.S.-PRC Tax Treaty. However, non-U.S. taxes on disposition gains may be deductible or reduce the amount realized on the disposition. The rules governing foreign tax credits and the deductibility of non-U.S. taxes are complex. U.S. Holders are also encouraged to consult their tax advisors regarding the tax consequences in the event PRC tax is imposed on a disposition of ordinary shares or ADSs, including the U.S.-PRC Tax Treaty's resourcing rule, any reporting requirements with respect to a treaty-based return position and the creditability or deductibility of any non-U.S. tax on disposition gains in their particular circumstances (including any applicable limitations).

Passive Foreign Investment Company Considerations

Status as a PFIC. The rules governing PFICs can result in adverse U.S. federal income tax consequences to U.S. Holders. We generally will be a PFIC for U.S. federal income tax purposes if, for any taxable year, either: (1) 75% or more of our gross income consists of certain types of passive income, or (2) 50% or more of the average value of our assets (generally determined on a quarterly basis) consists of our assets that produce, or are held for the production of, passive income. Passive income generally includes dividends, interest, rents and royalties (other than certain rents and royalties derived in the active conduct of a trade or business), annuities and gains from assets that produce passive income. If a non-U.S. corporation owns at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for the purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income. Cash and cash equivalents are generally treated as passive assets. Goodwill is generally treated as an active asset to the extent associated with activities that generate non-passive income.

Based on the composition of our income and assets and the estimated average value of our assets (including goodwill), we believe that we were not a PFIC for our taxable year ended December 31, 2022. However, our PFIC status is a factual determination that is made on an annual basis and depends on particular facts and circumstances (such as the value of our assets, including goodwill and other intangible assets). We hold a substantial amount of cash and financial investments and while this continues to be the case, our PFIC status depends primarily on the average value of our goodwill. The value of our goodwill may be determined, in large part, by reference to our market capitalization, which has been, and may continue to be, volatile. Therefore, if our market capitalization declines we may become a PFIC. In addition, there is uncertainty as to how to apply the PFIC rules for purposes of classifying certain of our income and assets as active or passive. In light of the foregoing, no assurance can be provided that we were not, or will not be, a PFIC for any taxable year.

U.S. federal income tax treatment of a shareholder of a PFIC generally. If we are a PFIC for any taxable year during which a U.S. Holder owns ordinary shares or ADSs, the U.S. Holder, absent certain elections, generally will be subject to adverse rules (regardless of whether we continue to be a PFIC) with respect to (1) any "excess distributions" (generally, the extent that any distributions received by the U.S. Holder on its ordinary shares or ADSs in a taxable year exceed 125% of the average annual distributions received by the U.S. Holder in the three preceding taxable years or, if shorter, the U.S. Holder's holding period) and (2) any gain realized on the sale or other disposition, including a pledge, of such ordinary shares or ADSs.

Under these rules (a) any gain or excess distribution will be allocated ratably over the U.S. Holder's holding period, (b) the amount allocated to the current taxable year and any taxable year prior to the first taxable year in which we became a PFIC will be taxed as ordinary income and (c) the amount allocated to each other taxable year during the U.S. Holder's holding period (i) will be subject to tax at the highest rate of tax in effect for the applicable category of taxpayer for that year and (ii) will be subject to an interest charge at a statutory rate with respect to the resulting tax attributable to each such other taxable year. In addition,a non-corporate U.S. Holder will not be eligible for reduced rates of taxation on any dividends received from us if we are a PFIC (or are treated as a PFIC with respect to the U.S. Holder) in the taxable year in which such dividends are paid or in the preceding taxable year.

If we are a PFIC in any taxable year during which a U.S. Holder owns ordinary shares or ADSs, we generally will continue to be treated as a PFIC with respect to that U.S. Holder in all succeeding taxable years, even if we cease to meet the threshold requirements for PFIC status described above, unless the U.S. Holder makes a timely "deemed sale election." If we are a PFIC for any taxable year and then cease to be a PFIC, a U.S. Holder may make a "deemed sale election" to be treated for U.S. federal income tax purposes as having sold such U.S. Holder's ordinary shares or ADSs on the last day of our taxable year during which we were a PFIC. A U.S. Holder that makes a deemed sale election would then cease to be treated as owning stock in a PFIC. However, gain recognized as a result of making the deemed sale election would be subject to the adverse rules described above and loss would not be recognized.

If we are a PFIC for any taxable year, a U.S. Holder will be treated as owning a proportionate amount (by value) of stock or shares owned by us in any direct or indirect subsidiaries that are also PFICs (any such entity, a "**Lower-tier PFIC**") and will be subject to similar adverse rules with respect to any distributions we receive from, and dispositions we make of, the stock or shares of such subsidiaries, in each case as if the U.S. Holder owned its proportionate share of the Lower-tier PFIC directly, even though the U.S. Holder will not receive the proceeds of those distributions or dispositions directly. U.S. Holders are urged to consult their tax advisors about the application of the PFIC rules to any of our subsidiaries.

PFIC "mark-to-market" election. In certain circumstances, a holder of "marketable stock" of a PFIC will be subject to tax consequences different that those described above by making a timely mark-to-market election with respect to such stock. For the purposes of these rules "marketable stock" is generally stock which is "regularly traded" (traded in greater than *de minimis* quantities on at least 15 days during each calendar quarter) on a "qualified exchange."

A U.S. Holder that makes a timely mark-to-market election must include in gross income, as ordinary income, for each taxable year that we are a PFIC an amount equal to the excess, if any, of the fair market value of the U.S. Holder's ordinary shares or ADSs that are "marketable stock" at the close of the taxable year over the U.S. Holder's adjusted tax basis in such ordinary shares or ADSs. An electing U.S. Holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted tax basis in such ordinary shares or ADSs over their fair market value at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains previously included in income pursuant to the timely mark-to-market election. The adjusted tax basis of a U.S. Holder's ordinary shares or ADSs with respect to which the timely mark-to-market election applies would be adjusted to reflect amounts included in gross income or allowed as a deduction because of such election. If a U.S. Holder makes an effective mark-to-market election with respect to our ordinary shares or ADSs, gains from an actual sale or other disposition of such ordinary shares or ADSs in a year in which we are a PFIC will be treated as ordinary income, and any losses incurred on such sale or other disposition will be treated as ordinary losses to the extent of any net mark-to-market gains previously included in income (with any excess loss treated as a capital loss).

If we are a PFIC for any taxable year in which a U.S. Holder owns ordinary shares or ADSs, but before a timely mark-to-market election is made, the general PFIC rules described above under "—U.S. federal income tax treatment of a shareholder of a PFIC generally" will apply to any mark-to-market gain recognized in the year the election is made. Otherwise, a timely mark-to-market election will be effective for the taxable year for which the election is made and all subsequent taxable years unless the ordinary shares or ADSs are no longer regularly traded on a qualified exchange or the IRS consents to the revocation of the election.

There is no law, regulation or administrative guidance that provides for a right to make a mark-to-market election for equity interests in any Lower-tier PFIC the shares of which are not regularly traded on a qualified exchange. As a result, even if a U.S. Holder makes a mark-to-market election with respect to our ordinary shares or ADSs, such U.S. Holder could nevertheless be subject to the PFIC rules described under "—U.S. federal income tax treatment of a shareholder of a PFIC generally" with respect to such U.S. Holder's indirect interest in any Lower-tier PFIC. U.S. Holders should consult their tax advisors regarding the availability of, and the procedure for, and the effect of making, a mark-to-market election, and whether making the election would be advisable, including in light of their particular circumstances.

No QEF election. We do not expect to provide the information regarding our income that would be necessary in order for a U.S. Holder to make a timely "qualifying electing fund" election, or QEF election, if we were a PFIC, which, if available, could materially affect the tax consequences of the ownership and disposition of the ordinary shares and ADSs if we are a PFIC for any taxable year. Therefore, U.S. Holders will not be able to make this election.

PFIC information reporting requirements. If we are (or are treated with respect to a particular U.S. Holder as) a PFIC for any year in which a U.S. Holder owns ordinary shares or ADSs, such U.S. Holder generally will be required to file an annual information return on IRS Form 8621 with respect to us and any Lower-tier PFIC.

NO ASSURANCE CAN BE GIVEN THAT WE ARE NOT CURRENTLY A PFIC OR THAT WE WILL NOT BECOME A PFIC IN THE FUTURE. U.S. HOLDERS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE OPERATION OF THE PFIC RULES AND RELATED REPORTING REQUIREMENTS IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES, INCLUDING THE ADVISABILITY AND EFFECTS OF MAKING ANY ELECTION THAT MAY BE AVAILABLE.

Backup Withholding and Information Reporting and Filing Requirements

Backup withholding and information reporting requirements may apply to distributions on, and proceeds from the sale or disposition of, ordinary shares and ADSs that are held by U.S. Holders. The payor will be required to withhold tax (currently at a rate of 24%) on such payments made within the United States, or by a U.S. payor or a U.S. intermediary (and certain subsidiaries thereof) to a U.S. Holder, other than an exempt recipient, if the U.S. Holder is not otherwise exempt and:

- the holder fails to furnish the holder's taxpayer identification number, which for an individual is ordinarily his or her social security number;
- the holder furnishes an incorrect taxpayer identification number;
- the applicable withholding agent is notified by the IRS that the holder previously failed to properly report payments of interest or dividends; or
- the holder fails to certify under penalties of perjury that the holder has furnished a correct taxpayer identification number and that the IRS has not notified the holder that the holder is subject to backup withholding.

Backup withholding is not an additional tax. Amounts withheld as backup withholding may be credited against a U.S. Holder's U.S. federal income tax liability (if any) or refunded provided the required information is furnished to the IRS in a timely manner. U.S. Holders should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption.

Certain U.S. Holders of specified foreign financial assets with an aggregate value in excess of the applicable dollar threshold may be required to report information relating to their holding of ordinary shares or ADSs, subject to certain exceptions (including an exception for shares held in accounts maintained by certain financial institutions) with their tax returns for each year in which they hold such interests. U.S. Holders should consult their own tax advisors regarding the information reporting obligations that may arise from their acquisition, ownership or disposition of our ordinary shares or ADSs.

THE ABOVE DISCUSSION DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PARTICULAR INVESTOR. INVESTORS ARE STRONGLY URGED TO CONSULT THEIR TAX ADVISORS ABOUT THE TAX CONSEQUENCES OF AN INVESTMENT IN OUR ORDINARY SHARES OR ADSs.

F. Dividends and Payment Agents.

Not applicable.

G. Statement by Experts.

Not applicable.

H. Documents on Display.

We are subject to the informational requirements of the Exchange Act and are required to file reports and other information with the SEC. Shareholders may access our reports and other information filed with the SEC by viewing them on the SEC's website, at *www.sec.gov*. We also make available on our website's investor relations page, free of charge, our annual report and the text of our reports on Form 6-K, including any amendments to these reports, as well as certain other SEC filings, as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. The address for our investor relations page is *www.hutch-med.com/ shareholder-information*. The information contained on our website is not incorporated by reference in this annual report.

We are a "foreign private issuer" as such term is defined in Rule 405 under the Securities Act, and are not subject to the same requirements that are imposed upon U.S. domestic issuers by the SEC. Under the Exchange Act, we are subject to reporting obligations that, in certain respects, are less detailed and less frequent than those of U.S. domestic reporting companies. As a result, we do not file the same reports that a U.S. domestic issuer would file with the SEC, although we are required to file or furnish to the SEC the continuous disclosure documents that we are required to file on the AIM market.

We will furnish Deutsche Bank Trust Company Americas, the depositary of our ADSs, with our annual reports, which will include a review of operation and annual audited consolidated financial statements prepared in conformity with U.S. GAAP, and all notices of shareholders' meetings and other reports and communications that are made generally available to our shareholders. The depositary will make such notices, reports and communications available to holders of ADSs and, upon our requests, will mail to all record holders of ADSs the information contained in any notice of a shareholders' meeting received by the depositary from us.

I. Subsidiary information.

Not applicable.

J. Annual Report to Security Holders.

The Company intends to submit annual report provided to security holders in electronic format as an exhibit to a current report on Form 6-K.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Foreign Exchange Risk

A substantial portion of our revenue and expenses are denominated in renminbi, and our consolidated financial statements are presented in U.S. dollars. We do not believe that we currently have any significant direct foreign exchange risk and have not used any derivative financial instruments to hedge our exposure to such risk. Although, in general, our exposure to foreign exchange risks should be limited, the value of your investment in our ADSs will be affected by the exchange rate between the U.S. dollar and the renminbi because the value of our business is effectively denominated in renminbi, while the ADSs will be traded in U.S. dollars.

The value of the renminbi against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in China's political and economic conditions. The conversion of renminbi into foreign currencies, including U.S. dollars, has been based on rates set by the PBOC. On July 21, 2005, the PRC government changed its decade-old policy of pegging the value of the renminbi to the U.S. dollar. Under the revised policy, the renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. This change in policy resulted in a more than 20% appreciation of the renminbi against the U.S. dollar in the following three years. Between July 2008 and June 2010, this appreciation halted, and the exchange rate between the renminbi and U.S. dollar remained within a narrow band. In June 2010, the PBOC announced that the PRC government would increase the flexibility of the exchange rate, and thereafter allowed the renminbi to appreciate slowly against the U.S. dollar within the narrow band fixed by the PBOC. At various times since then, the PBOC has significantly devalued the renminbi against the U.S. dollar. If we decide to convert renminbi into U.S. dollars for the purpose of making payments for dividends on our ordinary shares or ADSs or for other business purposes, appreciation of the U.S. dollar against the renminbi would have a negative effect on the U.S. dollar amounts available to us.

Credit Risk

Substantially all of our bank deposits are in major financial institutions, which we believe are of high credit quality. We limit the amount of credit exposure to any single financial institution. We make periodic assessments of the recoverability of trade and other receivables and amounts due from related parties. Our historical experience in collection of receivables falls within the recorded allowances, and we believe that we have made adequate provision for uncollectible receivables.

Interest Rate Risk

We have no significant interest-bearing assets except for bank deposits. Our exposure to changes in interest rates is mainly attributable to our bank borrowings, which bear interest at floating interest rates and expose us to cash flow interest rate risk. We have not used any interest rate swaps to hedge our exposure to interest rate risk. We have performed sensitivity analysis for the effects on our results for the year from changes in interest rates on floating rate borrowings. The sensitivity to interest rates used is based on the market forecasts available at the end of the reporting period and under the economic environments in which we operate, with other variables held constant. According to the analysis, the impact on our net loss of a 1.0% interest rate shift would be a maximum increase/decrease of $0.1 million for the year ended December 31, 2022.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities.

Not applicable.

B. Warrants and Rights.

Not applicable.

C. Other Securities.

Not applicable.

D. American Depositary Shares.

Our ADSs representing our ordinary shares are currently traded on Nasdaq. Dealings in our ADSs on Nasdaq are conducted in U.S. dollars.

ADSs may be held either:

(a) directly: (i) by having an American Depositary Receipt, also referred to as an ADR, which is a certificate evidencing a specific number of ADSs registered in the holder's name; or (ii) by having uncertificated ADSs registered in the holder's name; or

(b) indirectly, by holding a security entitlement in ADSs through a broker or other financial institution that is a direct or indirect participant in The Depository Trust Company, also called DTC.

The depositary for our ADSs is Deutsche Bank Trust Company Americas, whose office is located at 1 Columbus Circle, New York, NY 10019, United States.

Table of Contents

Fees and charges our ADS holders may have to pay

ADS holders will be required to pay the following service fees to Deutsche Bank Trust Company America, the depositary of our ADS program, and certain taxes and governmental charges (in addition to any applicable fees, expenses, taxes and other governmental charges payable on the deposited securities represented by ADSs):

Service	Fees
● To any person to which ADSs are issued or to any person to which a distribution is made in respect of ADS distributions pursuant to stock dividends or other free distributions of stock, bonus distributions, stock splits or other distributions (except where converted to cash)	Up to $0.05 per ADS issued
● Cancellation or withdrawal of ADSs, including the case of termination of the deposit agreement	Up to $0.05 per ADS cancelled
● Distribution of cash dividends	Up to $0.05 per ADS held
● Distribution of cash entitlements (other than cash dividends) and/or cash proceeds from the sale of rights, securities and other entitlements	Up to $0.05 per ADS held
● Distribution of ADSs pursuant to exercise of rights	Up to $0.05 per ADS held
● Depositary services	Up to $0.05 per ADS held on the applicable record date(s) established by the depositary bank (an annual fee)

ADS holders will also be responsible for paying certain fees and expenses incurred by the depositary bank and certain taxes and governmental charges (in addition to any applicable fees, expenses, taxes and other governmental charges payable on the deposited securities represented by any of your ADSs) such as:

- Fees for the transfer and registration of ordinary shares charged by the registrar and transfer agent for the ordinary shares in the Cayman Islands (i.e., upon deposit and withdrawal of ordinary shares).
- Expenses incurred for converting foreign currency into U.S. dollars.
- Expenses for cable, telex and fax transmissions and for delivery of securities.
- Taxes and duties upon the transfer of securities, including any applicable stamp duties, any stock transfer charges or withholding taxes (i.e., when ordinary shares are deposited or withdrawn from deposit).
- Fees and expenses incurred in connection with the delivery or servicing of ordinary shares on deposit.
- Fees and expenses incurred in connection with complying with exchange control regulations and other regulatory requirements applicable to ordinary shares, ordinary shares deposited securities, ADSs and ADRs.
- Any applicable fees and penalties thereon.

The depositary fees payable upon the issuance and cancellation of ADSs are typically paid to the depositary bank by the brokers (on behalf of their clients) receiving the newly issued ADSs from the depositary bank and by the brokers (on behalf of their clients) delivering the ADSs to the depositary bank for cancellation. The brokers in turn charge these fees to their clients. Depositary fees payable in connection with distributions of cash or securities to ADS holders and the depositary services fee are charged by the depositary bank to the holders of record of ADSs as of the applicable ADS record date.

The depositary fees payable for cash distributions are generally deducted from the cash being distributed or by selling a portion of distributable property to pay the fees. In the case of distributions other than cash (i.e., share dividends, rights), the depositary bank charges the applicable fee to the ADS record date holders concurrent with the distribution. In the case of ADSs registered in the name of the investor (whether certificated or uncertificated in direct registration), the depositary bank sends invoices to the applicable record date ADS holders. In the case of ADSs held in brokerage and custodian accounts (via DTC), the depositary bank generally collects its fees through the systems provided by DTC (whose nominee is the registered holder of the ADSs held in DTC) from the brokers and custodians holding ADSs in their DTC accounts. The brokers and custodians who hold their clients' ADSs in DTC accounts in turn charge their clients' accounts the amount of the fees paid to the depositary banks.

In the event of refusal to pay the depositary fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder.

Fees and other payments made by the depositary to us

The depositary has agreed to pay certain amounts to us in exchange for its appointment as depositary. We may use these funds towards our expenses relating to the establishment and maintenance of the ADR program, including investor relations expenses, or otherwise as we see fit. In November 2022, we received $630,000 net of taxes from the depositary as part of the consideration for renewing the depositary's appointment.

Ordinary Shares and Conversions

Our ordinary shares are admitted to trading on AIM and trade on the SEHK. Dealings in our ordinary shares on the AIM and SEHK are conducted in pound sterlings and H.K. dollars, respectively.

In connection with the initial public offering of our ordinary shares in Hong Kong in June 2021, we established a branch register of members in Hong Kong, or the Hong Kong share register, which will be maintained by our Hong Kong Share Registrar, Computershare Hong Kong Investor Services Limited. Our principal register of members, or the Cayman share register, will continue to be maintained by our Principal Share Registrar, Computershare Investor Services (Jersey) Limited. All ordinary shares offered in our initial public offering in Hong Kong were registered on the Hong Kong share register in order to be listed and traded on the SEHK.

Details on the conversion process between SEHK, Nasdaq and AIM are available at https://www.hutch-med.com/shareholder-information/investor-faqs/.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

A-D. Material Modifications to the Rights of Security Holders; Assets Securing Securities; Trustees; Paying Agents.

None.

E. Use of Proceeds.

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Evaluation of Disclosure Controls and Procedures.

As required by Rule 13a-15 under the Exchange Act, management, including our chief executive officer and our chief financial officer, has evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. Disclosure controls and procedures refer to controls and other procedures designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in our reports that we file or submit under the Exchange Act is accumulated and communicated to management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding our required disclosure. Based on such evaluation, our management has concluded that, as of December 31, 2022, our disclosure controls and procedures were effective.

B. Management's Annual Report on Internal Control over Financial Reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rule 13a-15(f) and 15d-15(f) promulgated under the Securities Exchange Act of 1934. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements in accordance with U.S. GAAP and includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of a company's assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of a company's management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of a company's assets that could have a material effect on the consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness of our internal control over financial reporting to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our chief executive officer and chief financial officer, has assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 Framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

C. Attestation Report of the Independent Registered Public Accounting Firm.

Our independent registered public accounting firm, PricewaterhouseCoopers Zhong Tian LLP ("PricewaterhouseCoopers Zhong Tian"), has audited the effectiveness of our internal control over financial reporting as of December 31, 2022, as stated in its report, which appears in this annual report.

D. Changes in Internal Control over Financial Reporting.

There were no changes in our internal controls over financial reporting during the fiscal year ended December 31, 2022 that have materially and adversely affected, or are reasonably likely to materially and adversely affect, our internal control over financial reporting.

ITEM 16. RESERVED

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERTS

Our audit committee consists of Graeme Allan Jack, Paul Rutherford Carter and Karen Jean Ferrante, with Graeme Allan Jack serving as chairman of the committee. Graeme Allan Jack, Paul Rutherford Carter and Karen Jean Ferrante each meet the independence requirements under the rules of the Nasdaq Stock Market and under Rule 10A-3 under the Exchange Act. We have determined that Graeme Allan Jack is an "audit committee financial expert" within the meaning of Item 407 of Regulation S-K. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq Stock Market. For information relating to qualifications and experience of each audit committee member, see Item 6. "Directors, Senior Management and Employees."

ITEM 16B. CODE OF ETHICS

Our board of directors has adopted a code of ethics applicable to all of our employees, officers and directors, including our principal executive officer, principal financial officer, principal accounting officer or controller, and persons performing similar functions. This code is intended to qualify as a "code of ethics" within the meaning of the applicable rules of the SEC. Our code of ethics is available on our website at *https://www.hutch-med.com/shareholder-information/corporate-governance/code-of-ethics/*. Information contained on, or that can be accessed through, our website is not incorporated by reference into this annual report. See Item 6.C. "Board Practices—Code of Ethics" for more information.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Principal Accountant Fees and Services

The following table summarizes the fees charged by PricewaterhouseCoopers Zhong Tian and PricewaterhouseCoopers for certain services rendered to our company, including some of our subsidiaries and joint ventures, during 2022 and 2021.

	For the year ended December 31,	
	2022	2021
	(in thousands)	
Audit fees(1)	2,200	4,614
Tax fees(2)	337	406
Total(3)	2,537	5,020

Notes:

(1) "Audit fees" means the aggregate fees billed in each of the fiscal years for professional services rendered by PricewaterhouseCoopers Zhong Tian for the audit of our annual financial statements and review of our interim financial statements. The fees were also related to the professional services paid by us in connection with initial public offering in Hong Kong and preparation for other capital market transactions and regulatory filings in 2021.

(2) "Tax fees" means the aggregate fees billed in each of the fiscal years for professional services rendered by PricewaterhouseCoopers for tax compliance and tax advice.

(3) The fees disclosed are exclusive of out-of-pocket expenses and taxes on the amounts paid, which totaled approximately $117,000 and $52,000 in 2021 and 2022, respectively.

(4) On June 15, 2021, we engaged PricewaterhouseCoopers Zhong Tian as our independent registered public accounting firm, and dismissed PricewaterhouseCoopers. The fees for 2021 are fees payable to PricewaterhouseCoopers Zhong Tian. See also "Item 16F. Change in Registrant's Certifying Accountant."

Audit Committee Pre-approval Policies and Procedures

Our audit committee reviews and pre-approves the scope and the cost of audit services related to us and permissible non-audit services performed by the independent auditors, other than those for *de minimis* services which are approved by the audit committee prior to the completion of the audit. All of the services related to our company provided by PricewaterhouseCoopers Zhong Tian and PricewaterhouseCoopers listed above have been approved by the audit committee.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

None.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

On June 15, 2021, we engaged PricewaterhouseCoopers Zhong Tian as our independent registered public accounting firm, and dismissed PricewaterhouseCoopers. The change of our independent registered public accounting firm had been approved by the audit committee of our board of directors, and the decision was not made due to any disagreement between us and PricewaterhouseCoopers.

The reports of PricewaterhouseCoopers on our consolidated financial statements for the fiscal year ended December 31, 2020 did not contain an adverse opinion or disclaimer of opinion and were not qualified or modified as to uncertainty, audit scope or accounting principle.

During the fiscal year ended December 31, 2020 and the subsequent interim period through June 15, 2021, there have been no (i) disagreements between us and PricewaterhouseCoopers on any matter of accounting principles or practices, financial statement disclosure, or audit scope or procedure, which disagreements if not resolved to the satisfaction of PricewaterhouseCoopers would have caused them to make reference thereto in their reports on the consolidated financial statements for such years, or (ii) reportable events as defined in Item 16F(a)(1)(v) of the instructions to Form 20-F.

We have provided PricewaterhouseCoopers with a copy of the disclosures hereunder and required under Item 16F of Form 20-F and requested from PricewaterhouseCoopers a letter addressed to the Securities and Exchange Commission indicating whether it agrees with such disclosures. A copy of PricewaterhouseCooper's letter dated June 21, 2021 is attached as Exhibit 16.1 to our current report on Form 6-K furnished to the SEC on June 21, 2021.

During each of the fiscal year ended December 31, 2020 and the subsequent interim period through June 15, 2021, neither we nor anyone on behalf of us has consulted with PricewaterhouseCoopers Zhong Tian regarding (i) the application of accounting principles to a specific transaction, either completed or proposed, or the type of audit opinion that might be rendered on our consolidated financial statements, and neither a written report nor oral advice was provided to us that PricewaterhouseCoopers Zhong Tian concluded was an important factor considered by us in reaching a decision as to any accounting, audit or financial reporting issue, (ii) any matter that was the subject of a disagreement pursuant to Item 16F(a)(1)(iv) of the instructions to Form 20-F, or (iii) any reportable event pursuant to Item 16F(a)(1)(v) of the instructions to Form 20-F.

ITEM 16G. CORPORATE GOVERNANCE

As permitted by Nasdaq, in lieu of the Nasdaq corporate governance rules, but subject to certain exceptions, we may follow the practices of our home country which for the purpose of such rules is the Cayman Islands. Certain corporate governance practices in the Cayman Islands may differ significantly from corporate governance listing standards as, except for general fiduciary duties and duties of care, Cayman Islands law has no corporate governance regime which prescribes specific corporate governance standards. For example, we follow Cayman Islands corporate governance practices in lieu of the corporate governance requirements of the Nasdaq Global Select Market in respect of the following:

(i) the majority independent director requirement under Section 5605(b)(1) of the Nasdaq listing rules,

(ii) the requirement under Section 5605(d) of the Nasdaq listing rules that a remuneration committee comprised solely of independent directors governed by a remuneration committee charter oversee executive compensation, and

(iii) the requirement under Section 5605(e) of the Nasdaq listing rules that director nominees be selected or recommended for selection by either a majority of the independent directors or a nominations committee comprised solely of independent directors.

Cayman Islands law does not impose a requirement that our board of directors consist of a majority of independent directors, nor does Cayman Islands law impose specific requirements on the establishment of a remuneration committee or nominating committee or nominating process. We voluntarily comply with Hong Kong Corporate Governance Code. See Item 6.C. “Board Practice—Hong Kong Corporate Governance Code” for more details.

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

ITEM 16I. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTION

For the immediately preceding annual financial statement period, our auditor, PricewaterhouseCoopers Zhong Tian LLP (a registered public accounting firm that the PCAOB was unable to inspect or investigate completely) issued an audit report for us.

As of the date of this annual report and to our best knowledge:

(i) none of our shares or the shares of our consolidated foreign operating entities are owned by governmental entities in the jurisdiction in which we or such consolidated foreign operating entities are incorporated or otherwise organized;

(ii) none of the governmental entities in the applicable foreign jurisdiction with respect to our registered public accounting firm have a controlling financial interest in us or any of our consolidated foreign operating entities;

(iii) none of the members of our board of directors or the board of directors of our operating entities is an official of the Chinese Communist Party; and

(iv) our or our operating entities’ articles of incorporation do not contain any charter of the Chinese Communist Party.

ITEM 16J. INSIDER TRADING POLICIES

Not Applicable.

PART III

ITEM 17. FINANCIAL STATEMENTS

See Item 18 “Financial Statements.”

ITEM 18. FINANCIAL STATEMENTS

Our consolidated financial statements and the consolidated financial statements of our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, and our former non-consolidated joint venture, Hutchison Baiyunshan, are included at the end of this annual report.

ITEM 19. EXHIBITS

EXHIBIT INDEX

1.1	Amended and Restated Memorandum and Articles of Association of HUTCHMED (China) Limited (incorporated by reference to Exhibit 1.1 to our annual report on Form 20-F filed with the SEC on March 3, 2022)
2.1	Form of Deposit Agreement and all holders and beneficial owners of ADSs issued thereunder (incorporated by reference to Exhibit 4.1 to Amendment No. 4 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on March 4, 2016)
2.2	Form of American Depositary Receipt (incorporated by reference to Exhibit 4.1 to Amendment No. 4 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on March 4, 2016)
2.3	Form of Specimen Certificate for Ordinary Shares (incorporated by reference to Exhibit 4.3 to Amendment No. 2 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on February 11, 2016)
2.4*	Description of Ordinary Shares
2.5	Description of American Depositary Shares (incorporated by reference to Exhibit 2.5 to our annual report on Form 20-F/A filed with the SEC on April 29, 2020)
4.1	Amended and Restated License and Collaboration Agreement by and between HUTCHMED Limited (formerly known as Hutchison MediPharma Limited) and AstraZeneca AB (publ) dated as of December 7, 2020 (incorporated by reference to Exhibit 4.1 to our annual report on Form 20-F filed with the SEC on March 4, 2021)
4.2+	Amendment to the Amended and Restated License and Collaboration Agreement by and between HUTCHMED Limited and AstraZeneca AB (publ) dated as of November 29, 2021 (incorporated by reference to Exhibit 4.2 to our annual report on Form 20-F filed with the SEC on March 3, 2022)
4.3	Amended and Restated Exclusive License and Collaboration Agreement by and HUTCHMED Limited, Eli Lilly Trading (Shanghai) Company Limited and HUTCHMED (China) Limited dated as of October 8, 2013 (incorporated by reference to Exhibit 4.2 to our annual report on Form 20-F/A filed with the SEC on May 30, 2019)
4.4	First Amendment to the Amended and Restated Exclusive License and Collaboration Agreement by and among Lilly (Shanghai) Management Company Limited, HUTCHMED Limited and HUTCHMED (China) Limited dated as of December 18, 2018 (incorporated by reference to Exhibit 4.16 to our annual report on Form 20-F filed with the SEC on March 11, 2019)
4.5	English translation of Sino-Foreign Joint Venture Contract by and between Shanghai Traditional Chinese Medicine Co., Ltd. and Shanghai HUTCHMED Investment Limited (formerly Hutchison Chinese Medicine (Shanghai) Investment Limited) dated as of January 6, 2001 (incorporated by reference to Exhibit 4.6 to our annual report on Form 20-F/A filed with the SEC on May 30, 2019)
4.6	English translation of First Amendment to Sino-Foreign Joint Venture Contract by and between Shanghai Traditional Chinese Medicine Co., Ltd. and Shanghai HUTCHMED Investment Limited dated as of July 12, 2001 (incorporated by reference to Exhibit 10.15 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on October 16, 2015)
4.7	English translation of Second Amendment to Sino-Foreign Joint Venture Contract by and between Shanghai Traditional Chinese Medicine Co., Ltd. and Shanghai HUTCHMED Investment (HK) Limited dated as of November 5, 2007 (incorporated by reference to Exhibit 10.16 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on October 16, 2015)
4.8	English translation of Third Amendment to Sino-Foreign Joint Venture Contract by and between Shanghai Traditional Chinese Medicine Co., Ltd. and Shanghai HUTCHMED Investment (HK) Limited dated as of June 19, 2012 (incorporated by reference to Exhibit 10.17 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on October 16, 2015)
4.9	English translation of Fourth Amendment to Sino-Foreign Joint Venture Contract by and between Shanghai Traditional Chinese Medicine Co., Ltd. and Shanghai HUTCHMED Investment (HK) Limited dated as of March 8, 2013 (incorporated by reference to Exhibit 4.10 to our annual report on Form 20-F/A filed with the SEC on May 30, 2019)
4.10	English translation of Sino-Foreign Joint Venture Contract by and between Sinopharm Group Co. Ltd. and Hutchison Chinese Medicine GSP (HK) Holdings Limited dated as of December 18, 2013 (incorporated by reference to Exhibit 4.11 to our annual report on Form 20-F/A filed with the SEC on May 30, 2019)

4.11	Form of Executive Employment Agreement for HUTCHMED Group (HK) Limited executive officers (incorporated by reference to Exhibit 10.23 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on October 16, 2015)
4.12	English translation of Form of Executive Employment Agreement for HUTCHMED Limited executive officers (incorporated by reference to Exhibit 10.24 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on October 16, 2015)
4.13	Form of Indemnification Agreement for Directors and Officers (incorporated by reference to Exhibit 10.25 to our Registration Statement on Form F-1 (file no. 333-207447) filed with the SEC on October 16, 2015)
4.14	Second Amendment to the Amended and Restated Exclusive License and Collaboration Agreement by and among Lilly (Shanghai) Management Company Limited, HUTCHMED Limited and HUTCHMED (China) Limited dated as of July 28, 2020 (incorporated by reference to Exhibit 4.14 to our annual report on Form 20-F filed with the SEC on March 4, 2021)
4.15+	License Agreement by and among Epizyme, Inc. and Hutchison China MediTech Investment Limited (now known as HUTCHMED Group Investment Limited) dated as of August 7, 2021 (incorporated by reference to Exhibit 4.15 to our annual report on Form 20-F filed with the SEC on March 3, 2022)
4.16*+	License Agreement by and among Takeda Pharmaceuticals International AG, HUTCHMED (China) Limited and HUTCHMED Limited dated as of January 23, 2023
8.1	List of Significant Subsidiaries of the Company (incorporated by reference to Exhibit 8.1 to our annual report on Form 20-F filed with the SEC on March 3, 2022)
12.1*	Certification of Chief Executive Officer Required by Rule 13a-14(a)
12.2*	Certification of Chief Financial Officer Required by Rule 13a-14(a)
13.1*	Certification of Chief Executive Officer Required by Rule 13a-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code
13.2*	Certification of Chief Financial Officer Required by Rule 13a-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code
15.1*	Consent of PricewaterhouseCoopers Zhong Tian LLP, an independent registered accounting firm, regarding the consolidated financial statements of HUTCHMED (China) Limited
15.2*	Consent of PricewaterhouseCoopers, an independent registered accounting firm, regarding the consolidated financial statements of HUTCHMED (China) Limited
15.3*	Consent of PricewaterhouseCoopers Zhong Tian LLP, independent accountants, regarding the consolidated financial statements of Shanghai Hutchison Pharmaceuticals Limited
15.4*	Consent of PricewaterhouseCoopers Zhong Tian LLP, independent accountants, regarding the consolidated financial statements of Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
15.5*	Consent of Conyers Dill & Pearman
15.6†	Submission under Item 16I(a) of Form 20-F in relation to the Holding Foreign Companies Accountable Act
16.1	Letter from PricewaterhouseCoopers to the Securities and Exchange Commission dated June 21, 2021 (incorporated herein by reference to Exhibit 16.1 to the current report on Form 6-K furnished to the SEC on June 21, 2021)
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definitions Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.
† Furnished herewith.
\+ Portions of the exhibit have been omitted because they are both (i) not material and (ii) would likely cause competitive harm to the company if publicly disclosed.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on annual report on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

HUTCHMED (China) Limited

By: /s/ Weiguo Su
Name: Weiguo Su
Title: Chief Executive Officer

Date: February 28, 2023

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of HUTCHMED (China) Limited

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of HUTCHMED (China) Limited and its subsidiaries (the "Company") as of December 31, 2022 and 2021, and the related consolidated statements of operations, of comprehensive loss, of changes in shareholders' equity and of cash flows for each of the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control—Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control—Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Annual Report on Internal Control over Financial Reporting appearing under Item 15 of Form 20-F. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Allowances for credit losses on accounts receivable and other receivables (except for prepayments)

As described in Note 6 to the consolidated financial statements, as of December 31, 2022, the gross balance of accounts receivable was US$98.0 million and an allowance for credit losses of less than US$0.1 million was made. As described in Note 7 to the consolidated financial statements, as of December 31, 2022, the gross balance of other receivables was US$54.2 million which consisted of the balance of prepayments of US$22.3 million, and no allowance for credit losses was made. The allowances for credit losses were made based on estimate of the current expected credit losses to be incurred over the expected life of these receivables.

The principal considerations for our determination that performing procedures relating to the allowances for credit losses on accounts receivable and other receivables (except for prepayments) is a critical audit matter are the significant estimates and judgments by management when developing the current expected credit losses to be incurred over the expected life of these receivables, which in turn led to a high degree of auditor judgment and significant audit effort in evaluating the audit evidence related to management’s significant assumptions, including accounts receivable and other receivables (except for prepayments) portfolio groups and estimated loss rates.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of internal controls relating to management’s estimate of allowances for credit losses on accounts receivable and other receivables (except for prepayments). The procedures also included, among others, testing management’s process of developing the allowances for credit losses, testing the accuracy and completeness of the underlying data and the mathematical accuracy of the allowances for credit losses, evaluating the appropriateness of the model and methodology used and assessing the reasonableness of portfolio groups of the receivables and estimated loss rates used by management. Assessing the reasonableness of portfolio groups of the receivables used by management involved evaluating their credit risk characteristics. Assessing the reasonableness of estimated loss rates used by management involved evaluating the historical default rates and application of forward-looking information.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Shenzhen, the People’s Republic of China
February 28, 2023

We have served as the Company’s auditor since 2021.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of HUTCHMED (China) Limited

Opinion on the Financial Statements

We have audited the consolidated statements of operations, of comprehensive loss, of changes in shareholders' equity and of cash flows of HUTCHMED (China) Limited (formerly known as "Hutchison China MediTech Limited") and its subsidiaries (the "Company") for the year ended December 31, 2020, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the results of operations and cash flows of the Company for the year ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audit included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers
Hong Kong
March 4, 2021

We served as the Company's auditor from 2005 to 2021.

CONSOLIDATED FINANCIAL STATEMENTS

HUTCHMED (CHINA) LIMITED
CONSOLIDATED BALANCE SHEETS
(IN US$'000, EXCEPT SHARE DATA)

	Note	December 31, 2022	December 31, 2021
Assets			
Current assets			
Cash and cash equivalents	5	313,278	377,542
Short-term investments	5	317,718	634,158
Accounts receivable	6	97,988	83,580
Other receivables, prepayments and deposits	7	54,214	81,041
Inventories	8	56,690	35,755
Total current assets		**839,888**	**1,212,076**
Property, plant and equipment	9	75,947	41,275
Right-of-use assets	10	8,722	11,879
Deferred tax assets	24(ii)	15,366	9,401
Investments in equity investees	11	73,777	76,479
Other non-current assets		15,745	21,551
Total assets		**1,029,445**	**1,372,661**
Liabilities and shareholders' equity			
Current liabilities			
Accounts payable	12	71,115	41,177
Other payables, accruals and advance receipts	13	264,621	210,839
Bank borrowings	14	—	26,905
Income tax payable	24(iii)	1,112	15,546
Other current liabilities		17,055	17,191
Total current liabilities		**353,903**	**311,658**
Lease liabilities	10	5,196	7,161
Deferred tax liabilities	24(ii)	2,710	2,765
Long-term bank borrowings	14	18,104	—
Other non-current liabilities		12,662	11,563
Total liabilities		**392,575**	**333,147**
Commitments and contingencies	15		
Company's shareholders' equity			
Ordinary shares; $0.10 par value; 1,500,000,000 shares authorized; 864,775,340 and 864,530,850 shares issued at December 31, 2022 and 2021 respectively	16	86,478	86,453
Additional paid-in capital		1,497,273	1,505,196
Accumulated losses		(971,481)	(610,328)
Accumulated other comprehensive (loss)/income		(1,903)	5,572
Total Company's shareholders' equity		**610,367**	**986,893**
Non-controlling interests		26,503	52,621
Total shareholders' equity		**636,870**	**1,039,514**
Total liabilities and shareholders' equity		**1,029,445**	**1,372,661**

The accompanying notes are an integral part of these consolidated financial statements.

HUTCHMED (CHINA) LIMITED
CONSOLIDATED STATEMENTS OF OPERATIONS
(IN US$'000, EXCEPT SHARE AND PER SHARE DATA)

	Note	Year Ended December 31, 2022	2021	2020
Revenues				
Goods —third parties		314,329	266,199	203,606
—related parties	23(i)	5,293	4,256	5,484
Services —commercialization—third parties		41,275	27,428	3,734
—collaboration research and development—third parties		23,741	18,995	9,771
—research and development—related parties	23(i)	507	525	491
Other collaboration revenue				
—royalties—third parties		26,310	15,064	4,890
—licensing—third parties		14,954	23,661	—
Total revenues	18	**426,409**	**356,128**	**227,976**
Operating expenses				
Costs of goods—third parties		(268,698)	(229,448)	(178,828)
Costs of goods—related parties		(3,616)	(3,114)	(3,671)
Costs of services—commercialization—third parties		(38,789)	(25,672)	(6,020)
Research and development expenses	20	(386,893)	(299,086)	(174,776)
Selling expenses		(43,933)	(37,827)	(11,334)
Administrative expenses		(92,173)	(89,298)	(50,015)
Total operating expenses		**(834,102)**	**(684,445)**	**(424,644)**
		(407,693)	**(328,317)**	**(196,668)**
Gain on divestment of an equity investee	22	—	121,310	—
Other (expense)/income				
Interest income	26	9,599	2,076	3,236
Other income		1,833	2,426	4,600
Interest expense	26	(652)	(592)	(787)
Other expense		(13,509)	(12,643)	(115)
Total other (expense)/income		**(2,729)**	**(8,733)**	**6,934**
Loss before income taxes and equity in earnings of equity investees		**(410,422)**	**(215,740)**	**(189,734)**
Income tax benefit/(expense)	24(i)	283	(11,918)	(4,829)
Equity in earnings of equity investees, net of tax	11	49,753	60,617	79,046
Net loss		**(360,386)**	**(167,041)**	**(115,517)**
Less: Net income attributable to non-controlling interests		(449)	(27,607)	(10,213)
Net loss attributable to the Company		**(360,835)**	**(194,648)**	**(125,730)**
Losses per share attributable to the Company—basic and diluted (US$ per share)	25	(0.43)	(0.25)	(0.18)
Number of shares used in per share calculation—basic and diluted	25	847,143,540	792,684,524	697,931,437

The accompanying notes are an integral part of these consolidated financial statements.

HUTCHMED (CHINA) LIMITED
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(IN US$'000)

	Year Ended December 31,		
	2022	**2021**	**2020**
Net loss	**(360,386)**	**(167,041)**	**(115,517)**
Other comprehensive (loss)/income			
Foreign currency translation (loss)/gain	(8,469)	2,964	9,530
Total comprehensive loss	**(368,855)**	**(164,077)**	**(105,987)**
Less: Comprehensive loss/(income) attributable to non-controlling interests	545	(28,029)	(11,413)
Total comprehensive loss attributable to the Company	**(368,310)**	**(192,106)**	**(117,400)**

The accompanying notes are an integral part of these consolidated financial statements.

HUTCHMED (CHINA) LIMITED
CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY
(IN US$'000, EXCEPT SHARE DATA IN '000)

	Ordinary Shares Number	Ordinary Shares Value	Additional Paid-in Capital	Accumulated Losses	Accumulated Other Comprehensive (Loss)/Income	Total Company's Shareholders' Equity	Non-controlling Interests	Total Shareholders' Equity
As at January 1, 2020	**666,906**	**66,691**	**514,904**	**(289,734)**	**(3,849)**	**288,012**	**24,891**	**312,903**
Net (loss)/income	—	—	—	(125,730)	—	(125,730)	10,213	(115,517)
Issuance in relation to public offering	23,669	2,366	115,975	—	—	118,341	—	118,341
Issuances in relation to private investment in public equity ("PIPE")	36,667	3,667	196,333	—	—	200,000	—	200,000
Issuance costs	—	—	(8,317)	—	—	(8,317)	—	(8,317)
Issuances in relation to share option exercises	480	48	545	—	—	593	—	593
Share-based compensation								
Share options	—	—	8,727	—	—	8,727	10	8,737
Long-term incentive plan ("LTIP")	—	—	7,203	—	—	7,203	16	7,219
	—	—	15,930	—	—	15,930	26	15,956
LTIP—treasury shares acquired and held by Trustee	—	—	(12,904)	—	—	(12,904)	—	(12,904)
Dividends declared to non-controlling shareholders of subsidiaries	—	—	—	—	—	—	(1,462)	(1,462)
Purchase of additional interests in a subsidiary of an equity investee (Note 11)	—	—	(52)	(83)	(4)	(139)	(35)	(174)
Transfer between reserves	—	—	44	(44)	—	—	—	—
Foreign currency translation adjustments	—	—	—	—	8,330	8,330	1,200	9,530
As at December 31, 2020	**727,722**	**72,772**	**822,458**	**(415,591)**	**4,477**	**484,116**	**34,833**	**518,949**
Net (loss)/income	—	—	—	(194,648)	—	(194,648)	27,607	(167,041)
Issuance in relation to public offering	119,600	11,960	602,907	—	—	614,867	—	614,867
Issuance in relation to PIPE	16,393	1,639	98,361	—	—	100,000	—	100,000
Issuance costs	—	—	(29,806)	—	—	(29,806)	—	(29,806)
Issuances in relation to share option exercises	816	82	2,370	—	—	2,452	—	2,452
Share-based compensation								
Share options	—	—	16,339	—	—	16,339	26	16,365
LTIP	—	—	19,808	—	—	19,808	70	19,878
	—	—	36,147	—	—	36,147	96	36,243
LTIP—treasury shares acquired and held by Trustee	—	—	(27,309)	—	—	(27,309)	—	(27,309)
Dividends declared to non-controlling shareholders of subsidiaries	—	—	—	—	—	—	(9,894)	(9,894)
Transfer between reserves	—	—	89	(89)	—	—	—	—
Divestment of an equity investee (Note 22)	—	—	(21)	—	(1,447)	(1,468)	(443)	(1,911)
Foreign currency translation adjustments	—	—	—	—	2,542	2,542	422	2,964
As at December 31, 2021	**864,531**	**86,453**	**1,505,196**	**(610,328)**	**5,572**	**986,893**	**52,621**	**1,039,514**
Net (loss)/income	—	—	—	(360,835)	—	(360,835)	449	(360,386)
Issuances in relation to share option exercises	244	25	149	—	—	174	—	174
Share-based compensation								
Share options	—	—	6,724	—	—	6,724	12	6,736
LTIP	—	—	32,970	—	—	32,970	15	32,985
	—	—	39,694	—	—	39,694	27	39,721
LTIP—treasury shares acquired and held by Trustee	—	—	(48,084)	—	—	(48,084)	—	(48,084)
Dividends declared to non-controlling shareholders of subsidiaries	—	—	—	—	—	—	(25,600)	(25,600)
Transfer between reserves	—	—	318	(318)	—	—	—	—
Foreign currency translation adjustments	—	—	—	—	(7,475)	(7,475)	(994)	(8,469)
As at December 31, 2022	**864,775**	**86,478**	**1,497,273**	**(971,481)**	**(1,903)**	**610,367**	**26,503**	**636,870**

The accompanying notes are an integral part of these consolidated financial statements.

HUTCHMED (CHINA) LIMITED
CONSOLIDATED STATEMENTS OF CASH FLOWS
(IN US$'000)

	Note	Year Ended December 31, 2022	2021	2020
Net cash used in operating activities	27	(268,599)	(204,223)	(62,066)
Investing activities				
Purchases of property, plant and equipment		(36,664)	(16,401)	(7,949)
Purchase of leasehold land		—	(355)	(11,631)
Refund/(payment) of leasehold land deposit		—	930	(2,326)
Deposits in short-term investments		(1,202,013)	(1,355,976)	(732,908)
Proceeds from short-term investments		1,518,453	921,364	629,373
Purchase of a warrant	19	—	(15,000)	—
Dividend and proceeds received from divestment of Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited ("HBYS")	22	16,488	159,118	—
Deposit received for divestment of other equity investee	11	324	—	—
Net cash generated from/(used in) investing activities		296,588	(306,320)	(125,441)
Financing activities				
Proceeds from issuances of ordinary shares		174	717,319	318,934
Purchases of treasury shares	17(ii)	(48,084)	(27,309)	(12,904)
Dividends paid to non-controlling shareholders of subsidiaries		(25,600)	(9,894)	(1,462)
Repayment of loan to a non-controlling shareholder of a subsidiary		—	(579)	—
Proceeds from bank borrowings		17,753	—	—
Repayment of bank borrowings		(26,923)	—	—
Payment of issuance costs		(83)	(29,509)	(8,134)
Net cash (used in)/generated from financing activities		(82,763)	650,028	296,434
Net (decrease)/increase in cash and cash equivalents		(54,774)	139,485	108,927
Effect of exchange rate changes on cash and cash equivalents		(9,490)	2,427	5,546
		(64,264)	141,912	114,473
Cash and cash equivalents				
Cash and cash equivalents at beginning of year		377,542	235,630	121,157
Cash and cash equivalents at end of year		313,278	377,542	235,630
Supplemental disclosure for cash flow information				
Cash paid for interest		150	425	815
Cash paid for tax, net of refunds	24(iii)	18,891	5,014	5,940
Supplemental disclosure for non-cash activities				
Increase in accrued capital expenditures		9,618	8,607	298
Vesting of treasury shares for LTIP	17(ii)	12,034	1,450	4,828

The accompanying notes are an integral part of these consolidated financial statements.

HUTCHMED (CHINA) LIMITED
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Nature of Business

HUTCHMED (China) Limited (the "Company") and its subsidiaries (together the "Group") are principally engaged in researching, developing, manufacturing and marketing pharmaceutical products. The Group and its equity investees have research and development facilities and manufacturing plants in the People's Republic of China (the "PRC") and sell their products mainly in the PRC, including Hong Kong and Macau. In addition, the Group has established international operations in the United States of America (the "U.S.") and Europe.

The Company's ordinary shares are listed on the Main Board of The Stock Exchange of Hong Kong Limited ("HKEX") and the AIM market of the London Stock Exchange, and its American depositary shares ("ADS") are traded on the Nasdaq Global Select Market.

Liquidity

As at December 31, 2022, the Group had accumulated losses of US$971,481,000 primarily due to its spending in drug research and development activities. The Group regularly monitors current and expected liquidity requirements to ensure that it maintains sufficient cash balances and adequate credit facilities to meet its liquidity requirements in the short and long term. As at December 31, 2022, the Group had cash and cash equivalents of US$313,278,000, short-term investments of US$317,718,000 and unutilized bank borrowing facilities of US$140,289,000. Short-term investments comprised of bank deposits maturing over three months. The Group's operating plan includes the continued receipt of dividends from an equity investee. Dividends received for the years ended December 31, 2022, 2021 and 2020 were US$43,718,000, US$49,872,000 and US$86,708,000 respectively.

Based on the Group's operating plan, the existing cash and cash equivalents, short-term investments and unutilized bank borrowing facilities are considered to be sufficient to meet the cash requirements to fund planned operations and other commitments for at least the next twelve months from the issuance date of the consolidated financial statements (the look-forward period used).

2. Particulars of Principal Subsidiaries and Equity Investee

Name	Place of establishment and operations	Equity interest attributable to the Group December 31, 2022	2021	Principal activities
Subsidiaries				
HUTCHMED Limited	PRC	99.75 %	99.75 %	Research, development, manufacture and commercialization of pharmaceutical products
HUTCHMED International Corporation	U.S.	99.75 %	99.75 %	Provision of professional, scientific and technical support services
Hutchison Whampoa Sinopharm Pharmaceuticals (Shanghai) Company Limited ("HSPL")	PRC	50.87 %	50.87 %	Provision of sales, distribution and marketing services to pharmaceutical manufacturers
Hutchison Healthcare Limited	PRC	100 %	100 %	Manufacture and distribution of healthcare products
Hutchison Hain Organic (Hong Kong) Limited ("HHOHK") (note)	Hong Kong	50 %	50 %	Wholesale and trading of healthcare and consumer products
HUTCHMED Science Nutrition Limited	Hong Kong	100 %	100 %	Wholesale and trading of healthcare and consumer products
Equity investee				
Shanghai Hutchison Pharmaceuticals Limited ("SHPL")	PRC	50 %	50 %	Manufacture and distribution of prescription drug products

Note: HHOHK is regarded as a subsidiary of the Company, as while both its shareholders have equal representation at the board, in the event of a deadlock, the Group has a casting vote and is therefore able to unilaterally control the financial and operating policies of HHOHK.

3. Summary of Significant Accounting Policies

Principles of Consolidation and Basis of Presentation

The accompanying consolidated financial statements reflect the accounts of the Company and all of its subsidiaries in which a controlling interest is maintained. All inter-company balances and transactions have been eliminated in consolidation. The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the U.S. ("U.S. GAAP").

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period.

Foreign Currency Translation

The Company's presentation currency and functional currency is the U.S. dollar ("US$"). The financial statements of its subsidiaries with a functional currency other than the US$ have been translated into the Company's presentation currency. All assets and liabilities of the subsidiaries are translated using year-end exchange rates and revenues and expenses are translated at average exchange rates for the year. Translation adjustments are reflected in accumulated other comprehensive (loss)/income in shareholders' equity.

Net foreign currency exchange losses of US$5,704,000 and net foreign currency exchange gains of US$1,671,000 and US$3,265,000 were recorded in other expense and income in the consolidated statements of operations for the years ended December 31, 2022, 2021 and 2020 respectively.

Foreign Currency Risk

The Group's operating transactions and its assets and liabilities in the PRC are mainly denominated in Renminbi ("RMB"), which is not freely convertible into foreign currencies. The Group's cash and cash equivalents denominated in RMB are subject to government controls. The value of the RMB is subject to fluctuations from central government policy changes and international economic and political developments that affect the supply and demand of RMB in the foreign exchange market. In the PRC, certain foreign exchange transactions are required by law to be transacted only by authorized financial institutions at exchange rates set by the People's Bank of China (the "PBOC"). Remittances in currencies other than RMB by the Group in the PRC must be processed through the PBOC or other PRC foreign exchange regulatory bodies which require certain supporting documentation in order to complete the remittance.

Allowance for Current Expected Credit Losses and Concentration of Credit Risk

Financial instruments that potentially expose the Group to credit risk consist primarily of cash and cash equivalents, short-term investments, and financial assets not carried at fair value including accounts receivable and other receivables.

The Group recognizes an allowance for current expected credit losses ("CECLs") on financial assets not carried at fair value. CECLs are calculated over the expected life of the financial assets on an individual or a portfolio basis considering information available about the counterparties' credit situation and collectability of the specific cash flows, including information about past events, current conditions and future forecasts.

The Group places substantially all of its cash and cash equivalents and short-term investments in major financial institutions, which management believes are of high credit quality. The Group has a practice to limit the amount of credit exposure to any particular financial institution. Additionally, the Group has policies in place to ensure that sales are made to customers with an appropriate credit history and the Group performs periodic credit evaluations of its customers. Normally the Group does not require collateral from trade debtors. The Group has not had any material credit losses.

Cash and Cash Equivalents

The Group considers all highly liquid investments purchased with original maturities of three months or less to be cash equivalents. Cash and cash equivalents consist primarily of cash on hand and bank deposits and are stated at cost, which approximates fair value.

Short-term Investments

Short-term investments include deposits placed with banks with original maturities of more than three months but less than one year.

Accounts Receivable

Accounts receivable are stated at the amount management expects to collect from customers based on their outstanding invoices. The allowance for CECLs reflects the Group's current estimate of credit losses expected to be incurred over the life of the receivables. The Group considers various factors in establishing, monitoring, and adjusting its allowance for CECLs including the aging of the accounts and aging trends, the historical level of charge-offs, and specific exposures related to particular customers. The Group also monitors other risk factors and forward-looking information, such as country risk, when determining credit limits for customers and establishing adequate allowances for CECLs. Accounts receivable are written off after all reasonable means to collect the full amount (including litigation, where appropriate) have been exhausted.

Inventories

Inventories are stated at the lower of cost or net realizable value. Cost is determined using the weighted average cost method. The cost of finished goods comprises raw materials, direct labor, other direct costs and related production overheads based on normal operating capacity. Net realizable value is the estimated selling price in the ordinary course of business, less applicable variable selling expenses. A provision for excess and obsolete inventory will be made based primarily on forecasts of product demand and production requirements. The excess balance determined by this analysis becomes the basis for excess inventory charge and the written-down value of the inventory becomes its cost. Written-down inventory is not written up if market conditions improve.

Property, Plant and Equipment

Property, plant and equipment consist of buildings, leasehold improvements, plant and equipment, furniture and fixtures, other equipment and motor vehicles. Property, plant and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the depreciable assets.

Buildings	20 years
Plant and equipment	5-10 years
Furniture and fixtures, other equipment and motor vehicles	4-5 years
Leasehold improvements	Shorter of (a) 5 years or (b) remaining term of lease

Additions and improvements that extend the useful life of an asset are capitalized. Repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

The Group evaluates the recoverability of long-lived assets in accordance with authoritative guidance on accounting for the impairment or disposal of long-lived assets. The Group evaluates long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. If indicators of impairment exist, the first step of the impairment test is performed to assess if the carrying value of the net assets exceeds the undiscounted cash flows of the assets. If yes, the second step of the impairment test is performed in order to determine if the carrying value of the net assets exceeds the fair value. If yes, impairment is recognized for the excess.

Investments in Equity Investees

Investments in equity investees over which the Group has significant influence are accounted for using the equity method. The Group evaluates equity method investments for impairment when events or circumstances suggest that their carrying amounts may not be recoverable. An impairment charge would be recognized in earnings for a decline in value that is determined to be other-than-temporary after assessing the severity and duration of the impairment and the likelihood of recovery before disposal. The investments are recorded at fair value only if impairment is recognized.

Leasehold Land

Leasehold land represents fees paid to acquire the right to use the land on which various plants and buildings are situated for a specified period of time from the date the respective right was granted and are stated at cost less accumulated amortization and impairment loss, if any. Amortization is computed using the straight-line basis over the lease period of 50 years.

Goodwill

Goodwill represents the excess of the purchase price plus fair value of non-controlling interests over the fair value of identifiable assets and liabilities acquired. Goodwill is not amortized, but is tested for impairment at the reporting unit level on at least an annual basis or when an event occurs or circumstances change that would more likely than not reduce the fair value of a reporting unit below its carrying amount. When performing an evaluation of goodwill impairment, the Group has the option to first assess qualitative factors, such as significant events and changes to expectations and activities that may have occurred since the last impairment evaluation, to determine if it is more likely than not that goodwill might be impaired. If as a result of the qualitative assessment, that it is more likely than not that the fair value of the reporting unit is less than its carrying amount, the quantitative fair value test is performed to determine if the fair value of the reporting unit exceeds its carrying value.

Other Intangible Assets

Other intangible assets with finite useful lives are carried at cost less accumulated amortization and impairment loss, if any. Amortization is computed using the straight-line basis over the estimated useful lives of the assets.

Borrowings

Borrowings are recognized initially at fair value, net of debt issuance costs incurred. Borrowings are subsequently stated at amortized cost; any difference between the proceeds (net of debt issuance costs) and the redemption value is recognized in the consolidated statements of operations over the period of the borrowings using the effective interest method.

Ordinary Shares

The Company’s ordinary shares are stated at par value of US$0.10 per ordinary share. The difference between the consideration received, net of issuance cost, and the par value is recorded in additional paid-in capital.

Treasury Shares

The Group accounts for treasury shares under the cost method. The treasury shares are purchased for the purpose of the LTIP and held by a trustee appointed by the Group (the “Trustee”) prior to vesting.

Share-Based Compensation

Share options

The Group recognizes share-based compensation expense on share options granted to employees and directors based on their estimated grant date fair value using the Polynomial model. This Polynomial pricing model uses various inputs to measure fair value, including the market value of the Company’s underlying ordinary shares at the grant date, contractual terms, estimated volatility, risk-free interest rates and expected dividend yields. The Group recognizes share-based compensation expense in the consolidated statements of operations on a graded vesting basis over the requisite service period, and accounts for forfeitures as they occur.

Share options are classified as equity-settled awards. Share-based compensation expense, when recognized, is charged to the consolidated statements of operations with the corresponding entry to additional paid-in capital.

LTIP

The Group recognizes the share-based compensation expense on the LTIP awards based on a fixed or determinable monetary amount on a straight-line basis for each annual tranche awarded over the requisite period. For LTIP awards with performance targets, prior to their determination date, the amount of LTIP awards that is expected to vest takes into consideration the achievement of the performance conditions and the extent to which the performance conditions are likely to be met. Performance conditions vary by awards, and may include targets for shareholder returns, financings, revenues, net profit after taxes and the achievement of clinical and regulatory milestones.

These LTIP awards are classified as liability-settled awards before the determination date (i.e. the date when the achievement of any performance conditions are known), as they settle in a variable number of shares based on a determinable monetary amount, which is determined upon the actual achievement of performance targets. As the extent of achievement of the performance targets is uncertain prior to the determination date, a probability based on management's assessment of the achievement of the performance targets has been assigned to calculate the amount to be recognized as an expense over the requisite period.

After the determination date or if the LTIP awards have no performance conditions, the LTIP awards are classified as equity-settled awards. If the performance target is achieved, the Group will pay the determined monetary amount to the Trustee to purchase ordinary shares of the Company or the equivalent ADS. Any cumulative compensation expense previously recognized as a liability will be transferred to additional paid-in capital. If the performance target is not achieved, no ordinary shares or ADS of the Company will be purchased and the amount previously recorded in the liability will be reversed and included in the consolidated statements of operations.

Defined Contribution Plans

The Group's subsidiaries in the PRC participate in a government-mandated multi-employer defined contribution plan pursuant to which certain retirement, medical and other welfare benefits are provided to employees. The relevant labor regulations require the Group's subsidiaries in the PRC to pay the local labor and social welfare authority's monthly contributions at a stated contribution rate based on the monthly basic compensation of qualified employees. The relevant local labor and social welfare authorities are responsible for meeting all retirement benefits obligations and the Group's subsidiaries in the PRC have no further commitments beyond their monthly contributions. The contributions to the plan are expensed as incurred.

The Group also makes payments to other defined contribution plans for the benefit of employees employed by subsidiaries outside the PRC. The defined contribution plans are generally funded by the relevant companies and by payments from employees.

The Group's contributions to defined contribution plans for the years ended December 31, 2022, 2021 and 2020 amounted to US$11,795,000, US$7,181,000 and US$2,660,000 respectively.

Revenue Recognition

Revenue is measured based on consideration specified in a contract with a customer, and excludes any sales incentives and amounts collected on behalf of third parties. Taxes assessed by a governmental authority that are both imposed on and concurrent with a specific revenue-producing transaction, that are collected by the Group from a customer, are also excluded from revenue. The Group recognizes revenue when it satisfies a performance obligation by transferring control over a good, service or license to a customer.

(i) Goods and services

The Group principally generates revenue from (1) sales of goods, which are the manufacture or purchase and distribution of pharmaceutical products and other consumer health products, and (2) provision of services, which are the provision of sales, distribution and marketing services to pharmaceutical manufacturers. The Group evaluates whether it is the principal or agent for these contracts. Where the Group obtains control of the goods for distribution, it is the principal (i.e. recognizes sales of goods on a gross basis). Where the Group does not obtain control of the goods for distribution, it is the agent (i.e. recognizes provision of services on a net basis). Control is primarily evidenced by taking physical possession and inventory risk of the goods.

Revenues from sales of goods is recognized when the customer takes possession of the goods. This usually occurs upon completed delivery of the goods to the customer site. The amount of revenue recognized is adjusted for expected sales incentives as stipulated in the contract, which are generally issued to customers as direct discounts at the point-of-sale or indirectly in the form of rebates. Sales incentives are estimated using the expected value method. Additionally, sales are generally made with a limited right of return under certain conditions. Revenues are recorded net of provisions for sales discounts and returns.

Revenue from provision of services is recognized when the benefits of the services transfer to the customer over time, which is based on the proportionate value of services rendered as determined under the terms of the relevant contract. Additionally, when the amounts that can be invoiced correspond directly with the value to the customer for performance completed to date, the Group recognizes revenue from provision of services based on amounts that can be invoiced to the customer.

Deferred revenue is recognized if consideration is received in advance of transferring control of the goods or rendering of services. Accounts receivable is recognized if the Group has an unconditional right to bill the customer, which is generally when the customer takes possession of the goods or services are rendered. Payment terms differ by subsidiary and customer, but generally range from 45 to 180 days from the invoice date.

(ii) License and collaboration contracts

The Group's Oncology/Immunology reportable segment includes revenue generated from license and collaboration contracts, which generally contain multiple performance obligations including (1) the license to the commercialization rights of a drug compound and (2) the research and development services for each specified treatment indication, which are accounted for separately if they are distinct, i.e. if a product or service is separately identifiable from other items in the arrangement and if a customer can benefit from it on its own or with other resources that are readily available to the customer.

The transaction price generally includes fixed and variable consideration in the form of upfront payment, research and development cost reimbursements, contingent milestone payments and sales-based royalties. Contingent milestone payments are not included in the transaction price until it becomes probable that a significant reversal of revenue will not occur, which is generally when the specified milestone is achieved. The allocation of the transaction price to each performance obligation is based on the relative standalone selling prices of each performance obligation determined at the inception of the contract. The Group estimates the standalone selling prices based on the income approach. Control of the license to the drug compounds transfers at the inception date of the collaboration agreements and consequently, amounts allocated to this performance obligation are generally recognized at a point in time. Conversely, research and development services for each specified indication are performed over time and amounts allocated to these performance obligations are generally recognized over time using cost inputs as a measure of progress. The Group has determined that research and development expenses provide an appropriate depiction of measure of progress for the research and development services. Changes to estimated cost inputs may result in a cumulative catch-up adjustment. Royalty revenues are recognized as future sales occur as they meet the requirements for the sales-usage based royalty exception.

Deferred revenue is recognized if allocated consideration is received in advance of the Group rendering research and development services or earning royalties on future sales. Accounts receivable is recognized based on the terms of the contract and when the Group has an unconditional right to bill the customer, which is generally when research and development services are rendered.

Research and Development Expenses

Research and development expenses include the following: (i) research and development costs, which are expensed as incurred; (ii) acquired in-process research and development ("IPR&D") expenses, which include the initial costs of externally developed IPR&D projects, acquired directly in a transaction other than a business combination, that do not have an alternative future use; and (iii) milestone payment obligations for externally developed IPR&D projects incurred prior to regulatory approval of the product in the in-licensed territory, which are accrued when the event requiring payment of the milestone occurs (milestone payment obligations incurred upon regulatory approval are recorded as other intangible assets).

Collaborative Arrangements

The Group enters into collaborative arrangements with collaboration partners that fall under the scope of Accounting Standards Codification ("ASC") 808, Collaborative Arrangements ("ASC 808"). The Group records all expenditures for such collaborative arrangements in research and development expenses as incurred, including payments to third party vendors and reimbursements to collaboration partners, if any. Reimbursements from collaboration partners are recorded as reductions to research and development expenses and accrued when they can be contractually claimed.

Government Grants

Grants from governments are recognized at their fair values. Government grants that are received in advance are deferred and recognized in the consolidated statements of operations over the period necessary to match them with the costs that they are intended to compensate. Government grants in relation to the achievement of stages of research and development projects are recognized in the consolidated statements of operations when amounts have been received and all attached conditions have been met. Non-refundable grants received without any further obligations or conditions attached are recognized immediately in the consolidated statements of operations.

Leases

In an operating lease, a lessee obtains control of only the use of the underlying asset, but not the underlying asset itself. An operating lease is recognized as a right-of-use asset with a corresponding liability at the date which the leased asset is available for use by the Group. The Group recognizes an obligation to make lease payments equal to the present value of the lease payments over the lease term. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Group will exercise that option.

Lease liabilities include the net present value of the following lease payments: (i) fixed payments; (ii) variable lease payments that depend on an index or a rate; and (iii) payments of penalties for terminating the lease if the lease term reflects the lessee exercising that option, if any. Lease liabilities exclude the following payments that are generally accounted for separately: (i) non-lease components, such as maintenance and security service fees and value added tax, and (ii) any payments that a lessee makes before the lease commencement date. The lease payments are discounted using the interest rate implicit in the lease or if that rate cannot be determined, the lessee's incremental borrowing rate being the rate that the lessee would have to pay to borrow the funds in its currency and jurisdiction necessary to obtain an asset of similar value, economic environment and terms and conditions.

An asset representing the right to use the underlying asset during the lease term is recognized that consists of the initial measurement of the operating lease liability, any lease payments made to the lessor at or before the commencement date less any lease incentives received, any initial direct cost incurred by the Group and any restoration costs.

After commencement of the operating lease, the Group recognizes lease expenses on a straight-line basis over the lease term. The right-of-use asset is subsequently measured at cost less accumulated amortization and any impairment provision. The amortization of the right-of-use asset represents the difference between the straight-line lease expense and the accretion of interest on the lease liability each period. The interest amount is used to accrete the lease liability and to amortize the right-of-use asset. There is no amount recorded as interest expense.

Payments associated with short-term leases are recognized as lease expenses on a straight-line basis over the period of the leases.

Subleases of right-of-use assets are accounted for similar to other leases. As an intermediate lessor, the Group separately accounts for the head-lease and sublease unless it is relieved of its primary obligation under the head-lease. Sublease income is recorded on a gross basis separate from the head-lease expenses. If the total remaining lease cost on the head-lease is more than the anticipated sublease income for the lease term, this is an indicator that the carrying amount of the right-of-use asset associated with the head-lease may not be recoverable, and the right-of-use asset will be assessed for impairment.

Income Taxes

The Group accounts for income taxes under the liability method. Under the liability method, deferred income tax assets and liabilities are determined based on the differences between the financial reporting and income tax bases of assets and liabilities and are measured using the income tax rates that will be in effect when the differences are expected to reverse. A valuation allowance is recorded when it is more likely than not that some of the net deferred income tax asset will not be realized.

The Group accounts for an uncertain tax position in the consolidated financial statements only if it is more likely than not that the position is sustainable based on its technical merits and consideration of the relevant tax authority's widely understood administrative practices and precedents. If the recognition threshold is met, the Group records the largest amount of tax benefit that is greater than 50 percent likely to be realized upon ultimate settlement.

The Group recognizes interest and penalties for income taxes, if any, under income tax payable on its consolidated balance sheets and under other expenses in its consolidated statements of operations.

Losses per Share

Basic losses per share is computed by dividing net loss attributable to the Company by the weighted average number of outstanding ordinary shares in issue during the year. Weighted average number of outstanding ordinary shares in issue excludes treasury shares.

Diluted losses per share is computed by dividing net loss attributable to the Company by the weighted average number of outstanding ordinary shares in issue and dilutive ordinary share equivalents outstanding during the year. Dilutive ordinary share equivalents include ordinary shares and treasury shares issuable upon the exercise or settlement of share-based awards or warrants issued by the Company using the treasury stock method. The computation of diluted losses per share does not assume conversion, exercise, or contingent issuance of securities that would have an anti-dilutive effect.

Segment Reporting

Operating segments are reported in a manner consistent with the internal reporting provided to the chief executive officer who is the Group's chief operating decision maker. The chief operating decision maker reviews the Group's internal reporting in order to assess performance and allocate resources.

Profit Appropriation and Statutory Reserves

The Group's subsidiaries and equity investees established in the PRC are required to make appropriations to certain non-distributable reserve funds.

In accordance with the relevant laws and regulations established in the PRC, the Company's subsidiaries registered as wholly-owned foreign enterprise have to make appropriations from their after-tax profits (as determined under generally accepted accounting principles in the PRC ("PRC GAAP") to reserve funds including general reserve fund, enterprise expansion fund and staff bonus and welfare fund. The appropriation to the general reserve fund must be at least 10% of the after-tax profits calculated in accordance with PRC GAAP. Appropriation is not required if the general reserve fund has reached 50% of the registered capital of the company. Appropriations to the enterprise expansion fund and staff bonus and welfare fund are made at the respective company's discretion. For the Group's equity investees, the amount of appropriations to these funds are made at the discretion of their respective boards.

In addition, Chinese domestic companies must make appropriations from their after-tax profits as determined under PRC GAAP to non-distributable reserve funds including statutory surplus fund and discretionary surplus fund. The appropriation to the statutory surplus fund must be 10% of the after-tax profits as determined under PRC GAAP. Appropriation is not required if the statutory surplus fund has reached 50% of the registered capital of the company. Appropriation to the discretionary surplus fund is made at the respective company's discretion.

The use of the general reserve fund, enterprise expansion fund, statutory surplus fund and discretionary surplus fund is restricted to the offsetting of losses or increases to the registered capital of the respective company. The staff bonus and welfare fund is a liability in nature and is restricted to fund payments of special bonus to employees and for the collective welfare of employees. All these reserves are not permitted to be transferred to the company as cash dividends, loans or advances, nor can they be distributed except under liquidation.

4. Fair Value Disclosures

The following table presents the Group's financial instruments by level within the fair value hierarchy under ASC 820, Fair Value Measurement:

	Fair Value Measurement Using			
	Level 1	Level 2	Level 3	Total
		(in US$'000)		
As at December 31, 2021				
Warrant (Note 19)	—	2,452	—	2,452

Cash equivalents, short-term investments, accounts receivable, other receivables, accounts payable and other payables are carried at cost, which approximates fair value due to the short-term nature of these financial instruments, and are therefore excluded from the above table. Bank borrowings are floating rate instruments and carried at amortized cost, which approximates fair values, and are therefore excluded from the above table.

5. Cash and Cash Equivalents and Short-term Investments

	December 31,	
	2022	2021
	(in US$'000)	
Cash and Cash Equivalents		
Cash at bank and on hand	178,326	104,620
Bank deposits maturing in three months or less	134,952	272,922
	313,278	377,542
Short-term Investments		
Bank deposits maturing over three months (note)	317,718	634,158
	630,996	1,011,700

Note: The maturities for short-term investments ranged from 91 to 99 days and 91 to 180 days for the years ended December 31, 2022 and 2021 respectively.

Certain cash and bank balances denominated in RMB, US$ and UK Pound Sterling ("£") were deposited with banks in the PRC. The conversion of these balances into foreign currencies is subject to the rules and regulations of foreign exchange control promulgated by the PRC government. Cash and cash equivalents and short-term investments were denominated in the following currencies:

	December 31,	
	2022	2021
	(in US$'000)	
US$	533,173	895,935
RMB	79,319	53,455
Hong Kong dollar ("HK$")	16,721	60,535
£	1,370	1,090
Euro	413	685
	630,996	1,011,700

6. Accounts Receivable

Accounts receivable from contracts with customers consisted of the following:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Accounts receivable—third parties	94,531	82,434
Accounts receivable—related parties (Note 23(ii))	3,517	1,166
Allowance for credit losses	(60)	(20)
Accounts receivable, net	97,988	83,580

Substantially all accounts receivable are denominated in RMB, US$ and HK$ and are due within one year from the end of the reporting periods. The carrying values of accounts receivable approximate their fair values due to their short-term maturities.

An aging analysis for accounts receivable—third parties based on the relevant invoice dates is as follows:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Not later than 3 months	84,007	78,288
Between 3 months to 6 months	7,478	2,867
Between 6 months to 1 year	1,947	78
Later than 1 year	1,099	1,201
Accounts receivable—third parties	94,531	82,434

Movements on the allowance for credit losses:

	2022	2021	2020
		(in US$'000)	
As at January 1	20	95	16
Increase in allowance for credit losses	150	16	95
Decrease in allowance due to subsequent collection	(107)	(92)	(18)
Exchange difference	(3)	1	2
As at December 31	60	20	95

7. Other receivables, prepayments and deposits

Other receivables, prepayments and deposits consisted of the following:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Dividend receivables (Note 22)	26,246	46,387
Prepayments	22,329	14,128
Value-added tax receivables	1,491	16,616
Deposits	1,214	1,255
Amounts due from related parties (Note 23(ii))	998	1,149
Others	1,936	1,506
	54,214	81,041

No allowance for credit losses has been made for other receivables, prepayments and deposits for the years ended December 31, 2022 and 2021.

8. Inventories

Inventories, net of provision for excess and obsolete inventories, consisted of the following:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Raw materials	27,392	15,837
Finished goods	29,298	19,918
	56,690	35,755

9. Property, Plant and Equipment

Property, plant and equipment consisted of the following:

	Buildings	Leasehold improvements	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)			
Cost						
As at January 1, 2022	2,432	17,828	5,987	27,957	19,970	74,174
Additions	—	171	541	4,945	40,625	46,282
Disposals	—	(1,105)	(2)	(529)	—	(1,636)
Transfers	—	1,336	1,412	1,637	(4,385)	—
Exchange differences	(199)	(1,394)	(484)	(2,272)	(1,660)	(6,009)
As at December 31, 2022	2,233	16,836	7,454	31,738	54,550	112,811
Accumulated depreciation						
As at January 1, 2022	1,788	11,571	2,352	17,188	—	32,899
Depreciation	116	3,741	590	3,880	—	8,327
Disposals	—	(1,018)	(2)	(505)	—	(1,525)
Transfers	—	—	(56)	56	—	—
Exchange differences	(151)	(1,012)	(214)	(1,460)	—	(2,837)
As at December 31, 2022	1,753	13,282	2,670	19,159	—	36,864
Net book value						
As at December 31, 2022	480	3,554	4,784	12,579	54,550	75,947

	Buildings	Leasehold improvements	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)			
Cost						
As at January 1, 2021	2,372	16,346	5,643	23,040	3,050	50,451
Additions	—	452	24	3,189	19,669	23,334
Disposals	—	(275)	(19)	(705)	—	(999)
Transfers	—	916	197	1,849	(2,962)	—
Exchange differences	60	389	142	584	213	1,388
As at December 31, 2021	2,432	17,828	5,987	27,957	19,970	74,174
Accumulated depreciation						
As at January 1, 2021	1,626	8,652	1,747	14,256	—	26,281
Depreciation	120	2,904	574	3,244	—	6,842
Disposals	—	(223)	(18)	(688)	—	(929)
Exchange differences	42	238	49	376	—	705
As at December 31, 2021	1,788	11,571	2,352	17,188	—	32,899
Net book value						
As at December 31, 2021	644	6,257	3,635	10,769	19,970	41,275

10. Leases

Leases consisted of the following:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Right-of-use assets		
Offices	6,634	10,605
Factories	387	702
Warehouses (note)	1,500	281
Others	201	291
Total right-of-use assets	8,722	11,879
Lease liabilities—current	3,708	4,917
Lease liabilities—non-current	5,196	7,161
Total lease liabilities	8,904	12,078

Note: Includes US$1.5 million right-of-use asset for warehouses in Suzhou that is leased through June 2026 in which the contract has a termination option with 3-month advance notice. The termination option was not recognized as part of the right-of-use asset and lease liability as it is uncertain that the Group will exercise such option.

Lease activities are summarized as follows:

	Year Ended December 31, 2022	2021
	(in US$'000)	
Lease expenses:		
Short-term leases with lease terms equal or less than 12 months	134	106
Leases with lease terms greater than 12 months	5,238	4,306
	5,372	4,412
Cash paid on lease liabilities	5,212	4,954
Non-cash: Lease liabilities recognized from obtaining right-of-use assets	2,689	7,665
Non-cash: Lease liabilities changed in relation to modifications and terminations	(499)	(33)

Lease contracts are typically within a period of 1 to 8 years. The weighted average remaining lease term and the weighted average discount rate as at December 31, 2022 was 3.24 years and 3.04% respectively. The weighted average remaining lease term and the weighted average discount rate as at December 31, 2021 was 3.38 years and 3.33% respectively.

Future lease payments are as follows:

	December 31, 2022
	(in US$'000)
Lease payments:	
Not later than 1 year	3,908
Between 1 to 2 years	2,471
Between 2 to 3 years	1,177
Between 3 to 4 years	911
Between 4 to 5 years	680
Later than 5 years	115
Total lease payments	9,262
Less: Discount factor	(358)
Total lease liabilities	8,904

11. Investments in Equity Investees

Investments in equity investees consisted of the following:

	December 31, 2022	2021
	(in US$'000)	
SHPL	73,461	75,999
Other	316	480
	73,777	76,479

The equity investees are private companies and there are no quoted market prices available for their shares.

Summarized financial information for the significant equity investees SHPL and HBYS (sold in 2021) is as follows:

(i) Summarized balance sheets

	SHPL December 31, 2022	SHPL December 31, 2021
	(in US$'000)	
Current assets	214,267	190,260
Non-current assets	80,062	91,605
Current liabilities	(147,952)	(128,993)
Non-current liabilities	(4,944)	(7,131)
Net assets	141,433	145,741

(ii) Summarized statements of operations

	SHPL			HBYS(note (a))	
	Year Ended December 31,				
	2022	2021	2020	2021(note (b))	2020
			(in US$'000)		
Revenue	370,600	332,648	276,354	209,528	232,368
Gross profit	281,113	255,089	204,191	111,066	116,804
Interest income	980	1,216	975	205	271
Finance cost	—	—	—	—	(5)
Profit before taxation	116,454	105,325	77,837	36,715	107,715
Income tax expense (note (c))	(16,738)	(15,896)	(10,833)	(4,840)	(16,494)
Net income (note (d))	99,716	89,429	67,004	31,875	91,221
Non-controlling interests	—	—	—	(36)	62
Net income attributable to the shareholders of equity investee	99,716	89,429	67,004	31,839	91,283

Notes:

(a) In 2020, HBYS entered into an agreement with the government to return the land use right for a plot of land in Guangzhou to the government and recognized land compensation of RMB569.2 million (approximately US$86.1 million). In June 2021, HBYS received a completion confirmation from the government and became entitled to a land compensation bonus of RMB110.3 million (approximately US$17.0 million) and recorded a gain before tax of RMB106.8 million (approximately US$16.4 million) after deducting costs of RMB3.5 million (approximately US$0.6 million).

(b) The summarized statement of operations for HBYS for the year ended December 31, 2021 includes the period when HBYS was the Group's equity investee from January 1, 2021 to September 28, 2021, the completion date of the divestment. The Group has accounted for the investment in HBYS under the equity method up to September 28, 2021.

(c) The main entity within the SHPL group has been granted the High and New Technology Enterprise ("HNTE") status. Accordingly, the entity was eligible to use a preferential income tax rate of 15% for the years ended December 31, 2022, 2021 and 2020.

(d) Net income is before elimination of unrealized profits on transactions with the Group. The amounts eliminated were approximately US$110,000, US$36,000 and nil for the years ended December 31, 2022, 2021 and 2020 respectively.

For the years ended December 31, 2022, 2021 and 2020, other equity investee had net income of approximately US$10,000 and US$41,000 and net losses of approximately US$194,000 respectively. In August 2022, the Group entered into an agreement with a third party (the "Buyer") to sell its entire investment in other equity investee for cash consideration of RMB2.2 million (approximately US$324,000) with closing subject to regulatory approval in the PRC.

(iii) Reconciliation of summarized financial information

Reconciliation of the summarized financial information presented to the carrying amount of investments in equity investees is as follows:

	SHPL			HBYS	
	2022	2021	2020	2021	2020
			(in US$'000)		
Opening net assets after non-controlling interests as at January 1	145,741	152,714	146,759	119,424	44,541
Net income attributable to the shareholders of equity investee	99,716	89,429	67,004	31,839	91,283
Purchase of additional interests in a subsidiary of an equity investee (note)	—	—	—	—	(347)
Dividends declared	(87,436)	(99,744)	(72,179)	(106,159)	(20,756)
Other comprehensive (loss)/income	(16,588)	3,342	11,130	1,387	4,703
Closing net assets after non-controlling interests as at December 31	141,433	145,741	152,714	46,491	119,424
Group's share of net assets	70,717	72,871	76,357	23,246	59,712
Goodwill	2,872	3,128	3,051	—	—
Elimination of unrealized profits on downstream sales	(128)	—	—	—	—
Divestment (Note 22)	—	—	—	(23,246)	—
Carrying amount of investments as at December 31	73,461	75,999	79,408	—	59,712

Note: During the year ended December 31, 2020, HBYS acquired an additional 30% interest in a subsidiary and after the acquisition, it became a wholly owned subsidiary of HBYS.

SHPL had the following capital commitments:

	December 31, 2022
	(in US$'000)
Property, plant and equipment	
Contracted but not provided for	1,307

12. Accounts Payable

	December 31,	
	2022	2021
	(in US$'000)	
Accounts payable—third parties	68,193	39,115
Accounts payable—non-controlling shareholders of subsidiaries (Note 23(iv))	2,922	2,062
	71,115	41,177

Substantially all accounts payable are denominated in RMB and US$ and due within one year from the end of the reporting period. The carrying values of accounts payable approximate their fair values due to their short-term maturities.

An aging analysis based on the relevant invoice dates is as follows:

	December 31,	
	2022	2021
	(in US$'000)	
Not later than 3 months	60,553	35,615
Between 3 months to 6 months	7,216	3,705
Between 6 months to 1 year	2,137	588
Later than 1 year	1,209	1,269
	71,115	41,177

13. Other Payables, Accruals and Advance Receipts

Other payables, accruals and advance receipts consisted of the following:

	December 31,	
	2022	2021
	(in US$'000)	
Accrued research and development expenses	156,134	116,134
Accrued salaries and benefits	42,442	41,786
Accrued capital expenditures	21,390	11,343
Accrued administrative and other general expenses	14,491	15,836
Accrued selling and marketing expenses	11,564	8,412
Deposits	3,616	2,111
Amounts due to related parties (Note 23(ii))	2,101	1,915
Deferred government grants	673	314
Others	12,210	12,988
	264,621	210,839

14. Bank Borrowings

Bank borrowings consisted of the following:

	December 31,	
	2022	2021
	(in US$'000)	
Current	—	26,905
Non-current	18,104	—

The weighted average interest rate for outstanding bank borrowings for the years ended December 31, 2022 and 2021 was 1.73% per annum and 1.08% per annum respectively. The carrying amounts of the Group's outstanding bank borrowings as at December 31, 2022 and 2021 were denominated in RMB and HK$ respectively.

(i) 3-year term loan and revolving loan facilities and 1-year revolving loan facility

In May 2019, the Group through its subsidiary, entered into a facility agreement with a bank for the provision of unsecured credit facilities in the aggregate amount of HK$400,000,000 (US$51,282,000). The 3-year credit facilities included (i) a HK$210,000,000 (US$26,923,000) term loan facility and (ii) a HK$190,000,000 (US$24,359,000) revolving loan facility, both with an interest rate at the Hong Kong Interbank Offered Rate ("HIBOR") plus 0.85% per annum, and an upfront fee of HK$819,000 (US$105,000) on the term loan. These credit facilities were guaranteed by the Company. The term loan was drawn in October 2019 and was repaid in May 2022. The revolving loan facility also expired in May 2022.

In May 2022, the Group through its subsidiary, entered into a 1-year revolving loan facility with the bank in the amount of HK$390,000,000 (US$50,000,000) with an interest rate at HIBOR plus 0.5% per annum. This credit facility is guaranteed by the Company. As at December 31, 2022, no amount was drawn from the revolving loan facility.

(ii) 10-year fixed asset loan facility

In October 2021, a subsidiary entered into a 10-year fixed asset loan facility agreement with a bank for the provision of a secured credit facility in the amount of RMB754,880,000 (US$108,393,000) with an annual interest rate at the 5-year China Loan Prime Rate less 0.8% (which was supplemented in June 2022) and interest payments commencing upon completion of the underlying construction in progress. This credit facility is guaranteed by the immediate holding company of the subsidiary and secured by the underlying leasehold land and buildings. As at December 31, 2022 and 2021, RMB126,083,000 (US$18,104,000) and nil were utilized from the fixed asset loan facility respectively, of which RMB769,000 (US$110,000) and nil were related to capitalized interest respectively.

(iii) 2-year revolving loan facility

In August 2020, the Group through its subsidiary, entered into a 2-year revolving loan facility with a bank in the amount of HK$117,000,000 (US$15,000,000) with an interest rate at HIBOR plus 4.5% per annum. This credit facility was guaranteed by the Company. The revolving loan facility expired in August 2022.

The Group's bank borrowings are repayable as from the dates indicated as follows:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Not later than 1 year	—	26,923
Between 1 to 3 years	360	—
Between 3 to 4 years	839	—
Between 4 to 5 years	1,079	—
Later than 5 years	15,826	—
	18,104	26,923

As at December 31, 2022 and 2021, the Group had unutilized bank borrowing facilities of US$140,289,000 and US$157,430,000 respectively.

15. Commitments and Contingencies

The Group had the following capital commitments:

	December 31, 2022
	(in US$'000)
Property, plant and equipment	
Contracted but not provided for	22,130

The Group does not have any other significant commitments or contingencies.

16. Ordinary Shares

As at December 31, 2022, the Company is authorized to issue 1,500,000,000 ordinary shares.

On April 14, 2021, the Company issued 16,393,445 ordinary shares to a third party for gross proceeds of US$100.0 million through a PIPE. Issuance costs totaled US$0.1 million.

On June 30, 2021 and July 15, 2021, the Company issued an aggregate of 119,600,000 ordinary shares in a public offering on the HKEX with over-allotment option exercised in full for aggregate gross proceeds of US$614.9 million. Issuance costs totaled US$29.7 million.

Each ordinary share is entitled to one vote. The holders of ordinary shares are also entitled to receive dividends whenever funds are legally available and when declared by the Board of Directors of the Company.

17. Share-based Compensation

(i) Share-based Compensation of the Company

The Company conditionally adopted a share option scheme on June 4, 2005 (as amended on March 21, 2007) and such scheme has a term of 10 years. It expired in 2016 and no further share options can be granted. Another share option scheme was conditionally adopted on April 24, 2015 (as amended on April 27, 2020) (the "Hutchmed Share Option Scheme"). Pursuant to the Hutchmed Share Option Scheme, the Board of Directors of the Company may, at its discretion, offer any employees and directors (including Executive and Non-executive Directors but excluding Independent Non-executive Directors) of the Company, holding companies of the Company and any of their subsidiaries or affiliates, and subsidiaries or affiliates of the Company share options to subscribe for shares of the Company.

As at December 31, 2022, the aggregate number of shares issuable under the Hutchmed Share Option Scheme was 48,611,458 ordinary shares and the aggregate number of shares issuable under the prior share option scheme which expired in 2016 was 660,570 ordinary shares. The Company will issue new shares to satisfy share option exercises. Additionally, the number of shares authorized but unissued was 635,224,660 ordinary shares.

Share options granted are generally subject to a four-year vesting schedule, depending on the nature and the purpose of the grant. Share options subject to the four-year vesting schedule, in general, vest 25% upon the first anniversary of the vesting commencement date as defined in the grant letter, and 25% every subsequent year. However, certain share option grants may have a different vesting schedule as approved by the Board of Directors of the Company. No outstanding share options will be exercisable or subject to vesting after the expiry of a maximum of eight to ten years from the date of grant.

A summary of the Company's share option activity and related information is as follows:

	Number of share options	Weighted average exercise price in US$ per share	Weighted average remaining contractual life (years)	Aggregate intrinsic value (in US$'000)
Outstanding at January 1, 2020	19,432,560	4.48	6.67	24,316
Granted	15,437,080	4.66		
Exercised	(480,780)	1.23		
Cancelled	(4,486,200)	5.02		
Expired	(741,670)	6.46		
Outstanding at December 31, 2020	29,160,990	4.49	7.21	53,990
Granted	10,174,840	5.96		
Exercised	(815,190)	3.01		
Cancelled	(1,287,650)	5.50		
Expired	(42,400)	5.52		
Outstanding at December 31, 2021	37,190,590	4.88	7.04	82,377
Granted (note)	7,680,820	2.26		
Exercised	(244,490)	1.98		
Cancelled	(3,849,905)	5.19		
Expired	(1,255,620)	5.66		
Outstanding at December 31, 2022	39,521,395	4.34	6.55	11,525
Vested and exercisable at December 31, 2021	16,077,770	4.24	4.91	46,491
Vested and exercisable at December 31, 2022	21,113,285	4.57	4.80	6,288

Note: Includes 861,220 share options (represented by 172,244 ADS) granted to an executive director in May 2022 where the number of share options exercisable is subject to a performance target based on a market condition covering the 3-year period from 2022 to 2024 which has been reflected in estimating the grant date fair value. The grant date fair value of such awards is US$0.24 per share using the Polynomial model. Vesting of such award will occur in March 2025.

In estimating the fair value of share options granted, the following assumptions were used in the Polynomial model for awards granted in the periods indicated:

	Year Ended December 31,		
	2022	2021	2020
Weighted average grant date fair value of share options (in US$ per share)	0.85	2.24	1.76
Significant inputs into the valuation model (weighted average):			
Exercise price (in US$ per share)	2.26	5.96	4.66
Share price at effective date of grant (in US$ per share)	2.22	5.91	4.66
Expected volatility (note (a))	46.7 %	41.1 %	42.6 %
Risk-free interest rate (note (b))	2.98 %	1.62 %	0.59 %
Contractual life of share options (in years)	10	10	10
Expected dividend yield (note (c))	0 %	0 %	0 %

Notes:

(a) The Company calculated its expected volatility with reference to the historical volatility prior to the issuances of share options.

(b) For share options exercisable into ADS, the risk-free interest rates reference the U.S. Treasury yield curves because the Company's ADS are currently listed on the NASDAQ and denominated in US$. For share options exercisable into ordinary shares, the risk-free interest rates reference the sovereign yield of the United Kingdom because the Company's ordinary shares are currently listed on AIM and denominated in £.

(c) The Company has not declared or paid any dividends and does not currently expect to do so prior to the exercise of the granted share options, and therefore uses an expected dividend yield of zero in the Polynomial model.

The Company will issue new shares to satisfy share option exercises. The following table summarizes the Company's share option exercises:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Cash received from share option exercises	174	2,452	593
Total intrinsic value of share option exercises	92	2,999	2,475

The Group recognizes compensation expense on a graded vesting approach over the requisite service period. The following table presents share-based compensation expense included in the Group's consolidated statements of operations:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Research and development expenses	4,803	8,460	4,061
Selling and administrative expenses	1,803	7,783	4,586
Cost of revenues	130	122	90
	6,736	16,365	8,737

As at December 31, 2022, the total unrecognized compensation cost was US$10,907,000, and will be recognized on a graded vesting approach over the weighted average remaining service period of 2.63 years.

(ii) LTIP

The Company grants awards under the LTIP to participating directors and employees, giving them a conditional right to receive ordinary shares of the Company or the equivalent ADS (collectively the "Awarded Shares") to be purchased by the Trustee up to a cash amount. Vesting will depend upon continued employment of the award holder with the Group and will otherwise be at the discretion of the Board of Directors of the Company. Additionally, some awards are subject to change based on annual performance targets prior to their determination date.

LTIP awards prior to the determination date

Performance targets vary by award, and may include targets for shareholder returns, financings, revenues, net profit after taxes and the achievement of clinical and regulatory milestones. As the extent of achievement of the performance targets is uncertain prior to the determination date, a probability based on management's assessment on the achievement of the performance target has been assigned to calculate the amount to be recognized as an expense over the requisite period with a corresponding entry to liability.

LTIP awards after the determination date

Upon the determination date, the Company will pay a determined monetary amount, up to the maximum cash amount based on the actual achievement of the performance target specified in the award, to the Trustee to purchase the Awarded Shares. Any cumulative compensation expense previously recognized as a liability will be transferred to additional paid-in capital. If the performance target is not achieved, no Awarded Shares of the Company will be purchased and the amount previously recorded in the liability will be reversed through share-based compensation expense.

Granted awards under the LTIP are as follows:

Grant date	Maximum cash amount (in US$ millions)	Covered financial years	Performance target determination date
April 20, 2020	5.3	2019	note (a)
April 20, 2020	37.4	2020	note (b)
April 20, 2020	1.9	note (c)	note (c)
April 20, 2020	0.2	note (d)	note (d)
August 12, 2020	2.1	2020	note (b)
August 12, 2020	0.3	note (c)	note (c)
March 26, 2021	57.3	2021	note (b)
September 1, 2021	7.3	2021	note (b)
September 1, 2021	0.5	note (c)	note (c)
October 20, 2021	1.7	note (c)	note (c)
December 14, 2021	0.1	note (c)	note (c)
December 14, 2021	0.1	note (d)	note (d)
May 23, 2022	60.4	2022	note (b)
September 13, 2022	3.8	2022	note (b)
September 13, 2022	1.7	note (c)	note (c)

Notes:

(a) This award does not stipulate performance targets and vesting occurs two business days after the announcement of the Group's annual results for the financial year falling two years after the covered financial year to which the LTIP award relates.

(b) The annual performance target determination date is the date of the announcement of the Group's annual results for the covered financial year and vesting occurs two business days after the announcement of the Group's annual results for the financial year falling two years after the covered financial year to which the LTIP award relates.

(c) This award does not stipulate performance targets and is subject to a vesting schedule of 25% on each of the first, second, third and fourth anniversaries of the date of grant.

(d) This award does not stipulate performance targets and will be vested on the first anniversary of the date of grant.

The Trustee has been set up solely for the purpose of purchasing and holding the Awarded Shares during the vesting period on behalf of the Company using funds provided by the Company. On the determination date, if any, the Company will determine the cash amount, based on the actual achievement of each annual performance target, for the Trustee to purchase the Awarded Shares. The Awarded Shares will then be held by the Trustee until they are vested.

The Trustee's assets include treasury shares and funds for additional treasury shares, trustee fees and expenses. The number of treasury shares (in the form of ordinary shares or ADS of the Company) held by the Trustee were as follows:

	Number of treasury shares	Cost (in US$'000)
As at January 1, 2020	941,310	6,079
Purchased	3,281,920	12,904
Vested	(712,555)	(4,828)
As at December 31, 2020	3,510,675	14,155
Purchased	4,907,045	27,309
Vested	(278,545)	(1,450)
As at December 31, 2021	8,139,175	40,014
Purchased	14,028,465	48,084
Vested	(2,566,265)	(12,034)
As at December 31, 2022	19,601,375	76,064

Based on the estimated achievement of performance conditions for 2022 financial year LTIP awards, the determined monetary amount was US$17,429,000 which is recognized to share-based compensation expense over the requisite vesting period to March 2025.

For the years ended December 31, 2022, 2021 and 2020, US$19,031,000, US$6,618,000 and US$7,038,000 of the LTIP awards were forfeited respectively based on the determined or estimated monetary amount as at the forfeiture date.

The following table presents the share-based compensation expenses recognized under the LTIP awards:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Research and development expenses	16,101	16,880	7,252
Selling and administrative expenses	7,376	8,451	3,552
Cost of revenues	373	294	101
	23,850	25,625	10,905
Recorded with a corresponding credit to:			
Liability	6,216	14,263	7,778
Additional paid-in capital	17,634	11,362	3,127
	23,850	25,625	10,905

For the years ended December 31, 2022, 2021 and 2020, US$15,351,000, US$8,516,000 and US$4,092,000 were reclassified from liability to additional paid-in capital respectively upon LTIP awards reaching the determination date. As at December 31, 2022 and 2021, US$3,701,000 and US$12,836,000 were recorded as liabilities respectively for LTIP awards prior to the determination date.

As at December 31, 2022, the total unrecognized compensation cost was approximately US$34,668,000, which considers expected performance targets and the amounts expected to vest, and will be recognized over the requisite periods.

18. Revenues

The following table presents disaggregated revenue, with sales of goods recognized at a point-in-time and provision of services recognized over time:

	Year Ended December 31, 2022		
	Oncology/ Immunology	Other Ventures	Total
		(in US$'000)	
Goods—Marketed Products	57,057	—	57,057
Goods—Distribution	—	262,565	262,565
Services —Commercialization—Marketed Products	41,275	—	41,275
—Collaboration Research and Development	23,741	—	23,741
—Research and Development	507	—	507
Royalties	26,310	—	26,310
Licensing	14,954	—	14,954
	163,844	262,565	426,409
Third parties	163,337	257,272	420,609
Related parties (Note 23(i))	507	5,293	5,800
	163,844	262,565	426,409

	Year Ended December 31, 2021		
	Oncology/ Immunology	Other Ventures	Total
		(in US$'000)	
Goods—Marketed Products	33,937	—	33,937
Goods—Distribution	—	236,518	236,518
Services —Commercialization—Marketed Products	27,428	—	27,428
—Collaboration Research and Development	18,995	—	18,995
—Research and Development	525	—	525
Royalties	15,064	—	15,064
Licensing	23,661	—	23,661
	119,610	236,518	356,128
Third parties	119,085	232,262	351,347
Related parties (Note 23(i))	525	4,256	4,781
	119,610	236,518	356,128

	Year Ended December 31, 2020		
	Oncology/ Immunology	Other Ventures	Total
		(in US$'000)	
Goods—Marketed Products	11,329	—	11,329
Goods—Distribution	—	197,761	197,761
Services —Commercialization—Marketed Products	3,734	—	3,734
—Collaboration Research and Development	9,771	—	9,771
—Research and Development	491	—	491
Royalties	4,890	—	4,890
	30,215	197,761	227,976
Third parties	29,724	192,277	222,001
Related parties (Note 23(i))	491	5,484	5,975
	30,215	197,761	227,976

The following table presents liability balances from contracts with customers:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Deferred revenue		
Current—Oncology/Immunology segment (note (a))	11,817	11,078
Current—Other Ventures segment (note (b))	1,530	1,196
	13,347	12,274
Non-current—Oncology/Immunology segment (note (a))	190	878
Total deferred revenue (note (c) and (d))	13,537	13,152

Notes:

(a) Oncology/Immunology segment deferred revenue relates to invoiced amounts for royalties where the customer has not yet completed the in-market sale, unamortized upfront and milestone payments and advance consideration received for cost reimbursements which are attributed to research and development services that have not yet been rendered as at the reporting date.

(b) Other Ventures segment deferred revenue relates to payments in advance from customers for goods that have not been transferred and services that have not been rendered to the customer as at the reporting date.

(c) Estimated deferred revenue to be recognized over time as from the date indicated is as follows:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Not later than 1 year	13,347	12,274
Between 1 to 2 years	150	476
Between 2 to 3 years	40	255
Between 3 to 4 years	—	147
	13,537	13,152

(d) As at January 1, 2022, deferred revenue was US$13.2 million, of which US$11.8 million was recognized during the year ended December 31, 2022.

License and collaboration agreement with Eli Lilly

On October 8, 2013, the Group entered into a licensing, co-development and commercialization agreement in China with Eli Lilly and Company ("Lilly") relating to Elunate ("Lilly Agreement"), also known as fruquintinib, a targeted oncology therapy for the treatment of various types of solid tumors. Under the terms of the Lilly Agreement, the Group is entitled to receive a series of payments up to US$86.5 million, including upfront payments and development and regulatory approval milestones. Development costs after the first development milestone are shared between the Group and Lilly. Elunate was successfully commercialized in China in November 2018, and the Group receives tiered royalties in the range of 15% to 20% on all sales in China.

In December 2018, the Group entered into various amendments to the Lilly Agreement (the "2018 Amendment"). Under the terms of the 2018 Amendment, the Group is entitled to determine and conduct future life cycle indications ("LCI") development of Elunate in China beyond the three initial indications specified in the Lilly Agreement and will be responsible for all associated development costs. In return, the Group will receive additional regulatory approval milestones of US$20 million for each LCI approved, for up to three LCI or US$60 million in aggregate, and will increase tiered royalties to a range of 15% to 29% on all Elunate sales in China upon the commercial launch of the first LCI. Additionally, through the 2018 Amendment, Lilly has provided consent, and freedom to operate, for the Group to enter into joint development collaborations with certain third-party pharmaceutical companies to explore combination treatments of Elunate and various immunotherapy agents. The 2018 Amendment also provided the Group rights to promote Elunate in provinces that represent 30% to 40% of the sales of Elunate in China upon the occurrence of certain commercial milestones by Lilly. Such rights were further amended below.

In July 2020, the Group entered into an amendment to the Lilly Agreement (the "2020 Amendment") relating to the expansion of the Group's role in the commercialization of Elunate across all of China. Under the terms of the 2020 Amendment, the Group is responsible for providing promotion and marketing services, including the development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities, in return for service fees on sales of Elunate made by Lilly. In October 2020, the Group commenced such promotion and marketing services. In addition, development and regulatory approval milestones for an initial indication under the Lilly Agreement were increased by US$10 million in lieu of cost reimbursement.

Upfront and cumulative milestone payments according to the Lilly Agreement received up to December 31, 2022 are summarized as follows:

	(in US$'000)
Upfront payment	6,500
Development milestone payments achieved	40,000

The Lilly Agreement has the following performance obligations: (1) the license for the commercialization rights to Elunate and (2) the research and development services for the specified indications. The transaction price includes the upfront payment, research and development cost reimbursements, milestone payments and sales-based royalties. Milestone payments were not included in the transaction price until it became probable that a significant reversal of revenue would not occur, which is generally when the specified milestone is achieved. The allocation of the transaction price to each performance obligation was based on the relative standalone selling prices of each performance obligation determined at the inception of the contract. Based on this estimation, proportionate amounts of transaction price to be allocated to the license to Elunate and the research and development services were 90% and 10% respectively. Control of the license to Elunate transferred at the inception date of the agreement and consequently, amounts allocated to this performance obligation were recognized at inception. Conversely, research and development services for each specified indication are performed over time and amounts allocated are recognized over time using the prior and estimated future development costs for Elunate as a measure of progress. Royalties are recognized as future sales occur as they meet the requirements for the sales-usage based royalty exception.

The 2018 Amendment is a separate contract as it added distinct research and development services for the LCIs to the Lilly Agreement. The 2020 Amendment related to the promotion and marketing services is a separate contract as it added distinct services to the Lilly Agreement. Such promotion and marketing services are recognized over time based on amounts that can be invoiced to Lilly. The 2020 Amendment related to the additional development and regulatory approval milestone amounts is a modification as it only affected the transaction price of research and development services for a specific indication under the Lilly Agreement, and therefore, such additional milestone amounts will be included in the transaction price accounted under the Lilly Agreement once the specified milestones are achieved.

Revenue recognized under the Lilly Agreement and subsequent amendments is as follows:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Goods—Marketed Products	14,407	15,792	11,329
Services—Commercialization—Marketed Products	41,275	27,428	3,734
—Collaboration Research and Development	8,054	4,491	1,991
Royalties	13,954	10,292	4,890
	77,690	58,003	21,944

License and collaboration agreement with AstraZeneca

On December 21, 2011, the Group and AstraZeneca AB (publ) (“AZ”) entered into a global licensing, co-development, and commercialization agreement for Orpathys (“AZ Agreement”), also known as savolitinib, a novel targeted therapy and a highly selective inhibitor of the c-Met receptor tyrosine kinase for the treatment of cancer. Under the terms of the AZ Agreement, the Group is entitled to receive a series of payments up to US$140 million, including upfront payments and development and first-sale milestones. Additionally, the AZ Agreement contains possible significant future commercial sale milestones. Development costs for Orpathys in China will be shared between the Group and AZ, with the Group continuing to lead the development in China. AZ will lead and pay for the development of Orpathys for the rest of the world. Orpathys was successfully commercialized in China in July 2021, and the Group receives fixed royalties of 30% based on all sales in China. Should Orpathys be successfully commercialized outside China, the Group would receive tiered royalties from 9% to 13% on all sales outside of China.

In August 2016 (as amended in December 2020), the Group entered into an amendment to the AZ Agreement whereby the Group shall pay the first approximately US$50 million of phase III clinical trial costs related to developing Orpathys for renal cell carcinoma (“RCC”), and remaining costs will be shared between the Group and AZ. Subject to approval of Orpathys in RCC, the Group would receive additional tiered royalties on all sales outside of China, with the incremental royalty rates determined based on actual sharing of development costs. In November 2021, the Group entered into an additional amendment which revised the sharing between the Group and AZ of development costs for Orpathys in China for non-small cell lung cancer, as well as adding potential development milestones.

Upfront and cumulative milestone payments according to the AZ Agreement received up to December 31, 2022 are summarized as follows:

	(in US$’000)
Upfront payment	20,000
Development milestone payments achieved	40,000
First-sale milestone payment achieved	25,000

The AZ Agreement has the following performance obligations: (1) the license for the commercialization rights to Orpathys and (2) the research and development services for the specified indications. The transaction price includes the upfront payment, research and development cost reimbursements, milestone payments and sales-based royalties. Milestone payments were not included in the transaction price until it became probable that a significant reversal of revenue would not occur, which is generally when the specified milestone is achieved. The allocation of the transaction price to each performance obligation was based on the relative standalone selling prices of each performance obligation determined at the inception of the contract. Based on this estimation, proportionate amounts of transaction price to be allocated to the license to Orpathys and the research and development services were 95% and 5% respectively. Control of the license to Orpathys transferred at the inception date of the agreement and consequently, amounts allocated to this performance obligation were recognized at inception. Conversely, research and development services for each specified indication are performed over time and amounts allocated are recognized over time using the prior and estimated future development costs for Orpathys as a measure of progress.

Revenue recognized under the AZ Agreement and subsequent amendments is as follows:

	Year Ended December 31,		
	2022	2021	2020
		(in US$’000)	
Goods—Marketed Products	9,904	6,509	—
Services—Collaboration Research and Development	14,467	14,113	7,780
Royalties	12,356	4,772	—
Licensing	14,954	23,661	—
	51,681	49,055	7,780

19. In-Licensing arrangement

On August 7, 2021, the Group and Epizyme, Inc. ("Epizyme") entered into a license agreement (the "In-license Agreement") for tazemetostat, a novel inhibitor of EZH2 that is approved by the U.S. Food and Drug Administration for the treatment of certain patients with epithelioid sarcoma and follicular lymphoma. The Group will be responsible for the development and commercialization of tazemetostat in the PRC, Hong Kong, Macau and Taiwan (the "Territory") and also holds rights to manufacture tazemetostat for the Territory. The Group also received a 4-year warrant, exercisable up to August 7, 2025, to purchase up to 5,653,000 shares of Epizyme common stock for an exercise price of US$11.50 per share ("Warrant Exercise Price").

Under the terms of the In-license Agreement and warrant, the Group paid Epizyme a US$25 million upfront payment and is obligated for a series of success-based payments up to US$110 million in development and regulatory milestones and up to US$175 million in sales milestones. Success-based payments are recognized when the related milestone is achieved. After tazemetostat is commercialized in the Territory, the Group will incur tiered royalties based on net sales. For the year ended December 31, 2022, US$5.0 million development milestone was paid and expensed to research and development expenses as in-process research and development.

The US$25 million upfront payment was first allocated to the warrant for its initial fair value of US$15 million, and the remainder was allocated to the rights to tazemetostat which were expensed to research and development expense as in-process research and development.

The warrant was recorded as a financial asset at fair value with changes to fair value recognized to the consolidated statements of operations. On August 12, 2022, a third party announced that it has acquired all outstanding shares of Epizyme under a definitive merger agreement. Consequently, the warrant was deemed expired under the terms of the In-license Agreement and warrant. For the years ended December 31, 2022 and 2021, fair value losses of US$2.5 million and US$12.5 million were recognized to other expense in the consolidated statements of operations respectively.

20. Research and Development Expenses

Research and development expenses are summarized as follows:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Clinical trial related costs	255,935	190,051	105,869
Personnel compensation and related costs	119,306	91,639	63,542
Other research and development expenses	11,652	17,396	5,365
	386,893	299,086	174,776

The Group has entered into multiple collaborative arrangements under ASC 808 to evaluate the combination of the Group's drug compounds with the collaboration partners' drug compounds. For the years ended December 31, 2022, 2021 and 2020, the Group has incurred research and development expenses of US$14,654,000, US$18,408,000 and US$8,291,000 respectively, related to such collaborative arrangements.

21. Government Grants

Government grants in the Oncology/Immunology segment are primarily given in support of the construction of a manufacturing plant in Shanghai and R&D activities which are conditional upon i) the Group spending a predetermined amount, regardless of success or failure of the research and development projects and/or ii) the achievement of certain stages of research and development projects being approved by the relevant PRC government authority. They are refundable to the government if the conditions, if any, are not met. Government grants in the Other Ventures segment are primarily given to promote local initiatives. These government grants may be subject to ongoing reporting and monitoring by the government over the period of the grant.

Government grants, which are deferred and recognized in the consolidated statements of operations over the period necessary to match them with the costs that they are intended to compensate, are recognized in other payables, accruals and advance receipts (Note 13) and other non-current liabilities. For the years ended December 31, 2022, 2021 and 2020, the Group received government grants of US$8,474,000, US$9,095,000 and US$4,724,000 respectively.

Government grants were recognized in the consolidated statements of operations as follows:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Research and development expenses	4,556	15,515	1,607
Other income	1,434	318	539
	5,990	15,833	2,146

22. Gain on divestment of an equity investee

In March 2021, the Group entered into a sale and purchase agreement (the "SPA") with a third party to sell its entire investment in HBYS with closing subject to regulatory approval in the PRC. On September 28, 2021, the Group completed the divestment for cash consideration of US$159.1 million.

On May 13, 2021 and September 23, 2021, HBYS had declared dividends to shareholders of US$46.5 million and US$59.7 million respectively which were related to prior year undistributed profits and distributions of a land bonus payment. Based on the SPA, the Group is entitled to a portion of such dividends and the third party will settle these amounts, net of taxes, after HBYS completes the distribution. As at December 31, 2022 and 2021, US$26.2 million and US$46.4 million of dividend receivables, net of taxes, from the third party was recorded respectively in other receivables, prepayments and deposits (Note 7).

In addition, the Group and Hutchison Whampoa Enterprises Limited, an affiliate of CK Hutchison Holdings Limited ("CK Hutchison"), entered into a license agreement on June 15, 2021, conditional upon the completion of the divestment, to grant a continuing right to use the "Hutchison Whampoa" brand by HBYS for 10 years at HK$12 million (approximately US$1.5 million) per year with aggregate amounts not to exceed HK$120 million (approximately US$15.4 million). On September 28, 2021, the Group recorded the present value of future branding liability payments of US$12.7 million. As at December 31, 2022 and 2021, US$1.5 million was included in amounts due to related parties (Note 23(ii)) and US$8.7 million and US$9.8 million were included in other non-current liabilities respectively.

The gain on divestment of an equity investee was recognized in the consolidated statements of operations as follows:

	Year Ended December 31, 2021
	(in US$'000)
Proceeds	159,118
Dividend receivables–third party (Note 7)	46,387
	205,505
Less: Group's share of net assets of HBYS (Note 11(iii))	(23,246)
Dividend receivables–HBYS	(52,887)
Withholding tax liability on dividend receivables–HBYS	2,644
Branding liability	(12,721)
Accumulated other comprehensive income and reserves	1,911
Transaction costs and others	104
Gain on divestment of an equity investee	121,310
Less: Capital gain tax	(14,373)
Less: Gain on divestment of an equity investee attributable to non-controlling interests	(24,010)
Gain on divestment of an equity investee attributable to the Group	82,927

23. Significant Transactions with Related Parties and Non-Controlling Shareholders of Subsidiaries

The Group has the following significant transactions with related parties and non-controlling shareholders of subsidiaries, which were carried out in the normal course of business at terms determined and agreed by the relevant parties:

(i) Transactions with related parties:

	Year Ended December 31, 2022	2021	2020
		(in US$'000)	
Sales to:			
Indirect subsidiaries of CK Hutchison	3,610	4,256	5,484
An equity investee	1,683	—	—
	5,293	4,256	5,484
Revenue from research and development services from:			
An equity investee	507	525	491
Purchases from:			
Equity investees	4,231	3,770	3,347
Rendering of marketing services from:			
Indirect subsidiaries of CK Hutchison	227	350	332
An equity investee	127	—	—
	354	350	332
Rendering of management services from:			
An indirect subsidiary of CK Hutchison	980	971	955
Entered brand license agreement with:			
An indirect subsidiary of CK Hutchison (note (a))	—	12,721	—

(ii) Balances with related parties included in:

	December 31, 2022	2021
	(in US$'000)	
Accounts receivable—related parties		
Indirect subsidiaries of CK Hutchison (note (b))	1,319	1,166
An equity investee (note (b))	2,198	—
	3,517	1,166
Other receivables, prepayments and deposits		
An equity investee (note (b))	998	1,149
Other payables, accruals and advance receipts		
Indirect subsidiaries of CK Hutchison (note (c) and (e))	1,953	1,915
An equity investee (note (b) and (d))	148	—
	2,101	1,915
Other non-current liabilities		
An equity investee (note (d))	755	736
An indirect subsidiary of CK Hutchison (note (e))	8,716	9,766
	9,471	10,502

Notes:

(a) The branding rights for HBYS from an indirect subsidiary of CK Hutchison were recognized in the consolidated statements of operations through the gain on divestment of an equity investee (Note 22). For the years ended December 31, 2022 and 2021, the Group paid US$1,538,000 for each of the two years.

(b) Balances with related parties are unsecured, repayable on demand and interest-free. The carrying values of balances with related parties approximate their fair values due to their short-term maturities.

(c) Amounts due to indirect subsidiaries of CK Hutchison are unsecured, repayable on demand and interest-bearing if not settled within one month.

(d) Other deferred income represents amounts recognized from granting of commercial, promotion and marketing rights.

(e) As at December 31, 2022 and 2021, a branding liability payable of US$1,538,000 was included in amounts due to related parties under other payables, accruals and advance receipts. As at December 31, 2022 and 2021, US$8,716,000 and US$9,766,000 of the branding liability payable was included in other non-current liabilities.

(iii) Transactions with non-controlling shareholders of subsidiaries:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Sales	47,611	41,974	36,500
Purchases	7,936	10,660	13,936
Dividends declared	25,600	9,894	1,462

(iv) Balances with non-controlling shareholders of subsidiaries included in:

	December 31,	
	2022	2021
	(in US$'000)	
Accounts receivable	11,139	8,436
Accounts payable	2,922	2,062

24. Income Taxes

(i) Income tax (benefit)/expense

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Current tax			
HK (note (a))	301	310	457
PRC (note (b) and (c))	2,580	15,909	872
U.S. and others (note (d))	399	417	219
Total current tax	3,280	16,636	1,548
Deferred income tax (benefit)/expense	(3,563)	(4,718)	3,281
Income tax (benefit)/ expense	(283)	11,918	4,829

Notes:

(a) The Company, three subsidiaries incorporated in the British Virgin Islands and its Hong Kong subsidiaries are subject to Hong Kong profits tax. Under the Hong Kong two-tiered profits tax rates regime, the first HK$2.0 million (US$0.3 million) of assessable profits of qualifying corporations will be taxed at 8.25%, with the remaining assessable profits taxed at 16.5%. Hong Kong profits tax has been provided for at the relevant rates on the estimated assessable profits less estimated available tax losses, if any, of these entities as applicable.

(b) Taxation in the PRC has been provided for at the applicable rate on the estimated assessable profits less estimated available tax losses, if any, in each entity. Under the PRC Enterprise Income Tax Law (the "EIT Law"), the standard enterprise income tax rate is 25%. In addition, the EIT Law provides for a preferential tax rate of 15% for companies which qualify as HNTE. HUTCHMED Limited and its wholly-owned subsidiary HUTCHMED (Suzhou) Limited qualify as a HNTE up to December 31, 2022 and 2023 respectively.

Pursuant to the EIT law, a 10% withholding tax is levied on dividends paid by PRC companies to their foreign investors. A lower withholding tax rate of 5% is applicable under the China-HK Tax Arrangement if direct foreign investors with at least 25% equity interest in the PRC companies are Hong Kong tax residents, and meet the conditions or requirements pursuant to the relevant PRC tax regulations regarding beneficial ownership. Since the equity holders of the equity investees of the Company are Hong Kong incorporated companies and Hong Kong tax residents, and meet the aforesaid conditions or requirements, the Company has used 5% to provide for deferred tax liabilities on retained earnings which are anticipated to be distributed. As at December 31, 2022, 2021 and 2020, the amounts accrued in deferred tax liabilities relating to withholding tax on dividends were determined on the basis that 100% of the distributable reserves of the equity investees operating in the PRC will be distributed as dividends.

Pursuant to PRC Bulletin on Issues of Enterprise Income Tax and Indirect Transfers of Assets by Non-PRC Resident Enterprises, an indirect transfer of a PRC resident enterprise by a non-PRC resident enterprise, via the transfer of an offshore intermediate holding company, shall be subject to PRC withholding tax under certain conditions.

(c) Current tax in the PRC for the year ended December 31, 2021 includes US$ 14.4 million arising from the indirect disposal of HBYS (Note 22), calculated at 10% of the excess of the disposal proceeds over the cost of acquiring the equity investment in HBYS.

(d) The Company's subsidiary in the U.S. with operations primarily in New Jersey is subject to U.S. taxes, primarily federal and state taxes, which have been provided for at approximately 21% (federal) and 0% to 11.5% (state tax) on the estimated assessable profit over the reporting years. Certain income receivable by the Company is subject to U.S. withholding tax of 30%. Two of the Group's subsidiaries are subject to corporate tax in the UK and EU countries at 19% and 15% to 25%, respectively, on the estimated assessable profits in relation to their presence in these countries.

The reconciliation of the Group's reported income tax expense to the theoretical tax amount that would arise using the tax rates of the Company against the Group's loss before income taxes and equity in earnings of equity investees is as follows:

	Year Ended December 31,		
	2022	**2021**	**2020**
		(in US$'000)	
Loss before income taxes and equity in earnings of equity investees	(410,422)	(215,740)	(189,734)
Tax calculated at the statutory tax rate of the Company	(67,720)	(35,597)	(31,306)
Tax effects of:			
Different tax rates applicable in different jurisdictions	6,316	136	4,025
Tax valuation allowance	93,243	63,975	46,321
Preferential tax rate difference	(171)	(148)	(154)
Preferential tax deduction and credits	(40,791)	(29,838)	(18,814)
Expenses not deductible for tax purposes	8,886	8,684	3,476
Withholding tax on undistributed earnings of PRC entities	2,492	3,153	3,962
Others	(2,538)	1,553	(2,681)
Income tax (benefit)/expense	(283)	11,918	4,829

(ii) Deferred tax assets and liabilities

The significant components of deferred tax assets and liabilities are as follows:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Deferred tax assets		
Cumulative tax losses	264,751	186,832
Others	15,254	12,269
Total deferred tax assets	280,005	199,101
Less: Valuation allowance	(264,639)	(189,700)
Deferred tax assets	15,366	9,401
Deferred tax liabilities		
Undistributed earnings from PRC entities	2,686	2,720
Others	24	45
Deferred tax liabilities	2,710	2,765

The movements in deferred tax assets and liabilities are as follows:

	2022	2021	2020
		(in US$'000)	
As at January 1	6,636	(3,548)	(2,343)
Utilization of previously recognized withholding tax on undistributed earnings	2,186	5,148	2,323
(Charged)/Credited to the consolidated statements of operations			
Withholding tax on undistributed earnings of PRC entities	(2,492)	(3,153)	(3,962)
Deferred tax on amortization of intangible assets	19	19	18
Deferred tax on temporary differences, tax loss carried forward and research tax credits	6,036	7,852	663
Divestment of an equity investee	—	370	—
Exchange differences	271	(52)	(247)
As at December 31	12,656	6,636	(3,548)

The deferred tax assets and liabilities are offset when there is a legally enforceable right to set off and when the deferred income taxes relate to the same fiscal authority.

The cumulative tax losses can be carried forward against future taxable income and will expire in the following years:

	December 31, 2022	December 31, 2021
	(in US$'000)	
No expiry date	71,325	60,450
2022	—	200
2023	—	—
2024	3,763	4,099
2025	36,098	39,321
2026	48,150	52,452
2027	61,808	67,217
2028	107,297	117,376
2029	175,853	191,554
2030	243,918	265,696
2031	389,761	432,278
2032	610,800	—
	1,748,773	1,230,643

The Company believes that it is more likely than not that future operations outside the U.S. will not generate sufficient taxable income to realize the benefit of the deferred tax assets. Certain of the Company's subsidiaries have had sustained tax losses, which will expire within five years if not utilized in the case of PRC subsidiaries (ten years for HNTEs), and which will not be utilized in the case of Hong Kong subsidiaries as they do not generate taxable profits. Accordingly, a valuation allowance has been recorded against the relevant deferred tax assets arising from the tax losses.

A U.S. subsidiary of the Company has approximately US$3.9 million and US$1.2 million U.S. Federal and New Jersey state research tax credits which will expire between 2041 and 2042 (Federal) and 2028 and 2029 (New Jersey) respectively, if not utilized.

The table below summarizes changes in the deferred tax valuation allowance:

	2022	2021	2020
		(in US$'000)	
As at January 1	189,700	122,378	69,399
Charged to consolidated statements of operations	93,243	63,975	46,321
Utilization of previously unrecognized tax losses	(1)	(186)	(114)
Write-off of tax losses	(125)	—	—
Others	—	(9)	—
Exchange differences	(18,178)	3,542	6,772
As at December 31	264,639	189,700	122,378

As at December 31, 2022, 2021 and 2020, the Group did not have any material unrecognized uncertain tax positions.

(iii) Income tax payable

	2022	2021	2020
		(in US$'000)	
As at January 1	15,546	1,120	1,828
Current tax	3,280	16,636	1,548
Withholding tax upon dividend declaration from PRC entities	2,186	5,148	2,323
Tax paid (note)	(18,891)	(5,014)	(5,940)
Reclassification from non-current withholding tax	—	—	812
Reclassification (from)/to prepaid tax	(241)	25	485
Divestment of an equity investee (Note 22)	—	(2,644)	—
Exchange difference	(768)	275	64
As at December 31	1,112	15,546	1,120

Note: The amount for 2022 includes US$14.4 million capital gain tax paid for gain on divestment of HBYS (Note 22). The amount for 2020 is net of the PRC Enterprise Income Tax refund of US$0.4 million received by HSPL.

25. Losses Per Share

(i) Basic losses per share

Basic losses per share is calculated by dividing the net loss attributable to the Company by the weighted average number of outstanding ordinary shares in issue during the year.

	Year Ended December 31,		
	2022	2021	2020
Weighted average number of outstanding ordinary shares in issue	847,143,540	792,684,524	697,931,437
Net loss attributable to the Company (US$'000)	(360,835)	(194,648)	(125,730)
Losses per share attributable to the Company (US$ per share)	(0.43)	(0.25)	(0.18)

(ii) Diluted losses per share

Diluted losses per share is calculated by dividing net loss attributable to the Company by the weighted average number of outstanding ordinary shares in issue and dilutive ordinary share equivalents outstanding during the year. Dilutive ordinary share equivalents include shares issuable upon the exercise or settlement of share options, LTIP awards and warrants issued by the Company using the treasury stock method.

For the years ended December 31, 2022, 2021 and 2020, the share options, LTIP awards and warrants issued by the Company were not included in the calculation of diluted losses per share because of their anti-dilutive effect. Therefore, diluted losses per share were equal to basic losses per share for the years ended December 31, 2022, 2021 and 2020.

26. Segment Reporting

The Group's operating segments are as follows:

(i) Oncology/Immunology: focuses on discovering, developing, and commercializing targeted therapies and immunotherapies for the treatment of cancer and immunological diseases. Oncology/Immunology is further segregated into two core business areas:

   (a) R&D: comprises research and development activities covering drug discovery, development, manufacturing and regulatory functions as well as administrative activities to support research and development operations; and

   (b) Marketed Products: comprises the sales, marketing, manufacture and distribution of drugs developed from research and development activities.

(ii) Other Ventures: comprises other commercial businesses which include the sales, marketing, manufacture and distribution of other prescription drugs and consumer health products.

The performance of the reportable segments is assessed based on segment net (loss)/income attributable to the Company.

The segment information is as follows:

	Year Ended December 31, 2022							
	Oncology/Immunology							
	R&D			Marketed Products		Other Ventures		
	PRC	U.S. and Others	Subtotal	PRC	Subtotal	PRC	Unallocated	Total
	(in US$'000)							
Revenue from external customers	39,202	—	39,202	124,642	163,844	262,565	—	426,409
Interest income	674	4	678	—	678	272	8,649	9,599
Interest expense	—	—	—	—	—	—	(652)	(652)
Equity in earnings of equity investees, net of tax	5	—	5	—	5	49,748	—	49,753
Income tax (expense)/benefit	(552)	6,053	5,501	(631)	4,870	(1,345)	(3,242)	283
Net (loss)/income attributable to the Company	(215,834)	(186,945)	(402,779)	17,367	(385,412)	54,604	(30,027)	(360,835)
Depreciation/amortization	(7,576)	(484)	(8,060)	—	(8,060)	(299)	(305)	(8,664)
Additions to non-current assets (other than financial instruments and deferred tax assets)	47,563	725	48,288	—	48,288	664	21	48,973

	December 31, 2022							
	Oncology/Immunology							
	R&D			Marketed Products		Other Ventures		
	PRC	U.S. and Others	Subtotal	PRC	Subtotal	PRC	Unallocated	Total
	(in US$'000)							
Total assets	221,337	30,281	251,618	45,984	297,602	235,500	496,343	1,029,445
Property, plant and equipment	72,775	2,103	74,878	—	74,878	735	334	75,947
Right-of-use assets	3,350	3,167	6,517	—	6,517	1,308	897	8,722
Leasehold land	11,830	—	11,830	—	11,830	—	—	11,830
Goodwill	—	—	—	—	—	3,137	—	3,137
Other intangible asset	—	—	—	—	—	85	—	85
Investments in equity investees	316	—	316	—	316	73,461	—	73,777

	Year Ended December 31, 2021							
	Oncology/Immunology							
	R&D			Marketed Products		Other Ventures		
	PRC	U.S. and Others	Subtotal	PRC	Subtotal	PRC	Unallocated	Total
	(in US$'000)							
Revenue from external customers	43,181	—	43,181	76,429	119,610	236,518	—	356,128
Interest income	809	3	812	—	812	282	982	2,076
Interest expense	—	—	—	—	—	—	(592)	(592)
Equity in earnings of equity investees, net of tax	20	—	20	—	20	60,597	—	60,617
Income tax benefit/(expense)	22	7,160	7,182	(1,320)	5,862	(14,573)	(3,207)	(11,918)
Net (loss)/income attributable to the Company	(143,528)	(152,235)	(295,763)	4,032	(291,731)	142,890	(45,807)	(194,648)
Depreciation/amortization	(6,436)	(197)	(6,633)	—	(6,633)	(318)	(239)	(7,190)
Additions to non-current assets (other than financial instruments and deferred tax assets)	25,295	4,321	29,616	—	29,616	1,056	327	30,999

	December 31, 2021							
	Oncology/Immunology							
	R&D			Marketed Products		Other Ventures		
	PRC	U.S. and Others	Subtotal	PRC	Subtotal	PRC	Unallocated	Total
	(in US$'000)							
Total assets	166,802	19,870	186,672	35,978	222,650	225,898	924,113	1,372,661
Property, plant and equipment	38,049	1,862	39,911	—	39,911	746	618	41,275
Right-of-use assets	4,798	3,768	8,566	—	8,566	1,827	1,486	11,879
Leasehold land	13,169	—	13,169	—	13,169	—	—	13,169
Goodwill	—	—	—	—	—	3,380	—	3,380
Other intangible asset	—	—	—	—	—	163	—	163
Investments in equity investees	480	—	480	—	480	75,999	—	76,479

	Year Ended December 31, 2020							
	Oncology/Immunology							
	R&D			Marketed Products		Other Ventures		
	PRC	U.S. and Others	Subtotal	PRC	Subtotal	PRC	Unallocated	Total
	(in US$'000)							
Revenue from external customers	10,262	—	10,262	19,953	30,215	197,761	—	227,976
Interest income	461	—	461	—	461	167	2,608	3,236
Interest expense	—	—	—	—	—	—	(787)	(787)
Equity in earnings of equity investees, net of tax	(97)	—	(97)	—	(97)	79,143	—	79,046
Income tax (expense)/benefit	(402)	642	240	(167)	73	(824)	(4,078)	(4,829)
Net (loss)/income attributable to the Company	(120,096)	(62,683)	(182,779)	7,282	(175,497)	72,785	(23,018)	(125,730)
Depreciation/amortization	(5,458)	(119)	(5,577)	—	(5,577)	(292)	(192)	(6,061)
Additions to non-current assets (other than financial instruments and deferred tax assets)	22,574	754	23,328	—	23,328	817	1,090	25,235

Revenue from external customers is after elimination of inter-segment sales. Sales between segments are carried out at mutually agreed terms. The amounts eliminated attributable to sales between PRC and U.S. and others under Oncology/Immunology segment were US$55,433,000, US$46,891,000, and US$19,230,000 for the years ended December 31, 2022, 2021, and 2020 respectively.

A summary of customers which accounted for over 10% of the Group's revenue for the years ended December 31, 2022, 2021 and 2020 is as follows:

	Year Ended December 31,		
	2022	2021	2020
	(in US$'000)		
Customer A	75,606	56,082	(note)
Customer B	51,681	49,055	(note)
Customer C	47,611	41,974	36,500
Customer D	(note)	(note)	25,993

Note: Customer did not account for over 10% of the Group's revenue during the year.

Customer A and B are included in Oncology/Immunology and Customer C and D are primarily included in Other Ventures.

Unallocated expenses mainly represent corporate expenses which include corporate employee benefit expenses and the relevant share-based compensation expenses. Unallocated assets mainly comprise cash and cash equivalents and short-term investments.

27. Note to Consolidated Statements of Cash Flows

Reconciliation of net loss for the year to net cash used in operating activities:

	Year Ended December 31,		
	2022	2021	2020
		(in US$'000)	
Net loss	(360,386)	(167,041)	(115,517)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	8,664	7,190	6,061
Amortization of finance costs	18	44	43
Loss on disposals of property, plant and equipment	111	70	85
Provision for excess and obsolete inventories	293	(23)	65
Provision for credit losses, net	43	(76)	77
Share-based compensation expense—share options	6,736	16,365	8,737
Share-based compensation expense—LTIP	23,850	25,625	10,905
Equity in earnings of equity investees, net of tax	(49,753)	(60,617)	(79,046)
Dividends received from SHPL and HBYS	43,718	49,872	86,708
Impairment of investment in other equity investee	130	—	—
Changes in right-of-use assets	2,721	(3,727)	(2,197)
Fair value losses on warrant	2,452	12,548	—
Gain from divestment of HBYS	—	(121,310)	—
Unrealized currency translation loss/(gain)	13,274	(2,505)	(6,149)
Changes in income tax balances	(19,174)	6,904	(1,111)
Changes in working capital			
Accounts receivable	(14,451)	(35,634)	(4,693)
Other receivables, prepayments and deposits	12,072	(5,758)	(9,602)
Inventories	(21,213)	(16,002)	(3,623)
Accounts payable	29,938	9,565	7,651
Other payables, accruals and advance receipts	52,629	66,224	37,472
Lease liabilities	(2,701)	3,079	2,258
Deferred revenue	386	11,071	(158)
Other	2,044	(87)	(32)
Total changes in working capital	58,704	32,458	29,273
Net cash used in operating activities	(268,599)	(204,223)	(62,066)

28. Litigation

From time to time, the Group may become involved in litigation relating to claims arising from the ordinary course of business. The Group believes that there are currently no claims or actions pending against the Group, the ultimate disposition of which could have a material adverse effect on the Group's financial position, results of operations or cash flows. However, litigation is subject to inherent uncertainties and the Group's view of these matters may change in the future. When an unfavorable outcome occurs, there exists the possibility of a material adverse impact on the Group's financial position, results of operations or cash flows for the periods in which the unfavorable outcome occurs, and potentially in future periods.

On May 17, 2019, Luye Pharma Hong Kong Ltd. (“Luye”) issued a notice to the Group purporting to terminate a distribution agreement that granted the Group exclusive commercial rights to Seroquel in the PRC for failure to meet a pre-specified target. The Group disagrees with this assertion and believes that Luye have no basis for termination. As a result, the Group commenced legal proceedings in 2019 in order to seek damages. On October 21, 2021 (and a decision on costs and interest in December 2021), the Group was awarded an amount of RMB253.2 million (equivalent to US$36.4 million) with interest of 5.5% per annum from the date of the award until payment and recovery of costs of approximately US$2.2 million (collectively the “Award”). On June 27, 2022, Luye provided the Group a bank guarantee of up to RMB286.0 million to cover the Award amounts, pending the outcome of an application by Luye to the High Court of Hong Kong to set aside the Award. On July 26, 2022, Luye’s application to set aside the Award was dismissed by the High Court with costs awarded in favor of the Group. On October 7, 2022, Luye filed a Notice of Appeal to the Court of Appeal regarding the dismissal and the notice was accepted on November 8, 2022. A Court of Appeal hearing date has been set for June 2023. The legal proceedings are ongoing, no Award amounts have been received as at the issuance date of these consolidated financial statements and no Award amounts have been recognized and no adjustment has been made to Seroquel-related balances as at December 31, 2022. Such Seroquel-related balances include accounts receivable, long-term prepayment, accounts payable and other payables of US$1.1 million, US$0.5 million, US$0.9 million and US$1.2 million respectively.

29. Restricted Net Assets

Relevant PRC laws and regulations permit payments of dividends by the Company’s subsidiaries in the PRC only out of their retained earnings, if any, as determined in accordance with PRC accounting standards and regulations. In addition, the Company’s subsidiaries in the PRC are required to make certain appropriations of net after-tax profits or increases in net assets to the statutory surplus fund prior to payment of any dividends. In addition, registered share capital and capital reserve accounts are restricted from withdrawal in the PRC, up to the amount of net assets held in each subsidiary. As a result of these and other restrictions under PRC laws and regulations, the Company’s subsidiaries in the PRC are restricted in their ability to transfer their net assets to the Group in terms of cash dividends, loans or advances, with restricted portions amounting to US$0.1 million and US$0.1 million as at December 31, 2022 and 2021 respectively, which excludes the Company’s subsidiaries with a shareholders’ deficit. Even though the Group currently does not require any such dividends, loans or advances from the PRC subsidiaries, for working capital and other funding purposes, the Group may in the future require additional cash resources from the Company’s subsidiaries in the PRC due to changes in business conditions, to fund future acquisitions and development, or merely to declare and pay dividends to make distributions to shareholders.

In addition, the Group has certain investments in equity investees in the PRC, where the Group’s equity in undistributed earnings amounted to US$53.7 million and US$54.4 million as at December 31, 2022 and 2021 respectively.

30. Subsequent Events

The Group evaluated subsequent events through February 28, 2023, which is the date when the consolidated financial statements were issued.

On January 23, 2023, the Group and Takeda Pharmaceuticals International AG (“Takeda”) entered into an exclusive out-licensing agreement (the “Agreement”) to further the global development, commercialization and manufacturing of Fruquintinib outside Mainland China, Hong Kong and Macau. The Group will receive up to US$1,130.0 million from Takeda, including upfront payments of US$400.0 million upon closing of the Agreement, as well as potential regulatory, development and commercial sales milestone payments, plus royalties on net sales.

SHANGHAI HUTCHISON PHARMACEUTICALS LIMITED

Report of Independent Auditors

To the Board of Directors of Shanghai Hutchison Pharmaceuticals Limited

Opinion

We have audited the accompanying consolidated financial statements of Shanghai Hutchison Pharmaceuticals Limited and its subsidiaries (the "Company"), which comprise the consolidated statements of financial position as of December 31, 2022 and 2021, and the related consolidated income statements, consolidated statements of comprehensive income, of changes in equity and of cash flows for each of the three years in the period ended December 31, 2022, including the related notes (collectively referred to as the "consolidated financial statements").

In our opinion, the accompanying consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022 in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

We conducted our audit in accordance with auditing standards generally accepted in the United States of America (US GAAS). Our responsibilities under those standards are further described in the Auditors' Responsibilities for the Audit of the Consolidated Financial Statements section of our report. We are required to be independent of the Company and to meet our other ethical responsibilities, in accordance with the relevant ethical requirements relating to our audit. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Responsibilities of Management for the Consolidated Financial Statements

Management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board, and for the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, management is responsible for assessing the Company's ability to continue as a going concern for at least, but not limited to, twelve months from the end of the reporting period, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless management either intends to liquidate the Company or to cease operations, or has no realistic alternative but to do so.

Auditors' Responsibilities for the Audit of the Consolidated Financial Statements

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditors' report that includes our opinion. Reasonable assurance is a high level of assurance but is not absolute assurance and therefore is not a guarantee that an audit conducted in accordance with US GAAS will always detect a material misstatement when it exists. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control. Misstatements are considered material if there is a substantial likelihood that, individually or in the aggregate, they would influence the judgment made by a reasonable user based on the consolidated financial statement

In performing an audit in accordance with US GAAS, we:

- Exercise professional judgment and maintain professional skepticism throughout the audit.

- Identify and assess the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, and design and perform audit procedures responsive to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements.

- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control. Accordingly, no such opinion is expressed.

- Evaluate the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluate the overall presentation of the consolidated financial statements.

- Conclude whether, in our judgment, there are conditions or events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern for a reasonable period of time.

We are required to communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit, significant audit findings, and certain internal control-related matters that we identified during the audit.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Shanghai, the People’s Republic of China
February 28, 2023

Shanghai Hutchison Pharmaceuticals Limited
Consolidated Income Statements
(in US$'000)

	Note	Year Ended December 31, 2022	2021	2020
Revenue	5	370,600	332,648	276,354
Cost of sales		(89,487)	(77,559)	(72,163)
Gross profit		281,113	255,089	204,191
Selling expenses		(144,979)	(131,821)	(111,892)
Administrative expenses		(21,727)	(22,627)	(17,907)
Other net operating income	6	2,126	4,759	3,473
Operating profit	7	**116,533**	**105,400**	**77,865**
Finance costs	15	(112)	(116)	(12)
Profit before taxation		**116,421**	**105,284**	**77,853**
Taxation charge	8	(16,738)	(15,896)	(10,833)
Profit for the year		**99,683**	**89,388**	**67,020**

The accompanying notes are an integral part of these consolidated financial statements.

Shanghai Hutchison Pharmaceuticals Limited
Consolidated Statements of Comprehensive Income
(in US$'000)

	Year Ended December 31,		
	2022	2021	2020
Profit for the year	**99,683**	**89,388**	**67,020**
Other comprehensive (loss)/income that has been or may be reclassified subsequently to profit or loss:			
Exchange translation differences	(16,581)	3,341	11,129
Total comprehensive income	**83,102**	**92,729**	**78,149**

The accompanying notes are an integral part of these consolidated financial statements.

Shanghai Hutchison Pharmaceuticals Limited
Consolidated Statements of Financial Position
(in US$'000)

	Note	December 31, 2022	December 31, 2021
Assets			
Current assets			
Cash and cash equivalents	10	33,923	50,038
Trade and bills receivables	11	21,856	17,482
Other receivables, prepayments and deposits	12	3,672	3,350
Inventories	13	154,816	119,390
Total current assets		**214,267**	**190,260**
Property, plant and equipment	14	62,831	73,650
Right-of-use assets	15	1,717	2,445
Leasehold land		6,291	7,025
Other intangible assets		823	722
Deferred tax assets	16	8,327	7,715
Total assets		**294,256**	**281,817**
Liabilities and shareholders' equity			
Current liabilities			
Trade payables	17	23,095	12,411
Other payables, accruals and advance receipts	18	121,354	111,793
Current tax liabilities	19	2,791	4,089
Lease liabilities	15	712	700
Total current liabilities		**147,952**	**128,993**
Deferred income		3,585	4,983
Lease liabilities	15	1,360	2,148
Total liabilities		**152,897**	**136,124**
Shareholders' equity			
Share capital		33,382	33,382
Reserves		107,977	112,311
Total shareholders' equity		**141,359**	**145,693**
Total liabilities and shareholders' equity		**294,256**	**281,817**

The accompanying notes are an integral part of these consolidated financial statements.

Shanghai Hutchison Pharmaceuticals Limited
Consolidated Statements of Changes in Equity
(in US$'000)

	Share capital	Exchange reserve	General reserves	Retained earnings	Total equity
As at January 1, 2020	**33,382**	**(8,524)**	**984**	**120,896**	**146,738**
Profit for the year	—	—	—	67,020	67,020
Other comprehensive income					
Exchange translation differences	—	11,129	—	—	11,129
Total comprehensive income	—	11,129	—	67,020	78,149
Transfer between reserves	—	—	14	(14)	—
Dividends declared to shareholders	—	—	—	(72,179)	(72,179)
As at December 31, 2020	**33,382**	**2,605**	**998**	**115,723**	**152,708**
Profit for the year	—	—	—	89,388	89,388
Other comprehensive income					
Exchange translation differences	—	3,341	—	—	3,341
Total comprehensive income	—	3,341	—	89,388	92,729
Transfer between reserves	—	—	31	(31)	—
Dividends declared to shareholders	—	—	—	(99,744)	(99,744)
As at December 31, 2021	**33,382**	**5,946**	**1,029**	**105,336**	**145,693**
Profit for the year	—	—	—	99,683	99,683
Other comprehensive loss					
Exchange translation differences	—	(16,581)	—	—	(16,581)
Total comprehensive (loss)/income	—	(16,581)	—	99,683	83,102
Transfer between reserves	—	—	14	(14)	—
Dividends declared to shareholders	—	—	—	(87,436)	(87,436)
As at December 31, 2022	**33,382**	**(10,635)**	**1,043**	**117,569**	**141,359**

The accompanying notes are an integral part of these consolidated financial statements.

Shanghai Hutchison Pharmaceuticals Limited
Consolidated Statements of Cash Flows
(in US$'000)

	Note	Year Ended December 31, 2022	2021	2020
Operating activities				
Net cash generated from operations	20	96,270	93,970	112,609
Interest received		1,219	1,116	912
Income tax paid	19	(19,003)	(15,976)	(10,232)
Net cash generated from operating activities		78,486	79,110	103,289
Investing activities				
Purchase of property, plant and equipment		(1,865)	(3,362)	(2,437)
Purchase of intangible asset		(410)	—	—
Proceeds from disposal of property, plant and equipment		20	32	63
Net cash used in investing activities		(2,255)	(3,330)	(2,374)
Financing activities				
Dividends paid to shareholders		(87,436)	(99,744)	(72,179)
Lease payments	15	(809)	(303)	(474)
Net cash used in financing activities		(88,245)	(100,047)	(72,653)
Net (decrease)/increase in cash and cash equivalents		(12,014)	(24,267)	28,262
Effect of exchange rate changes on cash and cash equivalents		(4,101)	1,827	2,972
		(16,115)	(22,440)	31,234
Cash and cash equivalents				
Cash and cash equivalents at beginning of year		50,038	72,478	41,244
Cash and cash equivalents at end of year		33,923	50,038	72,478

The accompanying notes are an integral part of these consolidated financial statements.

Shanghai Hutchison Pharmaceuticals Limited
Notes to the Consolidated Financial Statements

1. General Information

Shanghai Hutchison Pharmaceuticals Limited (the "Company") and its subsidiaries (together the "Group") are principally engaged in manufacturing, selling and distribution of prescription drug products. The Group has manufacturing plants in the People's Republic of China (the "PRC") and sells mainly in the PRC.

The Company was incorporated in the PRC on April 30, 2001 as a Chinese-Foreign Equity joint venture. The Company is jointly controlled by Shanghai HUTCHMED Investment (HK) Limited ("SHHCMI(HK)L") and Shanghai Traditional Chinese Medicine Co., Ltd ("SHTCML").

These consolidated financial statements are presented in United States dollars ("US$"), unless otherwise stated and have been approved for issue by the Company's Board of Directors on February 28, 2023.

2. Summary of Significant Accounting Policies

The consolidated financial statements of the Company have been prepared in accordance with International Financial Reporting Standards ("IFRS") and interpretations issued by the IFRS Interpretations Committee applicable to companies reporting under IFRS. The consolidated financial statements comply with IFRS as issued by the International Accounting Standards Board ("IASB"). These consolidated financial statements have been prepared under the historical cost convention.

During the year, the Group has adopted all of the new and revised standards, amendments and interpretations issued by the IASB that are relevant to the Group's operations and mandatory for annual periods beginning January 1, 2022. The adoption of these new and revised standards, amendments and interpretations did not have any material effects on the Group's results of operations or financial position.

The following standards, amendments and interpretations were issued but not yet effective for the financial year ended December 31, 2022 and have not been early adopted by the Group:

Amendments to IAS 1 and IFRS Practice Statement 2(1)	Disclosure Initiative—Accounting Policies
IAS 8 (Amendments)(1)	Definition of Accounting Estimates
IAS 12 (Amendments)(1)	Deferred Tax related to Assets and Liabilities arising from a Single Transaction
IFRS 17(1)	Insurance Contracts
IAS 1 (Amendments)(2)	Classification of Liabilities as Current or Non-current
IAS 1 (Amendments)(2)	Non-current Liabilities with Covenants
IFRS 16(2)	Lease Liability in a Sale and Leaseback
IFRS 10 and IAS 28 (Amendments)(3)	Sale or Contribution of Assets between an Investor and its Associate or Joint Venture

(1) Effective for the Group for annual periods beginning on or after January 1, 2023.

(2) Effective for the Group for annual periods beginning on or after January 1, 2024.

(3) Effective date to be determined by the IASB.

The adoption of standards, amendments and interpretations listed above in future periods is not expected to have any material effects on the Group's results of operations or financial position.

(a) Basis of Consolidation

The consolidated financial statements of the Group include the financial statements of the Company and its subsidiaries.

The accounting policies of subsidiaries have been changed where necessary to ensure consistency with the policies adopted by the Group.

Intercompany transactions, balances and unrealized gains on transactions between group companies are eliminated. Unrealized losses are also eliminated unless the transaction provides evidence of an impairment of the transferred asset.

(b) Subsidiaries

Subsidiaries are all entities over which the Group has control. The Group controls an entity when the Group is exposed, or has rights, to variable returns from its involvement with the entity and has the ability to affect those returns through its power to direct the activities of the entity. In the consolidated financial statements, subsidiaries are accounted for as described in Note 2(a) above.

Subsidiaries are fully consolidated from the date on which control is transferred to the Group. They are de-consolidated from the date that control ceases.

(c) Foreign Currency Translation

Items included in the financial statements of each of the Group's companies are measured using the currency of the primary economic environment in which the entity operates (the "functional currency"). The functional currency of the Company and its subsidiaries is Renminbi ("RMB") whereas the consolidated financial statements are presented in US$, which is the Company's presentation currency.

Foreign currency transactions are translated into the functional currency using the exchange rates at the dates of the transactions. Foreign currency gains and losses resulting from the settlement of such transactions and from the translation of monetary assets and liabilities denominated in foreign currencies at year end exchange rates are generally recognized in the consolidated income statements.

The financial statements of the Company and its subsidiaries are translated into the Company's presentation currency using the year end rates of exchange for the statements of financial position items and the average rates of exchange for the year for the income statement items. Exchange translation differences are recognized directly in other comprehensive income.

(d) Property, Plant and Equipment

Property, plant and equipment other than construction in progress are stated at historical cost less accumulated depreciation and any accumulated impairment losses. Historical cost includes the purchase price of the asset and any directly attributable costs of bringing the asset to its working condition and location for its intended use.

Subsequent costs are included in the asset's carrying amount or recognized as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. All other repairs and maintenance are charged to the consolidated income statements during the financial period in which they are incurred.

Depreciation is calculated using the straight-line method to allocate asset costs less accumulated impairment losses over their estimated useful lives. The principal estimated useful lives are as follows:

Buildings	20 years
Leasehold improvements	Over the unexpired period of the lease or 5 years, whichever is shorter
Plant and equipment	10 years
Furniture and fixtures, other equipment and motor vehicles	5 years

The assets' useful lives are reviewed and adjusted, if appropriate, at the end of each reporting period. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount.

Gains and losses on disposals are determined by comparing net sales proceeds with the carrying amount of the relevant assets and are recognized in the consolidated income statements.

(e) Construction in Progress

Construction in progress represents buildings, plant and machinery under construction and pending installation and is stated at cost less accumulated impairment losses, if any. Cost includes the costs of construction of buildings and the costs of plant and machinery. No provision for depreciation is made on construction in progress until such time as the relevant assets are completed and ready for its intended use. When the assets concerned are brought into use, the costs are transferred to property, plant and equipment and depreciated in accordance with the policy as stated in Note 2(d).

(f) Other Intangible Assets

The Group's other intangible asset represents promotion and marketing rights. Other intangible asset has a definite useful life and is carried at historical cost less accumulated amortization and accumulated impairment losses, if any. Amortization is calculated using the straight-line method to allocate its cost over its estimated useful life of five to ten years.

(g) Research and Development

Research expenditure is recognized as an expense as incurred. Costs incurred on development projects (relating to the design and testing of new or improved products) are recognized as intangible assets when it is probable that the project will generate future economic benefits by considering its commercial and technological feasibility, and costs can be measured reliably. Other development expenditures are recognized as an expense as incurred. Development costs previously recognized as an expense are not recognized as an asset in a subsequent period. Development costs with a finite useful life that have been capitalized, if any, are amortized on a straight-line basis over the period of expected benefit not exceeding five years. The capitalized development costs are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset exceeds its recoverable amount.

Where the research phase and the development phase of an internal project cannot be clearly distinguished, all expenditure incurred on the project is charged to the consolidated income statements.

(h) Impairment of Non-Financial Assets

Assets are reviewed for impairment to determine whether there is any indication that the carrying value of these assets may not be recoverable and have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss, if any. The recoverable amount is the higher of an asset's fair value less costs to sell and value in use. Such impairment loss is recognized in the consolidated income statements. Assets that have an indefinite useful life such as goodwill or intangible assets not ready to use are not subject to amortization and are tested for impairment annually and when there are indications that the carrying value may not be recoverable.

(i) Inventories

Inventories are stated at the lower of cost or net realizable value. Cost is determined using the weighted average cost method. The cost of finished goods comprises raw materials, direct labor, other direct costs and related production overheads (based on normal operating capacity). Net realizable value is the estimated selling price in the ordinary course of business, less applicable variable selling expenses.

(j) Trade and Other Receivables

Trade and other receivables are recognized initially at the amount of consideration, which is unconditional. Trade and other receivables solely represent payments of principal and interest, if any, and the Group holds such financial assets with the objective to collect its contractual cash flows. Therefore, the Group measures them subsequently at amortized cost using the effective interest method, less any loss allowance. The Group applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all trade receivables. To measure the expected credit losses, trade receivables have been grouped based on shared credit risk characteristics and the days past due. All other receivables at amortized cost are considered to have low credit risk, and the loss allowance recognized during the period was therefore limited to 12 months expected losses. The amount of the provision is recognized in the consolidated income statements.

(k) Cash and Cash Equivalents

In the consolidated statements of cash flows, cash and cash equivalents include cash on hand, bank deposits and other short-term highly liquid investments with original maturities of three months or less that are readily convertible to known amounts of cash and which are subject to an insignificant risk of changes in value, if any.

(l) Financial Liabilities and Equity Instruments

Financial liabilities and equity instruments issued by the Group are classified according to the substance of the contractual arrangements entered into and the definitions of a financial liability and an equity instrument. Financial liabilities (including trade and other payables) are initially measured at fair value, and are subsequently measured at amortized cost, using the effective interest method. An equity instrument is any contract that does not meet the definition of a financial liability and evidences a residual interest in the assets of the Group after deducting all of its liabilities.

Ordinary shares are classified as equity. Incremental costs, net of tax, directly attributable to the issue of new shares are shown in equity as a deduction from the proceeds.

(m) Current and Deferred Income Tax

(i) Current income tax

The current income tax charge is calculated on the basis of the tax laws enacted or substantively enacted at the balance sheet date in the country where the Group operates and generates taxable income. Management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate on the basis of amounts expected to be paid to the tax authorities.

(ii) Deferred income tax

Inside basis differences

Deferred income tax is recognized, using the liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. However, deferred tax liabilities are not recognized if they arise from the initial recognition of goodwill and deferred income tax is not accounted for if it arises from initial recognition of an asset or liability in a transaction other than a business combination that at the time of the transaction affects neither accounting nor taxable profit or loss. Deferred income tax is determined using tax rates (and laws) that have been enacted or substantively enacted by the balance sheet date and are expected to apply when the related deferred income tax asset is realized or the deferred income tax liability is settled.

Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Deferred income tax assets and deferred income tax liabilities are offset when there is a legally enforceable right to set off and when the deferred income taxes related to the same fiscal authority.

Outside basis differences

Deferred income tax liabilities are provided on taxable temporary differences arising from investments in subsidiaries, except for deferred income tax liabilities where the timing of the reversal of the temporary difference is controlled by the Group and it is probable that the temporary difference will not reverse in the foreseeable future.

Deferred income tax assets are recognized on deductible temporary differences arising from investments in subsidiaries, only to the extent that it is probable the temporary difference will reverse in the future and there is sufficient taxable profit available against which the temporary difference can be utilized.

(n) Employee Benefits

The employees of the Group participate in defined contribution retirement benefit plans managed by the relevant municipal and provincial governments in the PRC. The assets of these plans are held separately from the Group. The Group is required to make monthly contributions to the plans calculated as a percentage of the employees' salaries. The municipal and provincial governments undertake to assume the retirement benefit obligations to all existing and future retired employees under the plans described above. Other than the monthly contributions, the Group has no further obligations for the payment of the retirement and other post-retirement benefits of its employees.

(o) Provisions

Provisions are recognized when the Group has a present legal or constructive obligation as a result of past events, it is probable that an outflow of resources will be required to settle the obligation, and the amount has been reliably estimated. Provisions are not recognized for future operating losses.

(p) Leases

A lease is recognized as a right-of-use asset with a corresponding liability at the date which the leased asset is available for use by the Group. The Group recognizes an obligation to make lease payments equal to the present value of the lease payments over the lease term. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Group will exercise that option.

Lease liabilities include the net present value of the following lease payments: (i) fixed payments; (ii) variable lease payments that depend on an index or a rate; and (iii) payments of penalties for terminating the lease if the lease term reflects the lessee exercising that option, if any. Lease liabilities exclude the following payments that are generally accounted for separately: (i) non-lease components, such as maintenance and security service fees and value added tax, and (ii) any payments that a lessee makes before the lease commencement date. The lease payments are discounted using the interest rate implicit in the lease or if that rate cannot be determined, the lessee's incremental borrowing rate being the rate that the lessee would have to pay to borrow the funds in its currency and jurisdiction necessary to obtain an asset of similar value, economic environment and terms and conditions.

An asset representing the right to use the underlying asset during the lease term is recognized that consists of the initial measurement of the lease liability, any lease payments made to the lessor at or before the commencement date less any lease incentives received, any initial direct cost incurred by the Group and any restoration costs.

After commencement of the lease, each lease payment is allocated between lease liability and finance costs. The finance costs are recognized over the lease term so as to produce a constant periodic rate of interest on the remaining balance of the lease liability for each period. The right-of-use asset is depreciated on a straight-line basis over the period of the lease.

Payments associated with short-term leases are recognized as lease expenses on a straight-line basis over the period of the leases.

Leasehold land is accounted under IFRS 16.

(q) Government Incentives

Incentives from government are recognized at their fair values where there is a reasonable assurance that the incentives will be received and all attached conditions will be complied with.

Government incentives relating to costs are deferred and recognized in the consolidated income statements over the period necessary to match them with the costs that they are intended to compensate.

Government grants relating to property, plant and equipment are included in other payables, accruals and advance receipts and non-current liabilities as deferred income and credited to the consolidated income statements on a straight-line basis over the expected lives of the related assets.

(r) Revenue and Income Recognition

Revenue is measured based on consideration specified in a contract with a customer, and excludes any sales incentives and amounts collected on behalf of third parties. Taxes assessed by a governmental authority that are both imposed on and concurrent with a specific revenue-producing transaction, that are collected by the Group from a customer, are also excluded from revenue. The Group recognizes revenue when it satisfies a performance obligation by transferring control over a good to a customer.

The Group principally generates revenue from sales of goods. Revenue from sales of goods is recognized when the customer takes possession of the goods. This usually occurs upon completed delivery of the goods to the customer site. The amount of revenue recognized is adjusted for expected sales incentives as stipulated in the contract, which are generally issued to customers as direct discounts at the point-of-sale or indirectly in the form of rebates. Sales incentives are estimated using the expected value method. Additionally, sales are generally made with a limited right of return under certain conditions. Revenues are recorded net of provisions for sales discounts and returns.

Revenue from provision of services is recognized when the benefits of the services transfer to the customer over time, which is based on the proportionate value of services rendered as determined under the terms of the relevant contract. Additionally, when the amounts that can be invoiced correspond directly with the value to the customer for performance completed to date, the Group recognizes revenue from provision of services based on amounts that can be invoiced to the customer.

Payments in advance from customers are deferred if consideration is received in advance of transferring control of the goods or rendering of services. Accounts receivable is recognized if the Group has an unconditional right to bill the customer, which is generally when the customer takes possession of the goods or services are rendered. Payment terms differ by subsidiary and customer, but generally range from 45 to 180 days from the invoice date.

(s) Interest Income

Interest income is recognized on a time-proportion basis using the effective interest method.

(t) Segment Reporting

Operating segments are reported in a manner consistent with the internal reporting provided to the chief operating decision makers. The Company's Board of Directors, which is responsible for allocating resources and assessing performance of the operating segments, has been identified as the steering committee that makes strategic decisions.

(u) General Reserves

In accordance with the laws applicable to Foreign Investment Enterprises established in the PRC, the Company makes appropriations to certain non-distributable reserve funds including the general reserve fund, the enterprise expansion fund and the staff bonus and welfare fund. The amount of appropriations to these funds are made at the discretion of the Company's Board of Directors.

3. Financial Risk Management

(a) Financial risk factors

The Group's activities expose it to a variety of financial risks, including credit risk and liquidity risk. The Group does not use any derivative financial instruments for speculative purposes.

(i) Credit risk

The carrying amounts of cash and cash equivalents, trade and bills receivables and other receivables included in the consolidated statements of financial position represent the Group's maximum exposure to credit risk of the counterparty in relation to its financial assets.

Substantially all of the Group's cash and cash equivalents are deposited in major financial institutions, which management believes are of high credit quality. The Group has a practice to limit the amount of credit exposure to any financial institution.

Bills receivables are mostly settled by state-owned banks or other reputable banks and therefore the management considers that they will not expose the Group to any significant credit risk.

The Group has no significant concentrations of credit risk. The Group has policies in place to ensure that the sales of products are made to customers with appropriate credit history and the Group performs periodic credit evaluations of its customers.

Management periodically assesses the recoverability of trade and bills receivables and other receivables. The Group's historical loss rates are adjusted to reflect current and forward-looking information on specific factors affecting the ability of the customers to settle the receivables, and historical experience collecting receivables falls within the recorded allowances.

(ii) Liquidity risk

Prudent liquidity management implies maintaining sufficient cash and cash equivalents and the availability of funding when necessary. The Group's policy is to regularly monitor current and expected liquidity requirements to ensure that it maintains sufficient cash balances and adequate credit facilities to meet its liquidity requirements in the short and long term.

As at December 31, 2022 and 2021, the Group's current financial liabilities were mainly due for settlement within twelve months and the Group expects to meet all liquidity requirements.

(b) Capital risk management

The Group's objectives when managing capital are to safeguard the Group's ability to provide returns for shareholders and benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital.

The Group regularly reviews and manages its capital structure to ensure an optimal balance between higher shareholders' return that might be possible with higher levels of borrowings and the advantages and security afforded by a sound capital position, and makes adjustments to the capital structure in light of changes in economic conditions.

The Group monitors capital on the basis of the liabilities to assets ratio. This ratio is calculated as total liabilities divided by total assets as shown on the consolidated statements of financial position.

Currently, it is the Group's strategy to maintain a reasonable liabilities to assets ratio. The liabilities to assets ratio as at December 31, 2022 and 2021 was as follows:

	December 31,	
	2022	2021
	(in US$'000)	
Total liabilities	152,897	136,124
Total assets	294,256	281,817
Liabilities to assets ratio	52.0 %	48.3 %

(c) Fair value estimation

The Group does not have any financial assets or liabilities which are carried at fair value. The carrying amounts of the Group's current financial assets, including cash and cash equivalents, trade and bills receivables and other receivables, and current financial liabilities, including trade payables and other payables and accruals, approximate their fair values due to their short-term maturities. The carrying amounts of the Group's financial instruments carried at cost or amortized cost are not materially different from their fair values.

The face values less any estimated credit adjustments for financial assets and liabilities with a maturity of less than one year are assumed to approximate their fair values. The fair value of financial liabilities for disclosure purposes is estimated by discounting the future contractual cash flows at the current market interest rate that is available to the Group for similar financial instruments.

4. Critical Accounting Estimates and Judgements

Note 2 includes a summary of the significant accounting policies used in the preparation of the consolidated financial statements. The preparation of consolidated financial statements often requires the use of judgements to select specific accounting methods and policies from several acceptable alternatives. Furthermore, significant estimates and assumptions concerning the future may be required in selecting and applying those methods and policies in the consolidated financial statements. The Group bases its estimates and judgements on historical experience and various other assumptions that it believes are reasonable under the circumstances. Actual results may differ from these estimates and judgements under different assumptions or conditions.

The following is a review of the more significant assumptions and estimates, as well as the accounting policies and methods used in the preparation of the consolidated financial statements.

(a) Sales rebates

Certain sales rebates are provided to customers when their business performance for an agreed period within the year and the whole year meets certain criteria as stipulated in the contracts. Sales rebates are considered variable consideration and the estimate of sales rebates during the year is based on estimated sales transactions for the entire period stipulated and is subject to change based on actual performance and collection status.

(b) Useful lives of property, plant and equipment

The Group has made substantial investments in property, plant and equipment. Changes in technology or changes in the intended use of these assets may cause the estimated period of use or value of these assets to change.

(c) Deferred income tax

Deferred tax is recognized using the liability method on temporary differences arising between the tax bases of assets and liabilities against which the deductible temporary differences and the carry forward of unused tax losses and tax credits can be utilized. Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Where the final outcomes are different from the estimations, such differences will impact the carrying amount of deferred tax in the period in which such determination is made.

5. Revenue and Segment Information

Management has reviewed the Group's internal reporting in order to assess performance and allocate resources, and has determined that the Group has two reportable operating segments as follows:

—Manufacturing business—manufacture and distribution of drug products

—Distribution business—provision of sales, distribution and marketing services to pharmaceutical manufacturers

The operating segments are strategic business units that offer different products and services. They are managed separately because each business requires different technology and marketing approaches. The performance of each of the reportable segments is assessed based on a measure of operating profit/(loss).

The segment information is as follows:

	Year Ended December 31, 2022		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Revenue from external customers	367,512	3,088	370,600
Interest income	501	479	980
Operating profit/(loss)	117,210	(677)	116,533
Finance costs	110	2	112
Depreciation/amortization	9,151	89	9,240
Additions to non-current assets (other than financial instruments and deferred tax assets)	3,636	532	4,168

	December 31, 2022		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Total segment assets	291,877	2,379	294,256

	Year Ended December 31, 2021		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Revenue from external customers	331,097	1,551	332,648
Interest income	629	587	1,216
Operating profit/(loss)	107,361	(1,961)	105,400
Finance costs	114	2	116
Depreciation/amortization	9,118	50	9,168
Additions to non-current assets (other than financial instruments and deferred tax assets)	5,867	82	5,949

	December 31, 2021		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Total segment assets	280,632	1,185	281,817

	Year Ended December 31, 2020		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Revenue from external customers	270,954	5,400	276,354
Interest income	396	579	975
Operating profit/(loss)	78,069	(204)	77,865
Finance costs	11	1	12
Depreciation/amortization	8,670	65	8,735
Additions to non-current assets (other than financial instruments and deferred tax assets)	3,037	57	3,094

Revenue from external customers is after elimination of inter-segment sales. The amount eliminated was US$87.3 million for 2022 (2021: US$77.8 million; 2020: US$62.2 million). Sales between segments are carried out at mutually agreed terms. Revenue from external customers from the manufacturing business is for sales of goods which are recognized at a point in time. Revenue from external customers from the distribution business is for provision of services which are recognized over time.

6. Other Net Operating Income

	Year Ended December 31,		
	2022	2021	2020
	(in US$'000)		
Interest income	980	1,216	975
Net foreign exchange (loss)/gain	(83)	25	70
Government incentives	2,198	2,999	2,601
Other operating (loss)/income	(969)	519	(173)
	2,126	4,759	3,473

7. Operating Profit

	Year Ended December 31,		
	2022	2021	2020
	(in US$'000)		
Operating profit	116,533	105,400	77,865

Operating profit is stated after charging/(crediting) the following:

	Year Ended December 31,		
	2022	2021	2020
	(in US$'000)		
Cost of inventories recognized as expense	63,079	50,637	47,299
Research and development expense	7,169	9,350	6,301
Depreciation of property, plant and equipment	8,148	8,100	7,878
Loss/(gain) on disposal of property, plant and equipment	449	60	(2)
Amortization of leasehold land	166	172	160
Amortization of other intangible assets	245	233	217
Depreciation charge of right-of-use assets and lease expenses	917	1,171	725
Movement on the provision for trade receivables	—	—	(9)
Movement on the provision for excess and obsolete inventories	(65)	(141)	2,447
Auditor's remuneration	227	223	198
Employee benefit expenses (Note 9)	111,200	100,311	80,728

8. Taxation Charge

	Year Ended December 31, 2022	2021	2020
		(in US$'000)	
Current tax	18,082	15,082	12,520
Deferred income tax (Note 16)	(1,344)	814	(1,687)
Taxation charge	16,738	15,896	10,833

The taxation charge on the Group's profit before taxation differs from the theoretical amount that would arise using the Group's weighted average tax rate as follows:

	Year Ended December 31, 2022	2021	2020
		(in US$'000)	
Profit before taxation	116,421	105,284	77,853
Tax calculated at the statutory tax rates of respective companies	29,105	26,321	19,463
Tax effects of:			
Expenses not deductible for tax purposes	1,397	1,946	1,137
Utilization of unrecognized temporary differences	(898)	(55)	(938)
Tax concession (note)	(13,000)	(12,420)	(8,753)
Under/(over) provision in prior years	134	104	(76)
Taxation charge	16,738	15,896	10,833

Note: The Company has been granted the High and New Technology Enterprise ("HNTE") status. Accordingly, the Company is subject to a preferential income tax rate of 15% in 2022 and renew the HNTE status in 2023 (2021: 15%; 2020: 15%). Certain research and development expenses are also eligible for super-deduction such that 200% of qualified expenses incurred are deductible against taxable profits for tax purposes (2021: 200%; 2020: 175%).

The weighted average tax rate calculated at the statutory tax rates of respective companies was 25%. The effective tax rate for the year ended December 31, 2022 was 14.4% (2021: 15.1%; 2020: 13.9%).

9. Employee Benefit Expenses

	Year Ended December 31, 2022	2021	2020
		(in US$'000)	
Wages, salaries and bonuses	86,330	77,335	68,226
Pension costs—defined contribution plans	9,701	8,713	995
Staff welfare	15,169	14,263	11,507
	111,200	100,311	80,728

Employee benefit expenses of approximately US$19.8 million for the year ended December 31, 2022 (2021: US$20.1 million; 2020: US$16.4 million) are included in cost of sales.

10. Cash and Cash Equivalents

	December 31, 2022	2021
	(in US$'000)	
Cash and cash equivalents	33,923	50,038

The cash and cash equivalents denominated in RMB were deposited with banks in the PRC. The conversion of these RMB denominated balances into foreign currencies is subject to the rules and regulations of foreign exchange control promulgated by the PRC government.

11. Trade and Bills Receivables

	December 31, 2022	December 31, 2021
	(in US$'000)	
Trade receivables—third parties	12,845	9,555
Trade receivables—related parties (Note 22(b))	3,695	649
Bills receivables	5,316	7,278
	21,856	17,482

All trade and bills receivables are denominated in RMB and are due within one year from the end of the reporting period. The carrying values of trade and bills receivables approximate their fair values due to their short-term maturities.

Movements on the provision for trade receivables are as follows:

	2022	2021	2020
		(in US$'000)	
As at January 1	—	—	9
Increase in provision for trade receivables	—	—	—
Decrease in provision due to subsequent collection	—	—	(9)
As at December 31	—	—	—

12. Other Receivables, Prepayments and Deposits

	December 31, 2022	December 31, 2021
	(in US$'000)	
Prepayments to suppliers	2,624	1,929
Interest receivables	25	283
Deposits	778	877
Others	245	261
	3,672	3,350

13. Inventories

	December 31, 2022	December 31, 2021
	(in US$'000)	
Raw materials	22,804	54,585
Work in progress	108,168	39,668
Finished goods	23,844	25,137
	154,816	119,390

14. Property, Plant and Equipment

	Buildings situated in the PRC	Leasehold improvements	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)			
Cost						
As at January 1, 2022	75,587	848	26,438	15,033	136	118,042
Additions	27	38	117	516	2,924	3,622
Disposals	(886)	—	(227)	(178)	—	(1,291)
Transfers	1,058	—	974	478	(2,510)	—
Exchange differences	(6,204)	(71)	(2,204)	(1,267)	(29)	(9,775)
As at December 31, 2022	69,582	815	25,098	14,582	521	110,598
Accumulated depreciation						
As at January 1, 2022	19,983	94	14,817	9,498	—	44,392
Depreciation	3,606	238	2,830	1,474	—	8,148
Disposals	(439)	—	(205)	(178)	—	(822)
Exchange differences	(1,774)	(18)	(1,326)	(833)	—	(3,951)
As at December 31, 2022	21,376	314	16,116	9,961	—	47,767
Net book value						
As at December 31, 2022	48,206	501	8,982	4,621	521	62,831

	Buildings situated in the PRC	Leasehold improvements	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)			
Cost						
As at January 1, 2021	73,480	578	25,173	12,273	2,685	114,189
Additions	28	68	535	929	1,453	3,013
Disposals	—	(128)	(207)	(481)	(1,230)	(2,046)
Transfers	224	314	298	1,982	(2,818)	—
Exchange differences	1,855	16	639	330	46	2,886
As at December 31, 2021	75,587	848	26,438	15,033	136	118,042
Accumulated depreciation						
As at January 1, 2021	15,699	504	12,288	7,570	1,196	37,257
Depreciation	3,763	100	2,347	1,890	—	8,100
Disposals	—	(128)	(145)	(464)	(1,217)	(1,954)
Transfers	93	(390)	—	297	—	—
Exchange differences	428	8	327	205	21	989
As at December 31, 2021	19,983	94	14,817	9,498	—	44,392
Net book value						
As at December 31, 2021	55,604	754	11,621	5,535	136	73,650

	Buildings situated in the PRC	Leasehold improvements	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)			
Cost						
As at January 1, 2020	68,213	539	22,606	9,526	2,828	103,712
Additions	—	—	581	935	1,519	3,035
Disposals	—	—	(53)	(134)	—	(187)
Transfers	334	—	361	1,155	(1,850)	—
Exchange differences	4,933	39	1,678	791	188	7,629
As at December 31, 2020	73,480	578	25,173	12,273	2,685	114,189
Accumulated depreciation						
As at January 1, 2020	11,212	383	8,760	5,665	1,116	27,136
Depreciation	3,493	88	2,786	1,511	—	7,878
Disposals	—	—	(35)	(91)	—	(126)
Exchange differences	994	33	777	485	80	2,369
As at December 31, 2020	15,699	504	12,288	7,570	1,196	37,257
Net book value						
As at December 31, 2020	57,781	74	12,885	4,703	1,489	76,932

15. Leases

Leases consisted of the following:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Right-of-use assets:		
Offices	1,717	2,445
Lease liabilities—current	712	700
Lease liabilities—non-current	1,360	2,148
	2,072	2,848

Lease activities are summarized as follows:

	Year Ended December 31, 2022	Year Ended December 31, 2021
	(in US$'000)	
Lease expenses: Short-term leases with lease terms equal or less than 12 months	236	508
Depreciation charge of right-of-use assets	681	663
Interest expense (included in finance costs)	112	116
Cash paid on lease liabilities	809	303
Non-cash: Lease liabilities recognized from obtaining right-of-use assets	135	2,936

Lease contracts are typically within a period of 1 to 5 years. The weighted average remaining lease term and weighted average discount rate as at December 31, 2022 was 2.7 years (2021: 3.7 years) and 4.70% (2021: 4.75%) respectively.

Future lease payments are as follows:

	December 31, 2022	December 31, 2021
	(in US$'000)	
Lease payments:		
Not later than 1 year	791	814
Between 1 to 2 years	755	784
Between 2 to 3 years	660	793
Between 3 to 4 years	—	713
Total lease payments	2,206	3,104
Less: Discount factor	(134)	(256)
Total lease liabilities	2,072	2,848

16. Deferred Tax Assets

The movements in deferred tax assets are as follows:

	2022	2021	2020
		(in US$'000)	
As at January 1	7,715	8,315	6,147
Credited/(debited) to the consolidated income statements			
—Accrued expenses, provisions, deferred income, accelerated depreciation and other temporary differences	1,344	(814)	1,687
Exchange differences	(732)	214	481
As at December 31	8,327	7,715	8,315

The Group's deferred tax assets are mainly temporary differences including accrued expenses, provisions, deferred income, accelerated depreciation and other temporary differences. The potential deferred tax assets in respect of tax losses which have not been recognized in the consolidated financial statements were approximately US$24,000 as at December 31, 2022 (2021: US$26,000).

These unrecognized tax losses can be carried forward against future taxable income and will expire in the following years:

	December 31, 2022	December 31, 2021
	(in US$'000)	
2022	—	7
2023	—	—
2024	76	83
2025	7	7
2026	6	6
2027	5	—
	94	103

17. Trade Payables

	December 31, 2022	December 31, 2021
	(in US$'000)	
Trade payables—third parties	19,737	12,030
Trade payables—related parties (Note 22(b))	3,358	381
	23,095	12,411

All trade payables are denominated in RMB and due within one year from the end of the reporting period. The carrying value of trade payables approximates their fair values due to their short-term maturities.

18. Other Payables, Accruals and Advance Receipts

	December 31, 2022	December 31, 2021
	(in US$'000)	
Accrued salaries and benefits	21,100	17,796
Accrued selling and marketing expenses	73,721	68,217
Value-added tax and tax surcharge payables	5,204	9,693
Payments in advance from customers (note)	14,004	11,858
Others	7,325	4,229
	121,354	111,793

Note: Substantially all customer balances as at December 31, 2021 were recognized to revenue during the year ended December 31, 2022. Additionally, substantially all customer balances as at December 31, 2022 are expected to be recognized to revenue within one year upon transfer of goods or services as the contracts have an expected duration of one year or less.

19. Current Tax Liabilities

	2022	2021	2020
		(in US$'000)	
As at January 1	4,089	5,032	2,395
Current tax (Note 8)	18,082	15,082	12,520
Tax paid	(19,003)	(15,976)	(10,232)
Exchange difference	(377)	108	192
Transfer (from)/to other receivables	—	(157)	157
As at December 31	2,791	4,089	5,032

20. Notes to the Consolidated Statements of Cash Flows

(a) Reconciliation of profit for the year to net cash generated from operations:

	2022	2021	2020
		(in US$'000)	
Profit for the year	99,683	89,388	67,020
Adjustments to reconcile profit for the year to net cash generated from operations			
Taxation charge	16,738	15,896	10,833
Finance costs	112	116	12
Interest income	(980)	(1,216)	(975)
Depreciation on property, plant and equipment	8,148	8,100	7,878
Loss/(gain) on disposal of property, plant and equipment	449	60	(2)
Amortization of leasehold land	166	172	160
Amortization of other intangible assets	245	233	217
Depreciation charge of right-of-use assets	681	663	480
Provision for excess and obsolete inventories	(65)	(141)	2,447
Movement on the provision for trade receivables	—	—	(9)
Exchange differences	(5,682)	(693)	2,057
Changes in working capital:			
Trade and bills receivables	(4,374)	939	6,360
Other receivables, prepayments and deposits	(580)	(80)	(227)
Inventories	(35,361)	(37,575)	(11,804)
Trade payables	10,684	1,237	905
Other payables, accruals and advance receipts	7,804	18,608	26,511
Deferred income	(1,398)	(1,737)	746
Total changes in operating assets and liabilities	(23,225)	(18,608)	22,491
Net cash generated from operations	96,270	93,970	112,609

(b) Supplemental disclosure for non-cash activities

During the years ended December 31, 2022, there was an increase in accruals made for purchases of property, plant and equipment of US$1.8 million (2021 and 2020: a decrease of US$0.3 million and an increase of US$0.6 million respectively).

21. Capital Commitments

The Group had the following capital commitments:

	December 31, 2022
	(in US$'000)
Property, plant and equipment	
Contracted but not provided for	1,307

Capital commitments for property, plant and equipment are mainly for improvements to the Group's plant.

22. Significant Related Party Transactions

The Group has the following significant transactions with related parties which were carried out in the normal course of business at terms determined and agreed by the relevant parties:

(a) Transactions with related parties:

	Year Ended December 31, 2022	2021	2020
		(in US$'000)	
Sales of goods to:			
—A fellow subsidiary of SHTCML	13,861	12,181	10,465
—A fellow subsidiary of SHHCMI(HK)L	4,231	3,492	2,854
	18,092	15,673	13,319
Purchase of goods from:			
—SHTCML	11,072	10,002	7,922
—Fellow subsidiaries of SHTCML	683	1,311	1,016
—A fellow subsidiary of SHHCMI(HK)L	1,683	—	—
	13,438	11,313	8,938
Rendering of research and development services from:			
—A fellow subsidiary of SHHCMI(HK)L	507	525	491
Provision of marketing services to:			
—A fellow subsidiary of SHTCML	952	1,146	2,781
—A fellow subsidiary of SHHCMI(HK)L	127	—	—
	1,079	1,146	2,781
Purchase of intangible asset from:			
—A fellow subsidiary of SHHCMI(HK)L	410	—	—
Leasing office from:			
—SHTCML	—	247	337

No transactions have been entered into with the directors of the Company (being the key management personnel) during the year ended December 31, 2022 (2021 and 2020: nil).

(b) Balances with related parties included in:

	December 31, 2022	2021
	(in US$'000)	
Trade and bills receivables		
—A fellow subsidiary of SHTCML	3,622	649
—A fellow subsidiary of SHHCMI(HK)L	73	—
	3,695	649
Other receivables, prepayments and deposits		
—A fellow subsidiary of SHTCML	402	547
Trade payables		
—SHTCML	1,266	—
— Fellow subsidiaries of SHTCML	152	381
—A fellow subsidiary of SHHCMI(HK)L	1,940	—
	3,358	381
Other payables, accruals and advance receipts		
—Fellow subsidiaries of SHHCMI(HK)L	1,256	1,149

Balances with related parties are unsecured, interest-free and repayable on demand. The carrying values of balances with related parties approximate their fair values due to their short-term maturities.

23. Particulars of Principal Subsidiaries

Name	Place of establishment and operation	Nominal value of registered capital		Equity interest attributable to the Group		Type of legal entity	Principal activity
		December 31,					
		2022	2021	2022	2021		
		(in RMB'000)					
Shanghai Shangyao Hutchison Whampoa GSP Company Limited	PRC	20,000	20,000	100 %	100 %	Limited liability company	Distribution of drug products
Hutchison Heze Bio Resources & Technology Co., Limited	PRC	1,500	1,500	100 %	100 %	Limited liability company	Agriculture and sales of Chinese herbs

24. Subsequent Events

The Group evaluated subsequent events through February 28, 2023, which is the date when the consolidated financial statements were issued.

On January 31, 2023, the Company's Board of Directors declared a dividend of RMB988.3 million (US$147.0 million), of which RMB500.0 million (US$74.4 million) and RMB488.3 million (US$72.6 million) are payable by and after December 31, 2023 respectively.

**HUTCHISON WHAMPOA GUANGZHOU
BAIYUNSHAN CHINESE MEDICINE
COMPANY LIMITED**

Report of Independent Auditors

To the Board of Directors and Shareholders of Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited

We have audited the accompanying consolidated financial statements of Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited and its subsidiaries (the "Company"), which comprise the consolidated statements of financial position as of September 28, 2021, and the related consolidated income statements, consolidated statements of comprehensive income, of changes in equity and of cash flows for the period from January 1, 2021 to September 28, 2021 and the year ended December 31, 2020.

Management's Responsibility for the Consolidated Financial Statements

Management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with the basis of preparation mentioned in Note 2(1) to the accompanying consolidated financial statements; this includes the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

Auditors' Responsibility

Our responsibility is to express an opinion on the consolidated financial statements based on our audits. We conducted our audits in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the consolidated financial statements. The procedures selected depend on our judgment, including the assessment of the risks of material misstatement of the consolidated financial statements, whether due to fraud or error. In making those risk assessments, we consider internal control relevant to the Company's preparation and fair presentation of the consolidated financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control. Accordingly, we express no such opinion. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited and its subsidiaries as of September 28, 2021, and the results of their operations and their cash flows for the period from January 1, 2021 to September 28 2021, and the year ended December 31, 2020 in accordance with the basis of preparation mentioned in Note 2(1) to the accompanying consolidated financial statements.

Emphasis of Matter

We draw attention to Note 2(1) to the accompanying consolidated financial statements, which describes the basis of preparation. On September 28, 2021, an intermediate holding company under HUTCHMED (China) Limited which wholly-owned Guangzhou Hutchison Chinese Medicine (HK) Investment Limited ("GZHCMHK"), sold its entire shareholding in GZHCMHK which jointly controls Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited, to a third party. Our opinion is not modified with respect of this matter.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Guangzhou, the People's Republic of China
December 7, 2021

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
Consolidated Income Statements
(in US$'000)

	Note	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
Revenue	5	209,528	232,368
Cost of sales		(98,462)	(115,564)
Gross profit		111,066	116,804
Selling expenses		(74,425)	(74,066)
Administrative expenses		(21,659)	(25,664)
Other net operating income	6	5,306	6,071
Operating profit	7	**20,288**	**23,145**
Share of profits/(losses) of a joint venture and associated companies, net of tax		29	(84)
Finance costs		(24)	(57)
Gain on return of land	8	16,433	84,667
Gain on divestment of a subsidiary		—	37
Profit before taxation		**36,726**	**107,708**
Taxation charge	9	(4,840)	(16,494)
Profit for the period/year		**31,886**	**91,214**
Attributable to:			
Shareholders of the Company		31,850	91,276
Non-controlling interests		36	(62)
		31,886	**91,214**

The accompanying notes are an integral part of these consolidated financial statements.

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
Consolidated Statements of Comprehensive Income
(in US$'000)

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
Profit for the period/year	**31,886**	**91,214**
Other comprehensive income that has been or may be reclassified subsequently to profit or loss:		
Exchange translation differences	1,393	4,728
Total comprehensive income	**33,279**	**95,942**
Attributable to:		
Shareholders of the Company	33,237	95,976
Non-controlling interests	42	(34)
	33,279	**95,942**

The accompanying notes are an integral part of these consolidated financial statements.

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
Consolidated Statements of Financial Position
(in US$'000)

	Note	September 28, 2021
Assets		
Current assets		
Cash and cash equivalents	11	73,616
Trade and bills receivables	12	27,874
Other receivables, prepayments and deposits	13	26,547
Inventories	14	62,400
Total current assets		**190,437**
Property, plant and equipment	15	58,619
Right-of-use assets	16	420
Leasehold land		19,657
Goodwill		8,825
Other intangible assets		1,798
Investments in a joint venture and associated companies		618
Deferred tax assets	17	4,420
Other non-current assets		46
Total assets		**284,840**
Liabilities and shareholders' equity		
Current liabilities		
Trade payables	18	19,048
Other payables, accruals and advance receipts	19	80,484
Dividend payable	23(b)	105,774
Lease liabilities	16	452
Current tax liabilities		16,681
Total current liabilities		**222,439**
Deferred income	20	14,913
Total liabilities		**237,352**
Company's shareholders' equity		
Share capital		24,103
Reserves		22,361
Total Company's shareholders' equity		**46,464**
Non-controlling interests		1,024
Total shareholders' equity		**47,488**
Total liabilities and shareholder's equity		**284,840**

The accompanying notes are an integral part of these consolidated financial statements.

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
Consolidated Statements of Changes in Equity
(in US$'000)

	Attributable to shareholders of the Company						
	Share capital	Exchange reserve	General reserves	Retained earnings	Total	Non-controlling interests	Total equity
As at January 1, 2020	**24,103**	**(2,043)**	**131**	**22,322**	**44,513**	**2,518**	**47,031**
Profit/(loss) for the year	—	—	—	91,276	91,276	(62)	91,214
Other comprehensive income							
Exchange translation differences	—	4,700	—	—	4,700	28	4,728
Total comprehensive income/ (loss)	—	4,700	—	91,276	95,976	(34)	95,942
Dividends declared to shareholders	—	—	—	(20,756)	(20,756)	—	(20,756)
Acquisition of additional interest in a subsidiary	—	(9)	(131)	(207)	(347)	(1,537)	(1,884)
Divestment of a subsidiary to non-controlling interest	—	—	—	—	—	35	35
As at December 31, 2020	**24,103**	**2,648**	**—**	**92,635**	**119,386**	**982**	**120,368**
Profit for the period	—	—	—	31,850	31,850	36	31,886
Other comprehensive income							
Exchange translation differences	—	1,387	—	—	1,387	6	1,393
Total comprehensive income	—	1,387	—	31,850	33,237	42	33,279
Dividends declared to shareholders	—	—	—	(106,159)	(106,159)	—	(106,159)
As at September 28, 2021	**24,103**	**4,035**	**—**	**18,326**	**46,464**	**1,024**	**47,488**

The accompanying notes are an integral part of these consolidated financial statements.

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
Consolidated Statements of Cash Flows
(in US$'000)

	Note	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
Operating activities			
Net cash generated from operations	21(a)	17,785	60,756
Interest received		205	271
Finance costs paid		(24)	(57)
Income tax paid		(4,825)	(4,013)
Net cash generated from operating activities		13,141	56,957
Investing activities			
Purchase of property, plant and equipment		(1,998)	(2,342)
Purchase of intangible assets		(4)	—
Proceeds from return of land	8	46,154	40,422
Proceeds from disposal of leasehold land		—	231
Proceeds from disposal of property, plant and equipment		—	730
Government grants received relating to property, plant and equipment		10	963
Net cash generated from investing activities		44,162	40,004
Financing activities			
Dividends paid to shareholders		—	(100,842)
Acquisition of additional interest in a subsidiary		—	(1,884)
Lease payments	16	(427)	(609)
Net cash used in financing activities		(427)	(103,335)
Net increase/(decrease) in cash and cash equivalents		56,876	(6,374)
Effect of exchange rate changes on cash and cash equivalents		138	1,555
		57,014	(4,819)
Cash and cash equivalents			
Cash and cash equivalents at beginning of period/year		16,602	21,421
Cash and cash equivalents at end of period/year		73,616	16,602

The accompanying notes are an integral part of these consolidated financial statements.

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited
Notes to the Consolidated Financial Statements

1. General Information

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited (the “Company”) and its subsidiaries (together the “Group”) are principally engaged in manufacturing, selling and distribution of over-the-counter drug products. The Group has manufacturing plants in the People’s Republic of China (the “PRC”) and sells mainly in the PRC.

The Company was incorporated in the PRC on April 12, 2005 as a Chinese-Foreign Equity joint venture. The Company is jointly controlled by Guangzhou Hutchison Chinese Medicine (HK) Investment Limited (“GZHCMHK”) and Guangzhou Baiyunshan Pharmaceutical Holdings Company Limited (“GBPHCL”). On September 28, 2021, an intermediate holding company under HUTCHMED (China) Limited (“HUTCHMED”) which wholly-owned GZHCMHK, sold its entire shareholding in GZHCMHK to a third party.

These consolidated financial statements are presented in United States dollars (“US$”), unless otherwise stated and have been approved for issue by the Company’s Board of Directors on September 28, 2021.

2. Summary of Significant Accounting Policies

(1) Basis of Preparation

Except for the comparative periods which have been prepared in accordance with the Regulation S-X Rule 3-09 issued by the United States Securities and Exchange Commission (“SEC”), the consolidated financial statements of the Company have been prepared in accordance with International Financial Reporting Standards (“IFRS”) and interpretations issued by the IFRS Interpretations Committee applicable to companies reporting under IFRS. The consolidated financial statements comply with IFRS as issued by the International Accounting Standards Board (“IASB”). These consolidated financial statements have been prepared under the historical cost convention.

As at September 28, 2021, the Group was in a net current liabilities position of US$32.0 million, primarily due to the dividend declaration on May 13, 2021 and September 23, 2021 of US$46.5 million and US$59.7 million respectively. Based on the Group’s operating plan, the existing cash and cash equivalents along with the expected net cash to be generated from operating activities are considered to be sufficient to meet the cash requirements to fund planned operations and other commitments for at least the next twelve months (the look-forward period used) from the report issue date, and it is appropriate for the Group to prepare the consolidated financial statements on a going concern basis.

(2) Summary of Significant Accounting Policies

During the period, the Group has adopted all of the new and revised standards, amendments and interpretations issued by the IASB that are relevant to the Group's operations and mandatory for annual periods beginning January 1, 2021. The adoption of these new and revised standards, amendments and interpretations did not have any material effects on the Group's results of operations or financial position.

The following standards, amendments and interpretations were issued but not yet effective for the financial period from January 1, 2021 to September 28, 2021 and have not been early adopted by the Group:

IFRS 3 (Amendments)(1)	Reference to the Conceptual Framework
IAS 16 (Amendments)(1)	Property, Plant and Equipment: Proceeds before Intended Use
IAS 37 (Amendments)(1)	Onerous Contracts – Costs of Fulfilling a Contract
Annual improvement 2018-2020(1)	Improvements to IFRSs
IAS 1(2)	Disclosure Initiative – Accounting Policies
IAS 1 (Amendments)(2)	Classification of Liabilities as Current or Non-current
IAS 8 (Amendments)(2)	Definition of Accounting Estimates
IAS 12 (Amendments)(2)	Deferred Tax related to Assets and Liabilities arising from a Single Transaction
IFRS 17(2)	Insurance Contracts
IFRS 10 and IAS 28 (Amendments)(3)	Sale or Contribution of Assets between an Investor and its Associate or Joint Venture

(1) Effective for the Group for annual periods beginning on or after January 1, 2022.

(2) Effective for the Group for annual periods beginning on or after January 1, 2023.

(3) Effective date to be determined by the IASB.

The adoption of standards, amendments and interpretations listed above in future periods is not expected to have any material effects on the Group's results of operations or financial position.

(a) Basis of Consolidation

The consolidated financial statements of the Group include the financial statements of the Company and its subsidiaries, and also include the Group's interests in a joint venture and associated companies on the basis set out in Notes 2(d) and 2(e) below.

The accounting policies of subsidiaries, the joint venture and associated companies have been changed where necessary to ensure consistency with the policies adopted by the Group.

Intercompany transactions, balances and unrealized gains on transactions between group companies are eliminated. Unrealized losses are also eliminated unless the transaction provides evidence of an impairment of the transferred asset.

Non-controlling interests represent the interests of outside shareholders in the operating results and net assets of subsidiaries.

(b) Subsidiaries

Subsidiaries are all entities over which the Group has control. The Group controls an entity when the Group is exposed, or has rights, to variable returns from its involvement with the entity and has the ability to affect those returns through its power to direct the activities of the entity. In the consolidated financial statements, subsidiaries are accounted for as described in Note 2(a) above.

Subsidiaries are fully consolidated from the date on which control is transferred to the Group. They are de-consolidated from the date that control ceases.

(c) Transactions with Non-controlling Interests

Transactions with non-controlling interests that do not result in a loss of control are accounted for as transactions with equity owners of the Group. For purchases from non-controlling interests, the difference between any consideration paid and the relevant share acquired of the carrying value of net assets of the subsidiary is recorded in equity. Gains or losses on disposals to non-controlling interests are also recorded in equity.

(d) Joint Arrangements

Investments in joint arrangements are classified either as joint operations or joint ventures depending on the contractual rights and obligations of each investor. The Group has assessed the nature of its joint arrangement and determined it to be a joint venture. The joint venture is accounted for using the equity method.

Under the equity method of accounting, the interest in joint venture is initially recognized at cost and adjusted thereafter to recognize the Group’s share of the post-acquisition profits or losses and movements in other comprehensive income. The Group determines at each reporting date whether there is any objective evidence that the investment in the joint venture is impaired. If this is the case, the Group calculates the amount of impairment as the difference between the recoverable amount of the joint venture and its carrying value and recognizes the amount in the consolidated income statements.

(e) Associated Companies

An associate is an entity, other than a subsidiary or a joint venture, in which the Group has a long-term equity interest and over which the Group is in position to exercise significant influence over its management, including participation in the financial and operating policy decisions.

The results and net assets of associates are incorporated in these financial statements using the equity method of accounting, except when the investment is classified as held for sale, in which case it is accounted for under IFRS 5, Non-current assets held for sale and discontinued operations. The total carrying amount of such investments is reduced to recognize any identified impairment loss in the value of individual investments.

(f) Foreign Currency Translation

Items included in the financial statements of each of the Group’s companies are measured using the currency of the primary economic environment in which the entity operates (the “functional currency”). The functional currency of the Company and its subsidiaries, joint venture and associated companies is Renminbi (“RMB”) whereas the consolidated financial statements are presented in US$, which is the Company’s presentation currency.

Foreign currency transactions are translated into the functional currency using the exchange rates at the dates of the transactions. Foreign currency gains and losses resulting from the settlement of such transactions and from the translation of monetary assets and liabilities denominated in foreign currencies at year end exchange rates are generally recognized in the consolidated income statements.

The financial statements of the Company, subsidiaries, joint venture and associated companies are translated into the Company’s presentation currency using the year end rates of exchange for the statements of financial position items and the average rates of exchange for the year for the income statement items. Exchange translation differences are recognized directly in other comprehensive income.

(g) Property, Plant and Equipment

Property, plant and equipment other than construction in progress are stated at historical cost less accumulated depreciation and any accumulated impairment losses. Historical cost includes the purchase price of the asset and any directly attributable costs of bringing the asset to its working condition and location for its intended use.

Subsequent costs are included in the asset's carrying amount or recognized as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. All other repairs and maintenance are charged to the consolidated income statements during the financial period in which they are incurred.

Depreciation is calculated using the straight-line method to allocate asset costs less accumulated impairment losses over their estimated useful lives. The principal estimated useful lives are as follows:

Buildings and facilities	10-30 years
Plant and equipment	10 years
Furniture and fixtures, other equipment and motor vehicles	5 years

The assets' useful lives are reviewed and adjusted, if appropriate, at the end of each reporting period. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount.

Gains and losses on disposals are determined by comparing net sales proceeds with the carrying amount of the relevant assets and are recognized in the consolidated income statements.

(h) Construction in Progress

Construction in progress represents buildings, plant and machinery under construction and pending installation and is stated at cost less accumulated impairment losses, if any. Cost includes the costs of construction of buildings and the costs of plant and machinery. No provision for depreciation is made on construction in progress until such time as the relevant assets are completed and ready for its intended use. When the assets concerned are brought into use, the costs are transferred to property, plant and equipment and depreciated in accordance with the policy as stated in Note 2(g).

(i) Goodwill

Goodwill represents the excess of the cost of an acquisition over the fair value of the Group's share of the net identifiable assets of the acquired subsidiary/business at the date of acquisition, or the excess of fair value of business over its fair value of the net identifiable assets injected into the Company upon its formation. If the cost of acquisition is less than the fair value of the Group's share of the net identifiable assets of the acquired subsidiary, the difference is recognized directly in the consolidated income statements.

Goodwill is retained at the carrying amount as a separate asset, and subject to impairment test annually and when there are indications that the carrying value may not be recoverable.

The profit or loss on disposal of a subsidiary is calculated by reference to the net assets at the date of disposal including the attributable amount of goodwill.

(j) Other Intangible Assets

The Group's other intangible assets mainly include distribution network and drugs licenses contributed from non-controlling shareholders. Other intangible assets have a definite useful life and are carried at historical cost less accumulated amortization and accumulated impairment losses, if any. Amortization is calculated using the straight-line method to allocate costs over the estimated useful lives of ten years.

(k) Research and Development

Research expenditure is recognized as an expense as incurred. Costs incurred on development projects (relating to the design and testing of new or improved products) are recognized as intangible assets when it is probable that the project will generate future economic benefits by considering its commercial and technological feasibility, and costs can be measured reliably. Other development expenditures are recognized as an expense as incurred. Development costs previously recognized as an expense are not recognized as an asset in a subsequent period. Development costs with a finite useful life that have been capitalized, if any, are amortized on a straight-line basis over the period of expected benefit not exceeding five years. The capitalized development costs are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset exceeds its recoverable amount.

Where the research phase and the development phase of an internal project cannot be clearly distinguished, all expenditure incurred on the project is charged to the consolidated income statements.

(l) Impairment of Non-Financial Assets

Assets are reviewed for impairment to determine whether there is any indication that the carrying value of these assets may not be recoverable and have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss, if any. The recoverable amount is the higher of an asset's fair value less costs to sell and value in use. Such impairment loss is recognized in the consolidated income statements. Assets that have an indefinite useful life such as goodwill or intangible assets not ready to use are not subject to amortization and are tested for impairment annually and when there are indications that the carrying value may not be recoverable.

(m) Inventories

Inventories are stated at the lower of cost or net realizable value. Cost is determined using the weighted average cost method. The cost of finished goods comprises raw materials, direct labor, other direct costs and related production overheads (based on normal operating capacity). Net realizable value is the estimated selling price in the ordinary course of business, less applicable variable selling expenses.

(n) Trade and Other Receivables

Trade and other receivables are recognized initially at fair value, which is the amount of consideration that is unconditional. Trade and other receivables solely represent payments of principal and interest, if any, and the Group holds such financial assets with the objective to collect its contractual cash flows. Therefore, the Group measures them subsequently at amortized cost using the effective interest method, less any loss allowance. The Group applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all trade receivables. To measure the expected credit losses, trade receivables have been grouped based on shared credit risk characteristics and the days past due. All other receivables at amortized cost are considered to have low credit risk, and the loss allowance recognized during the period was therefore limited to 12 months expected losses. The amount of the provision is recognized in the consolidated income statements.

(o) Cash and Cash Equivalents

In the consolidated statements of cash flows, cash and cash equivalents include cash on hand, bank deposits and other short-term highly liquid investments with original maturities of three months or less that are readily convertible to known amounts of cash and which are subject to an insignificant risk of changes in value, if any.

(p) Financial Liabilities and Equity Instruments

Financial liabilities and equity instruments issued by the Group are classified according to the substance of the contractual arrangements entered into and the definitions of a financial liability and an equity instrument. Financial liabilities (including trade and other payables) are initially measured at fair value, and are subsequently measured at amortized cost, using the effective interest method. An equity instrument is any contract that does not meet the definition of financial liability and evidences a residual interest in the assets of the Group after deducting all of its liabilities.

Ordinary shares are classified as equity. Incremental costs, net of tax, directly attributable to the issue of new shares are shown in equity as a deduction from the proceeds.

(q) Current and Deferred Income Tax

(i) Current income tax

The current income tax charge is calculated on the basis of the tax laws enacted or substantively enacted at the balance sheet date in the country where the Group operates and generates taxable income. Management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate on the basis of amounts expected to be paid to the tax authorities.

(ii) Deferred income tax

Inside basis differences

Deferred income tax is provided in full, using the liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. However, deferred tax liabilities are not recognized if they arise from the initial recognition of goodwill. Deferred income tax is also not accounted for if it arises from initial recognition of an asset or liability in a transaction other than a business combination that, at the time of the transaction, affects neither accounting nor taxable profit or loss and does not give rise to equal taxable and deductible temporary differences. Deferred income tax is determined using tax rates (and laws) that have been enacted or substantively enacted by the balance sheet date and are expected to apply when the related deferred income tax asset is realized or the deferred income tax liability is settled.

Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Deferred income tax assets and deferred income tax liabilities are offset when there is a legally enforceable right to set off and when the deferred income taxes related to the same fiscal authority.

Outside basis differences

Deferred income tax liabilities are provided on taxable temporary differences arising from investments in subsidiaries, associates and joint arrangements, except for deferred income tax liabilities where the timing of the reversal of the temporary difference is controlled by the Group and it is probable that the temporary difference will not reverse in the foreseeable future. Generally the Group is unable to control the reversal of the temporary difference for associates. Only when there is an agreement in place that gives the Group the ability to control the reversal of the temporary difference in the foreseeable future, deferred tax liability in relation to taxable temporary differences arising from the associate's undistributed profits is not recognized.

Deferred income tax assets are recognized on deductible temporary differences arising from investments in subsidiaries, associates and joint arrangements only to the extent that it is probable the temporary difference will reverse in the future and there is sufficient taxable profit available against which the temporary difference can be utilized.

(r) Employee Benefits

The employees of the Group participate in defined contribution retirement benefit plans managed by the relevant municipal and provincial governments in the PRC. The assets of these plans are held separately from the Group. The Group is required to make monthly contributions to the plans, calculated as a percentage of the employees' salaries. The municipal and provincial governments undertake to assume the retirement benefit obligations to all existing and future retired employees under the plans described above. Other than the monthly contributions, the Group has no further obligations for the payment of the retirement and other post-retirement benefits of its employees.

(s) Provisions

Provisions are recognized when the Group has a present legal or constructive obligation as a result of past events, it is probable that an outflow of resources will be required to settle the obligation, and the amount has been reliably estimated. Provisions are not recognized for future operating losses.

(t) Leases

A lease is recognized as a right-of-use asset with a corresponding liability at the date which the leased asset is available for use by the Group. The Group recognizes an obligation to make lease payments equal to the present value of the lease payments over the lease term. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Group will exercise that option.

Lease liabilities include the net present value of the following lease payments: (i) fixed payments; (ii) variable lease payments that depend on an index or a rate; and (iii) payments of penalties for terminating the lease if the lease term reflects the lessee exercising that option, if any. Lease liabilities exclude the following payments that are generally accounted for separately: (i) non-lease components, such as maintenance and security service fees and value added tax, and (ii) any payments that a lessee makes before the lease commencement date. The lease payments are discounted using the interest rate implicit in the lease or if that rate cannot be determined, the lessee's incremental borrowing rate being the rate that the lessee would have to pay to borrow the funds in its currency and jurisdiction necessary to obtain an asset of similar value, economic environment and terms and conditions.

An asset representing the right to use the underlying asset during the lease term is recognized that consists of the initial measurement of the lease liability, any lease payments made to the lessor at or before the commencement date less any lease incentives received, any initial direct cost incurred by the Group and any restoration costs.

After commencement of the lease, each lease payment is allocated between lease liability and finance costs. The finance costs are recognized over the lease term so as to produce a constant periodic rate of interest on the remaining balance of the lease liability for each period. The right-of-use asset is depreciated on a straight-line basis over the period of the lease.

Payments associated with short-term leases are recognized as lease expenses on a straight-line basis over the period of the leases.

Leasehold land is accounted under IFRS 16.

(u) Government Incentives

Incentives from government are recognized at their fair values where there is a reasonable assurance that the incentives will be received and all attached conditions will be complied with.

Government incentives relating to costs are deferred and recognized in the consolidated income statements over the period necessary to match them with the costs that they are intended to compensate.

Government grants relating to property, plant and equipment are included in non-current liabilities as deferred income and credited to the consolidated income statements on a straight-line basis over the expected lives of the related assets.

(v) Revenue and Income Recognition

The Group principally generates revenue from sales of goods. Revenue from sales of goods is recognized when the customer takes possession of the goods. This usually occurs upon completed delivery of the goods to the customer site. The amount of revenue recognized is adjusted for expected sales incentives as stipulated in the contract, which are generally issued to customers as direct discounts at the point-of-sale or indirectly in the form of rebates. Sales incentives are estimated using the expected value method. Additionally, sales are generally made with a limited right of return under certain conditions. Revenues are recorded net of provisions for sales discounts and returns.

Revenue from provision of services is recognized when the benefits of the services transfer to the customer over time, which is based on the proportionate value of services rendered as determined under the terms of the relevant contract. Additionally, when the amounts that can be invoiced correspond directly with the value to the customer for performance completed to date, the Group recognizes revenue from provision of services based on amounts that can be invoiced to the customer.

Payments in advance from customers are deferred if consideration is received in advance of transferring control of the goods or rendering of services. Accounts receivable is recognized if the Group has an unconditional right to bill the customer, which is generally when the customer takes possession of the goods or services are rendered. Payment terms differ by subsidiary and customer, but generally range from 45 to 180 days from the invoice date.

(w) Interest income

Interest income is recognized on a time-proportion basis using the effective interest method.

(x) Segment Reporting

Operating segments are reported in a manner consistent with the internal reporting provided to the chief operating decision-makers. The Company's Board of Directors, which is responsible for allocating resources and assessing performance of the operating segments, has been identified as the steering committee that makes strategic decisions.

(y) General Reserves

In accordance with the laws applicable to Foreign Investment Enterprises established in the PRC, the Company makes appropriations to certain non-distributable reserve funds including the general reserve fund, the enterprise expansion fund and the staff bonus and welfare fund. The amount of appropriations to these funds are made at the discretion of the Company's Board of Directors.

3. Financial Risk Management

(a) Financial risk factors

The Group's activities expose it to a variety of financial risks, including credit risk and liquidity risk. The Group does not use any derivative financial instruments for speculative purposes.

(i) Credit risk

The carrying amounts of cash and cash equivalents, trade receivables (including bills receivables) and other receivables included in the consolidated statements of financial position represent the Group's maximum exposure to credit risk of the counterparty in relation to its financial assets.

Substantially all of the Group's cash and cash equivalents are deposited in major financial institutions, which management believes are of high credit quality.

Bills receivables are mostly settled by state-owned banks or other reputable banks and therefore the management considers that they will not expose the Group to any significant credit risk.

The Group has no significant concentrations of credit risk. The Group has policies in place to ensure that the sales of products are made to customers with appropriate credit history and the Group performs periodic credit evaluations of its customers.

Management periodically assesses the recoverability of trade receivables and other receivables. The Group's historical loss rates are adjusted to reflect current and forward-looking information on specific factors affecting the ability of the customers to settle the receivables, and historical experience collecting receivables falls within the recorded allowances.

(ii) Liquidity risk

Prudent liquidity management implies maintaining sufficient cash and cash equivalents and the availability of funding when necessary. The Group's policy is to regularly monitor current and expected liquidity requirements to ensure that it maintains sufficient cash balances and adequate credit facilities to meet its liquidity requirements in the short and long term.

As at September 28, 2021, the Group's current financial liabilities were mainly due for settlement within twelve months and the Group expects to meet all liquidity requirements. As at September 28, 2021, the Group's consolidated current liabilities exceed the consolidated current assets by US$32.0 million, which was mainly attributable to current dividends payable to shareholders (refer to Note 23(b)), for which settlement will occur when sufficient cash and cash equivalents are available. In assessing the Group's liquidity, management prepared a cash flow forecast up to December 31, 2022 taking into consideration of ongoing operations and the settlement of the current dividends payable, which indicates that the Group will have sufficient cash resources to fund planned operations and other commitments for at least the next twelve months (the look-forward period used).

(b) Capital risk management

The Group's objectives when managing capital are to safeguard the Group's ability to provide returns for shareholders and benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital.

The Group regularly reviews and manages its capital structure to ensure an optimal balance between higher shareholders' return that might be possible with higher levels of borrowings and the advantages and security afforded by a sound capital position, and makes adjustments to the capital structure in light of changes in economic conditions.

The Group monitors capital on the basis of the liabilities to assets ratio. This ratio is calculated as total liabilities divided by total assets as shown on the consolidated statements of financial position.

Currently, it is the Group's strategy to maintain a reasonable liabilities to assets ratio. The liabilities to assets ratio as at September 28, 2021 was as follows:

	September 28, 2021
	(in US$'000)
Total liabilities (note)	237,352
Total assets	284,840
Liabilities to assets ratio	83.3 %

Note: On May 13, 2021 and September 23, 2021, the Company declared dividends to shareholders of US$46.5 million and US$59.7 million respectively, which were not settled as at September 28, 2021.

(c) Fair value estimation

The Group does not have any financial assets or liabilities which are carried at fair value. The carrying amounts of the Group's current financial assets, including cash and cash equivalents, trade and bills receivables and other receivables, and current financial liabilities, including trade payables, and other payables and accruals and dividend payable, approximate their fair values due to their short-term maturities. The carrying amounts of the Group's financial instruments carried at cost or amortized cost are not materially different from their fair values.

The face values less any estimated credit adjustments for financial assets and liabilities with a maturity of less than one year are assumed to approximate their fair values. The fair value of financial liabilities for disclosure purposes is estimated by discounting the future contractual cash flows at the current market interest rate that is available to the Group for similar financial instruments.

4. Critical Accounting Estimates and Judgements

Note 2 includes a summary of the significant accounting policies used in the preparation of the consolidated financial statements. The preparation of consolidated financial statements often requires the use of judgements to select specific accounting methods and policies from several acceptable alternatives. Furthermore, significant estimates and assumptions concerning the future may be required in selecting and applying those methods and policies in the consolidated financial statements. The Group bases its estimates and judgements on historical experience and various other assumptions that it believes are reasonable under the circumstances. Actual results may differ from these estimates and judgements under different assumptions or conditions.

The following is a review of the more significant assumptions and estimates, as well as the accounting policies and methods used in the preparation of the consolidated financial statements.

(a) Sales rebates

Certain sales rebates are provided to customers when their business performance for the whole year meets certain criteria as stipulated in the contracts. Sales rebates are considered variable consideration and the estimate of sales rebates during the year is based on estimated sales transactions for the entire period stipulated and is subject to change based on actual performance and collection status.

(b) Useful lives of property, plant and equipment

The Group has made substantial investments in property, plant and equipment. Changes in technology or changes in the intended use of these assets may cause the estimated period of use or value of these assets to change.

(c) Impairment of non-financial assets

The Group tests at least annually whether goodwill has suffered any impairment. Other non-financial assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset exceeds its recoverable amount in accordance with the accounting policy stated in Note 2(l). The recoverable amount of an asset or a cash-generating unit is determined based on the higher of the asset's or the cash-generating unit's fair value less costs to disposal and value-in-use. The value-in-use calculation requires the entity to estimate the future cash flows expected to arise from the asset and a suitable discount rate in order to calculate present value, and the growth rate assumptions in the cash flow projections which has been prepared on the basis of management's assumptions and estimates.

(d) Deferred income tax

Deferred tax is recognized using the liability method on temporary differences arising between the tax bases of assets and liabilities against which the deductible temporary differences and the carry forward of unused tax losses and tax credits can be utilized. Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Where the final outcomes are different from the estimations, such differences will impact the carrying amount of deferred tax in the period in which such determination is made.

5. Revenue and Segment Information

Management has reviewed the Group's internal reporting in order to assess performance and allocate resources, and has determined that the Group has two reportable operating segments as follows:

—Manufacturing business—manufacture and distribution of drug products

—Distribution business—provision of sales, distribution and marketing services to pharmaceutical manufacturers

The operating segments are strategic business units that offer different products and services. They are managed separately because each business requires different technology and marketing approaches. The performance of each of the reportable segments is assessed based on operating profit.

The segment information is as follows:

	Period from January 1, 2021 to September 28, 2021		
	Manufacturing business	Distribution business	Total
		PRC	
		(in US$'000)	
Revenue from external customers	190,619	18,909	209,528
Interest income	141	64	205
Operating profit	18,212	2,076	20,288
Share of profits of a joint venture and associated companies, net of tax	29	—	29
Finance costs	18	6	24
Depreciation/amortization	5,515	98	5,613
Additions to non-current assets (other than financial instruments and deferred tax assets)	2,405	—	2,405

	As at September 28, 2021		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Total segment assets	251,178	33,662	284,840

	Year Ended December 31, 2020		
	Manufacturing business	Distribution business	Total
	PRC		
	(in US$'000)		
Revenue from external customers	215,427	16,941	232,368
Interest income	188	83	271
Operating profit	20,833	2,312	23,145
Share of losses of a joint venture and associated companies, net of tax	84	—	84
Finance costs	51	6	57
Depreciation/amortization	6,361	123	6,484
Additions to non-current assets (other than financial instruments and deferred tax assets)	2,432	1	2,433

Revenue from external customers is after elimination of inter-segment sales. The amount eliminated was US$0.2 million for the period from January 1, 2021 to September 28, 2021 (for the year ended December 31, 2020: US$0.1 million). Sales between segments are carried out at mutually agreed terms. Revenue from external customers is primarily for sales of goods which are recognized at a point in time, except for provision of services which are recognized over time of US$1.2 million for the period from January 1, 2021 to September 28, 2021 (for the year ended December 31, 2020: US$3.7 million) and included in the manufacturing business operating segment.

6. Other Net Operating Income

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Interest income	205	271
Gain on disposal of leasehold land	—	166
Loss on disposal of property, plant and equipment	(47)	(643)
Other operating income	5,631	6,734
Other operating expenses	(483)	(457)
	5,306	6,071

7. Operating Profit

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Operating profit	20,288	23,145

Operating profit is stated after charging/(crediting) the following:

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Cost of inventories recognized as expense	87,941	100,906
Depreciation of property, plant and equipment	4,425	5,283
Loss on disposal of property, plant and equipment	47	643
Gain on disposal of leasehold land	—	(166)
Amortization of leasehold land	450	236
Amortization of other intangible assets	331	414
Depreciation charge of right-of-use assets and lease expenses	1,360	1,438
Movements on the provision for trade receivables	38	(20)
Movements on the provision for excess and obsolete inventories	41	474
Research and development expense	2,057	1,670
Auditor's remuneration	43	88
Employee benefit expenses (Note 10)	31,605	36,822

8. Gain On Return of Land

In June 2020, the Group entered into an agreement with the government to return the land use right for a plot of land in Guangzhou to the government (the "Land Compensation Agreement") for cash consideration which aggregated to RMB679.5 million (approximately US$103.1 million). In November 2020, the Group completed all material obligations as stipulated in the Land Compensation Agreement and recognized land compensation of RMB569.2 million (approximately US$86.1 million), resulting in a gain of RMB559.7 million (approximately US$84.7 million). In June 2021, the Group received a completion confirmation from the government and recognized an additional land compensation bonus of RMB110.3 million (approximately US$17.0 million), resulting in a gain of RMB106.8 million (approximately US$16.4 million), after deducting costs of RMB3.5 million (approximately US$0.6 million). As at September 28, 2021, the Group has received RMB584.6 million (approximately US$86.6 million) and has recorded RMB94.9 million (approximately US$14.6 million) in other receivables, prepayments and deposits.

9. Taxation Charge

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Current tax	6,093	17,108
Deferred income tax (Note 17)	(1,253)	(614)
Taxation charge	4,840	16,494

The taxation charge on the Group's profit before taxation differs from the theoretical amount that would arise using the Group's weighted average tax rate as follows:

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Profit before taxation	36,726	107,708
Tax calculated at the statutory tax rates of respective companies	9,181	26,927
Tax effects of:		
Expenses not deductible for tax purposes	45	66
Tax concession (note)	(3,781)	(10,834)
Tax losses for which no deferred tax assets were recognized	192	339
Under provision in prior years	6	44
Utilization of tax losses for which no deferred tax assets were recognized previously	(803)	(48)
Taxation charge	4,840	16,494

Note: The Company has been granted the High and New Technology Enterprise status. Accordingly, the Company is subject to a preferential income tax rate of 15% and renewed the status in 2021. Certain research and development expenses are also eligible for super-deduction such that 200% of qualified expenses incurred are deductible for tax purposes.

The weighted average tax rate calculated at the statutory tax rates of respective companies was 25%. The effective tax rate for the period from January 1, 2021 to September 28, 2021 was 13.2% (for the year ended December 31, 2020: 15.3%).

10. Employee Benefit Expenses

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Wages, salaries and bonuses	23,705	28,380
Pension costs—defined contribution plans	6,679	6,954
Staff welfare	1,221	1,488
	31,605	36,822

Employee benefit expenses of approximately US$9.1 million for the period from January 1, 2021 to September 28, 2021 (for the year ended December 31, 2020: US$11.1 million) are included in cost of sales.

11. Cash and Cash Equivalents

	September 28, 2021
	(in US$'000)
Cash and cash equivalents	73,616

The cash and cash equivalents denominated in RMB were deposited with banks in the PRC. The conversion of these RMB denominated balances into foreign currencies is subject to the rules and regulations of foreign exchange control promulgated by the PRC government.

12. Trade and Bills Receivables

	September 28, 2021
	(in US$'000)
Trade receivables—third parties	4,290
Trade receivables—related parties (Note 23(b))	1,975
Bills receivables	21,609
	27,874

All trade and bills receivables are denominated in RMB and are due within one year from the end of the reporting period. The carrying values of trade and bills receivables approximate their fair values due to their short-term maturities.

Movements on the provision for trade receivables are as follows:

	2021	2020
	(in US$'000)	
As at January 1	—	19
Increase in provision for trade receivables	38	—
Decrease in provision due to subsequent collection	—	(20)
Exchange differences	—	1
As at September 28/December 31	38	—

The impaired and provided receivables as at September 28, 2021 were aged over 1 year.

13. Other Receivables, Prepayments and Deposits

	September 28, 2021
	(in US$'000)
Prepayments to suppliers	9,671
Value-added tax receivables	780
Land compensation receivable	14,592
Others	1,504
	26,547

14. Inventories

	September 28, 2021
	(in US$'000)
Raw materials	23,126
Work in progress	17,816
Finished goods	21,458
	62,400

15. Property, Plant and Equipment

	Buildings and facilities	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)		
Cost					
As at January 1, 2021	61,267	27,769	12,615	1,979	103,630
Additions	396	440	623	943	2,402
Disposals	(3)	(97)	(78)	—	(178)
Transfers	—	358	906	(1,264)	—
Exchange differences	516	234	105	17	872
As at September 28, 2021	62,176	28,704	14,171	1,675	106,726
Accumulated depreciation					
As at January 1, 2021	16,368	16,559	10,522	—	43,449
Depreciation	1,763	1,278	1,384	—	4,425
Disposals	(1)	(61)	(69)	—	(131)
Exchange differences	137	138	89	—	364
As at September 28, 2021	18,267	17,914	11,926	—	48,107
Net book value					
As at September 28, 2021	43,909	10,790	2,245	1,675	58,619

	Buildings and facilities	Plant and equipment	Furniture and fixtures, other equipment and motor vehicles	Construction in progress	Total
			(in US$'000)		
Cost					
As at January 1, 2020	59,099	25,426	11,353	1,311	97,189
Additions	224	168	651	1,390	2,433
Disposals	(2,204)	(187)	(522)	—	(2,913)
Disposal of a subsidiary	(28)	—	(27)	—	(55)
Transfers	28	502	318	(848)	—
Exchange differences	4,148	1,860	842	126	6,976
As at December 31, 2020	61,267	27,769	12,615	1,979	103,630
Accumulated depreciation					
As at January 1, 2020	14,021	14,096	8,755	—	36,872
Depreciation	2,201	1,520	1,562	—	5,283
Disposals	(926)	(150)	(464)	—	(1,540)
Disposal of a subsidiary	(10)	—	(23)	—	(33)
Exchange differences	1,082	1,093	692	—	2,867
As at December 31, 2020	16,368	16,559	10,522	—	43,449
Net book value					
As at December 31, 2020	44,899	11,210	2,093	1,979	60,181

16. Leases

Leases consisted of the following:

	September 28, 2021
	(in US$'000)
Right-of-use assets:	
Warehouses	420
Lease liabilities—current	452

Lease activities are summarized as follows:

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Lease expenses: Short-term leases with lease terms equal or less than 12 months	953	887
Depreciation charge of right-of-use assets	407	551
Interest expense (included in finance costs)	24	57
Cash paid on lease liabilities	427	609

Lease contracts are typically within a period of 1 to 6 years. The weighted average remaining lease term and weighted average discount rate as at September 28, 2021 was 0.83 year (as at December 31, 2020: 1.56 years) and 4.75% (as at December 31, 2020: 4.75%) respectively.

Future lease payments are as follows:

	September 28, 2021
	(in US$'000)
Lease payments:	
Not later than 1 year	462
Total lease payments	462
Less: Discount factor	(10)
Total lease liabilities	452

17. Deferred Tax Assets and Liabilities

	September 28, 2021
	(in US$'000)
Deferred tax assets	4,420
Net deferred tax assets	4,420

The movements in net deferred tax assets are as follows:

	2021	2020
	(in US$'000)	
At January 1	3,027	2,217
Credited/(debited) to the consolidated income statements		
—Tax losses	326	(396)
—Accrued expenses, provisions, depreciation allowances	927	1,010
Exchange differences	140	196
At September 28/December 31	4,420	3,027

The Group's deferred tax assets and liabilities are temporary differences including tax losses, accrued expenses, provisions and depreciation allowances. The potential deferred tax assets in respect of tax losses which have not been recognized in the consolidated financial statements were approximately US$1.6 million as at September 28, 2021.

These unrecognized tax losses can be carried forward against future taxable income and will expire in the following years:

	September 28, 2021
	(in US$'000)
2021	928
2022	1,450
2023	856
2024	1,239
2025	1,074
2026	669
	6,216

18. Trade Payables

	September 28, 2021
	(in US$'000)
Trade payables—third parties	15,519
Trade payables—related parties (Note 23(b))	3,529
	19,048

All trade payables are denominated in RMB and due within one year from the end of the reporting period. The carrying value of trade payables approximates their fair values due to their short-term maturities.

19. Other Payables, Accruals and Advance Receipts

	September 28, 2021 (in US$'000)
Other payables and accruals	
Accrued salaries and benefits	5,384
Accrued selling and administrative expenses	35,266
Value-added tax and tax surcharge payables	2,588
Deposits received	4,748
Other payables to manufacturers	8,794
Others	5,934
	62,714
Advance receipts	
Payments in advance from customers (note)	16,310
Deferred government incentives	1,460
	17,770
	80,484

Note: Substantially all customer balances as at September 28, 2021 are expected to be recognized to revenue within one year upon transfer of goods or services as the contracts have an expected duration of one year or less.

20. Deferred Income

	September 28, 2021 (in US$'000)
Deferred government incentives:	
Buildings and other non-current assets	11,272
Others	3,641
	14,913

21. Notes to the Consolidated Statements of Cash Flows

(a) Reconciliation of profit for the period/year to net cash generated from operations:

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Profit for the period/year	31,886	91,214
Adjustments to reconcile profit for the period/year to net cash generated from operations		
Taxation charge	4,840	16,494
Finance costs	24	57
Interest income	(205)	(271)
Share of (profits)/losses of a joint venture and associated companies, net of tax	(29)	84
Depreciation on property, plant and equipment	4,425	5,283
Depreciation charge of right-of-use assets	407	551
Loss on disposal of property, plant and equipment	47	643
Gain on return of land	(16,433)	(84,667)
Gain on disposal of leasehold land	—	(166)
Amortization of leasehold land	450	236
Amortization of other intangible assets	331	414
Movement on the provision for trade receivables	38	(20)
Movement on the provision for excess and obsolete inventories	41	474
Amortization of deferred income	(845)	(1,689)
Gain on divestment of a subsidiary	—	(37)
Exchange differences	(470)	794
Changes in working capital:		
Trade and bills receivables	39,505	(19,124)
Other receivables, prepayments and deposits	(5,248)	1,902
Inventories	(18,693)	2,195
Other non-current assets	(139)	—
Trade payables	(3,531)	9,880
Other payables, accruals and advance receipts	(18,616)	36,509
Total changes in working capital	(6,722)	31,362
Net cash generated from operations	17,785	60,756

(b) Supplemental disclosure for non-cash activities

During the period from January 1, 2021 to September 28, 2021, there was an increase of US$0.4 million in accruals made for purchases of property, plant and equipment (for the year ended December 31, 2020: an increase of US$0.1 million).

22. Capital Commitments

The Group had the following capital commitments:

	September 28, 2021
	(in US$'000)
Property, plant and equipment	
Contracted but not provided for	1,290

Capital commitments for property, plant and equipment are mainly for improvements to the Group's plant.

23. Significant Related Party Transactions

The Group has the following significant transactions with related parties which were carried out in the normal course of business at terms determined and agreed by the relevant parties:

(a) Transactions with related parties:

	Period from January 1, 2021 to September 28, 2021	Year Ended December 31, 2020
	(in US$'000)	
Sales of goods to:		
—Fellow subsidiaries of GBPHCL	25,043	33,535
—A fellow subsidiary of GZHCMHK	278	493
	25,321	34,028
Other services income from:		
—An equity investee	—	273
—Fellow subsidiaries of GBPHCL	3,576	6,166
	3,576	6,439
Purchase of goods from:		
—An equity investee	2,145	2,317
—Fellow subsidiaries of GBPHCL	24,222	29,594
	26,367	31,911
Advertising expenses to:		
—A fellow subsidiary of GBPHCL	4,805	5,733
Interest paid to:		
—A non-controlling shareholder of a subsidiary	—	5
	—	5

No transactions have been entered into with the directors of the Company (being the key management personnel) during the period from January 1, 2021 to September 28, 2021 (for the year ended December 31, 2020: nil).

(b) Balances with related parties included in:

	September 28, 2021 (in US$'000)
Trade and bills receivables	
—Fellow subsidiaries of GBPHCL (note (i))	1,975
	1,975
Trade payables	
—Fellow subsidiaries of GBPHCL (note (i))	3,529
	3,529
Other receivables and prepayments—related parties	
—Fellow subsidiaries of GBPHCL (note (i))	1,129
—An equity investee (note (i))	156
	1,285
Other payables, accruals and advance receipts	
—Fellow subsidiaries of GBPHCL (note (i))	2,691
	2,691
Dividend payable (Note 3(b))	
—GZHCMHK	52,887
—GBPHCL	52,887
	105,774

Notes:

(i) Balances are unsecured, interest-free and repayable on demand. The carrying values of balances with related parties approximate their fair values due to their short-term maturities.

24. Particulars of Principal Subsidiaries, Joint Venture and Associated Companies

All of the Group's principal subsidiaries, joint venture and associated companies had a place of establishment and operation in the PRC.

Name	Nominal value of registered capital September 28, 2021 (in RMB'000)	Equity interest attributable to the Group September 28, 2021	Type of legal entity	Principal activity
Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine (Bozhou) Co. Ltd	100,000	100 %	Limited liability company	Manufacture, sales and distribution of drug products
Hutchison Whampoa Guangzhou Baiyunshan Pharmaceuticals Limited	10,000	100 %	Limited liability company	Sales and marketing of drug products
Hutchison Whampoa Guangzhou Baiyunshan Health & Wellness Co. Ltd	10,000	100 %	Limited liability company	Health supplemented food distribution
Hutchison Whampoa Baiyunshan Lai Da Pharmaceuticals (Shan Tou) Company Limited	10,000	100 %	Limited liability company	Manufacture, sales and distribution of drug products
Fuyang Baiyunshan Hutchison Whampoa Chinese Medicine Technology Company Limited	3,650	75 %	Limited liability company	Agriculture and sales of Chinese herbs
Wenshan Baiyunshan Hutchison Whampoa Sanqi Co. Ltd.	2,000	51 %	Limited liability company	Agriculture and sales of Chinese herbs
Daqing Baiyunshan Hutchison Whampoa Banlangen Technology Company Limited	1,020	51 %	Limited liability company	Agriculture and sales of Chinese herbs
Shen Nong Garden Traditional Chinese Medicine Museum	1,000	100 %	Non-profit making organization	Promote awareness of Chinese herbs
Guangzhou Hulu Cultural Communications Company Limited	1,000	100 %	Limited liability company	Promote awareness of Chinese herbs
Shen Nong Garden Pharmacy Company Limited	200	100 %	Limited liability company	Retail of drug products, health foods and souvenirs
Joint Venture				
Qing Yuan Hutchison Whampoa Baiyunshan Chinese Medicine Company Limited	1,000	50 %	Limited liability company	Agriculture and sales of Chinese herbs
Associated companies				
Linyi Shenghe Jiuzhou Pharmaceuticals Company Limited	3,000	30 %	Limited liability company	Agriculture and sales of Chinese herbs
Tibet Linzhi Guangzhou Pharmaceutical Development Co. Ltd.	2,000	20 %	Limited liability company	Trading of Chinese herbs

Exhibit 2.4

Description of Ordinary Shares

The following are summaries of material provisions of our currently effective amended and restated memorandum and articles of association and the Cayman Islands Companies Act (As Revised), or the Companies Act, insofar as they relate to the material terms of our ordinary shares. You should read this summary together with our amended and restated memorandum and articles of association which have been filed with the Securities and Exchange Commission, or SEC, as exhibit 1.1 to our annual report on Form 20-F for the year ended December 31, 2022.

General

All of our outstanding shares are fully paid and non-assessable. Our ordinary shares are issued in registered form and are issued when registered in our register of members. Our shareholders who are non-residents of the Cayman Islands may freely hold and vote their ordinary shares. Each ordinary share has US$0.10 par value.

Dividends

Under our amended and restated memorandum and articles of association, our company in general meeting may from time to time declare final dividends in any currency to be paid to the members but no final dividend shall be declared in excess of the amount recommended by our board of directors. Dividends may be declared and paid out of the profits of our company, realized or unrealized, or from any reserve set aside from profits which our directors determine is no longer needed. With the sanction of an ordinary resolution, dividends may also be declared and paid out of share premium account or any other fund or account which can be authorized for this purpose in accordance with the Companies Act. Except in so far as the rights attaching to, or the terms of issue of, any share otherwise provide: (a) all dividends shall be declared and paid according to the amounts paid up on the shares in respect of which the dividend is paid, but no amount paid up on a share in advance of calls shall be treated for this purpose as paid up on that share; and (b) all dividends shall be apportioned and paid pro rata according to the amounts paid up on the shares during any portion or portions of the period in respect of which the dividend is paid.

Our board of directors may from time to time pay to the members such interim dividends as appear to the board of directors to be justified by the profits of our company, whenever such profits, in the opinion of our board of directors, justifies such payment.

Our board of directors may deduct from any dividend or other moneys payable to a member by our company on or in respect of any shares all sums of money (if any) presently payable by such shareholder to our company on account of calls or otherwise.

No dividend or other moneys payable by our company on or in respect of any share shall bear interest against our company.

Any dividend, interest or other sum payable in cash to the holder of shares may be paid by check or warrant sent through the post addressed to the holder at his or her registered address or, in the case of joint holders, addressed to the holder whose name stands first in the register of members in respect of the shares at his or her address as appearing in the register of members or addressed to such person and at such address as the holder or joint holders may in writing direct. Every such check or warrant shall, unless the holder or joint holders otherwise direct, be made payable to the order of the holder or, in the case of joint holders, to the order of the holder whose name stands first on the register of members in respect of such shares, and shall be sent at his, her or their risk and payment of the check or warrant by the bank on which it is drawn shall constitute a good discharge to our company.

All dividends or bonuses unclaimed for one year after having been declared may be invested or otherwise made use of by our board of directors for the benefit of our company until claimed. Any dividend or bonuses unclaimed after a period of six years from the date of declaration shall be forfeited and shall revert to our company.

Whenever our board of directors or our company in general meeting has resolved that a dividend be paid or declared, our board of directors may further resolve that such dividend be satisfied wholly or in part by the distribution of specific assets of any kind and in particular of paid up shares, debentures or warrants to subscribe securities of our company or any other company, or in any one or more of such ways, and where any difficulty arises in regard to the distribution the board of directors may settle the same as it thinks expedient, and in particular may issue certificates in respect of fractions of shares, disregard fractional entitlements or round the same up or down, and may fix the value for distribution of such specific assets, or any part thereof, and may determine that cash payments shall be made to any of our members upon the footing of the value so fixed in order to adjust the rights of all parties, and may vest any such specific assets in trustees as may seem expedient to our board of directors and may appoint any person to sign any requisite instruments of transfer and other documents on behalf of the persons entitled to the dividend, and such appointment shall be effective and binding on our members.

Whenever our board of directors or our company in general meeting has resolved that a dividend be paid or declared on any class of the share capital of our company, our board of directors may further resolve either: (a) that such dividend be satisfied wholly or in part in the form of an allotment of shares credited as fully paid up, provided that our members entitled thereto will be entitled to elect to receive such dividend (or part thereof if our board of directors so determines) in cash in lieu of such allotment; or (b) that the members entitled to such dividend shall be entitled to elect to receive an allotment of shares credited as fully paid up in lieu of the whole or such part of the dividend as our board of directors may think fit. We may upon the recommendation of our board of directors by ordinary resolution resolve in respect of any one particular dividend of our company that notwithstanding the provisions as set out in our amended and restated memorandum and articles of association in respect of the foregoing, a dividend may be satisfied wholly in the form of an allotment of shares credited as fully paid up without offering any right to members to elect to receive such dividend in cash in lieu of such allotment.

Voting Rights

Under our amended and restated memorandum and articles of association, subject to any special rights or restrictions as to voting for the time being attached to any shares by or in accordance with the articles of the association of our company, at any general meeting on a poll every member present in person or by proxy or, in the case of a member being a corporation, by its duly authorized representative shall have one vote for every fully paid share of which he is the holder but no amount paid up or credited as paid up on a share in advance of calls or installments is treated for the foregoing purposes as paid up on the share; and where a show of hands is allowed, every member present in person or by proxy (or, in the case of a member being a corporation, by its duly authorized representative) shall have one vote. A resolution put to the vote of a meeting shall be decided by way of a show of hands or, where required by the rules of any designated stock exchange, by way of a poll, save that the chairman of the meeting may in good faith, allow a resolution which relates purely to a procedural or administrative matter to be voted on by a show of hands in which case every member present in person (or being a corporation, is present by a duly authorized representative), or by proxy(ies) shall have one vote provided that where more than one proxy is appointed by a member which is a clearing house (or its nominee(s)), each such proxy shall have one vote on a show of hands. For purposes of the articles of association of our company, procedural and administrative matters are those that (i) are not on the agenda of the general meeting or in any supplementary circular that may be issued by our company to its members; and (ii) relate to the chairman's duties to maintain the orderly conduct of the meeting and/or allow the business of the meeting to be properly and effectively dealt with, whilst allowing all members a reasonable opportunity to express their views.

Where a show of hands is allowed, before or on the declaration of the result of the show of hands, a poll may be demanded (a) by the chairman of such meeting, or (b) by at least five members present in person or in the case of a member being a corporation by its duly authorized representative or by proxy for the time being entitled to vote at the meeting, or (c) by a member or members present in person or in the case of a member being a corporation by its duly authorized representative or by proxy and representing not less than one-tenth of the total voting rights of all members having the right to vote at the meeting, or (d) by a member or members present in person or in the case of a member being a corporation by its duly authorized representative or by proxy and holding shares in our company conferring a right to vote at the meeting being shares on which an aggregate sum has been paid up equal to not less than one-tenth of the total sum paid up on all shares conferring that right.

No member shall, unless our board of directors otherwise determines, be entitled to attend and vote and to be reckoned in a quorum at any general meeting unless he or she is duly registered and all calls or other sums presently payable by him or her in respect of shares in our company have been paid. Where our company has knowledge that any member is, under the rules of the designated stock exchange, required to abstain from voting on any particular resolution of our company or restricted to voting only for or only against any particular resolution of our company, any votes cast by or on behalf of such member in contravention of such requirement or restriction shall not be counted. Furthermore, our amended and restated memorandum and articles of association provide that if any member, or any other person appearing to be interested in shares held by such member, has been duly served with a notice issued by or on behalf of our company requiring disclosure of interests in shares pursuant to Section 793 of the Companies Act 2006 of England and Wales and is in default for the prescribed period referred to in the article of association of our company in supplying to our company the information thereby required, then the directors of our company may in their absolute discretion at any time thereafter serve a notice, called a Direction Notice, upon such member in accordance with the articles of association of our company, pursuant to which such member may be precluded from attending, voting or being reckoned in a quorum at any general meeting. The Direction Notice may direct that such member shall not be entitled to vote or exercise any right conferred by membership in relation to meetings of our company in respect of the shares to which the notice relates. Where the holding represents at least 0.25% of the share capital of our company, then the Direction Notice may additionally direct that (i) in respect of such shares, any dividends or other money which would otherwise be payable on such shares shall be retained by our company without any liability to pay interest thereon when such money is finally paid to the member; and/or (ii) no transfer of any of the shares held by such member shall be registered unless: (a) the member is not himself in default as regards supplying the information required and (b) the transfer is of part only of the member's holding and when presented for registration is accompanied by a certificate of the member in a form satisfactory to the directors of our company to that effect that after due and careful enquiry the directors of our company are satisfied that no person in default as regards supplying such information is interested in any of the shares which are the subject of the transfer.

Under our amended and restated memorandum and articles of association, a resolution shall be an ordinary resolution when it has been passed at a meeting by a simple majority of votes cast by such members as, being entitled so to do, vote in person or, in the case of any member being a corporation, by its duly authorized representative or, where proxies are allowed, by proxy at a general meeting of which notice has been duly given in accordance with the articles of association of our company, while a resolution shall be a special resolution when it has been passed by a majority of not less than three-fourths of votes cast by such members as, being entitled so to do, vote in person or, in the case of any member being a corporation, by its duly authorized representative or, where proxies are allowed, by proxy at a general meeting of which notice has been duly given in accordance with the articles of association of our company. Both ordinary resolutions and special resolutions may also be passed by a unanimous written resolution signed by all the shareholders of our company, as permitted by the Companies Act and our amended and restated memorandum and articles of association. A special resolution will be required for important matters such as a change of name or making changes to our amended and restated memorandum and articles of association. Holders of the ordinary shares may, among other things, divide or consolidate their shares by ordinary resolution.

Subject to the provisions set forth below, any of our shareholders may transfer all or any of his or her ordinary shares by an instrument of transfer in the usual or common form or in a form prescribed by the designated stock exchange or in in any other form approved by our board of directors and may be under hand or, if the transferor or transferee is a clearing house or its nominee(s), by hand or by machine imprinted signature or by such other manner of execution as our board of directors may approve from time to time. Notwithstanding the above, for so long as any shares are listed on the designated stock exchange, title to such listed shares may be evidenced and transferred in accordance with the laws applicable to and the rules and regulations of the designated stock exchange that are or shall be applicable to such listed shares. The register of members of our company in respect of its listed shares (whether the principal register or a branch register) may be kept by recording the particulars required by Section 40 of the Companies Act in a form otherwise than legible if such recording otherwise complies with the laws applicable to and the rules and regulations of the designated stock exchange that are or shall be applicable to such listed shares.

Our board of directors may, in its absolute discretion, and without giving any reason therefor, refuse to register a transfer of any share (not being a fully paid up share) to a person whom it does not approve, or any share issued under any share incentive scheme for employees upon which a restriction on transfer imposed thereby still subsists, and it may also, without prejudice to the foregoing generality, refuse to register a transfer of any share to more than four joint holders or a transfer of any share (not being a fully paid up share) on which our company has a lien. Our board of directors may decline to recognize any instrument of transfer unless:

- a fee of such maximum sum as the rules of any designated stock exchange may determine to be payable or such lesser sum as our board of directors may from time to time require is paid to our company in respect thereof;

- the instrument of transfer is in respect of only one class of share;

- the instrument of transfer is lodged at the registered office of our company or such other place at which the register of members is kept in accordance with the Companies Act or the registration office (as the case may be) accompanied by the relevant share certificate(s) and such other evidence as our board of directors may reasonably require to show the right of the transferor to make the transfer (and, if the instrument of transfer is executed by some other person on his or her behalf, the authority of that person so to do); and

- if applicable, the instrument of transfer is duly and properly stamped.

If our board of directors refuses to register a transfer of any share, it shall, within two months after the date on which the transfer was lodged with our company, send to each of the transferor and the transferee notice of such refusal.

Notwithstanding above, our board of directors may permit shares of any class to be held in uncertificated form to be transferred without an instrument of transfer by means of a relevant system, including (without limitation) CREST, an electronic settlement system for U.K. and Irish securities operated by Euroclear UK & Ireland Limited for the paperless settlement of securities in uncertificated form.

Where any class of shares is a participating security and our company is entitled under the Companies Act, our articles of association or any applicable regulations to sell, transfer, dispose of, forfeit, re-allot, accept the surrender of or otherwise enforce a lien over a share held in uncertificated form without an instrument of transfer, our company shall be entitled, subject to the Companies Act, our articles of association, any applicable regulations and the facilities and requirements of the relevant system:

- to require the holder of that uncertificated share by notice to change that share into certificated form within the period specified in the notice and to hold that share in certificated form so long as required by our company;

- to require the holder of that uncertificated share by notice to give any instructions necessary to transfer title to that share by means of the relevant system within the period specified in the notice;

- to require the holder of that uncertificated share by notice to appoint any person to take any step, including without limitation the giving of any instructions by means of the relevant system, necessary to transfer that share within the period specified in the notice; and

- to take any action that our board of directors considers appropriate to achieve the sale, transfer, disposal of, forfeiture, re-allotment or surrender of that share or otherwise to enforce a lien in respect of it.

The registration of transfers of shares or of any class of shares may, after notice has been given by advertisement in any newspapers or by any other means in accordance with the requirements of any designated stock exchange to that effect, be suspended and the register closed at such times and for such periods (not exceeding in the whole thirty (30) days in any year or such longer period as our members may by ordinary resolution determine, provided that such period shall not be extended beyond sixty (60) days in any year) as our board may determine.

Liquidation

Under our amended and restated memorandum and articles of association, subject to any special rights, privileges or restrictions as to the distribution of available surplus assets on liquidation for the time being attached to any class or classes of shares (i) if our company shall be wound up and the assets available for distribution amongst the members of our company shall be more than sufficient to repay the whole of the capital paid up at the commencement of the winding up, the excess shall be distributed pari passu amongst such members in proportion to the amount paid up on the shares held by them respectively and (ii) if our company shall be wound up and the assets available for distribution amongst the members as such shall be insufficient to repay the whole of the paid-up capital such assets shall be distributed so that, as nearly as may be, the losses shall be borne by the members in proportion to the capital paid up, or which ought to have been paid up, at the commencement of the winding up on the shares held by them respectively.

If our company shall be wound up (whether the liquidation is voluntary or by the court) the liquidator may, with the authority of a special resolution and any other sanction required by the Companies Act, divide among the members in specie or kind the whole or any part of the assets of our company and whether or not the assets shall consist of properties of one kind or shall consist of properties to be divided as aforesaid of different kinds, and may for such purpose set such value as he or she deems fair upon any one or more class or classes of property and may determine how such division shall be carried out as between the members or different classes of members. The liquidator may, with the like authority, vest any part of the assets in trustees upon such trusts for the benefit of the members as the liquidator with the like authority shall think fit, and the liquidation of our company may be closed and our company dissolved, but so that no contributory shall be compelled to accept any shares or other property in respect of which there is a liability.

Calls on Shares and Forfeiture of Shares

Our board of directors may from time to time make calls upon members in respect of any moneys unpaid on their shares, and each member shall (subject to being given at least 14 clear days' notice specifying the time and place of payment) pay to our company as required by such notice the amount called on such shares. The shares that have been called upon and remain unpaid are subject to forfeiture. Notwithstanding any such forfeiture described above, our board of directors may at any time, before any shares so forfeited shall have been sold, re-allotted or otherwise disposed of, permit the forfeited shares to be bought back upon the terms of payment of all calls and interest due upon, and expenses incurred in respect of, the shares and upon further terms (if any) as it thinks fit. The forfeiture of a share shall not prejudice the right of our company to any call already made, or installment payable, thereon.

Redemption, Repurchase and Surrender of Ordinary Shares

Under our amended and restated memorandum and articles of association, subject to the Companies Act, our amended and restated memorandum and articles of association and the rules of any designated stock exchange and/or any competent regulatory authority, any power of our company to purchase or otherwise acquire its own shares shall be exercisable by our board of directors in such manner, upon such terms and subject to such conditions as it thinks fit. Furthermore, under the Companies Act, the redemption or repurchase of any share may be paid out of our company's profits or out of the share premium account or out of the proceeds of a fresh issue of shares made for the purpose of such redemption or repurchase, or out of capital if our company is able to, immediately following such payment, pay its debts as they fall due in the ordinary course of business. In addition, under the Companies Act no such share may be redeemed or repurchased (a) unless it is fully paid, (b) if as a result of the redemption or repurchase would result in there being no issued shares of our company other than shares held as treasury shares. Under our amended and restated memorandum and articles of association, our board of directors may accept the surrender of any share liable to be forfeited hereunder and, in such case, references in our amended and restated memorandum and articles of association to forfeiture will include surrender.

Variations of Rights of Shares

According to our articles of association and without prejudice to our amended and restated memorandum and articles of association, all or any of the special rights for the time being attached to the shares or any class of shares may, unless otherwise provided by the terms of issue of the shares of that class, from time to time, whether or not our company is being wound up, be varied, modified or abrogated either with the consent in writing of the holders of not less than three-fourths in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a separate general meeting of the holders of the shares of that class. The special rights conferred upon the holders of any shares or class of shares shall not, unless otherwise expressly provided in the rights attaching to or the terms of issue of such shares, be deemed to be varied, modified or abrogated by the creation or issue of further shares ranking pari passu with such existing class of shares.

Issuance of Additional Shares and Pre-emptive Rights

Our amended and restated memorandum and articles of association authorizes our board of directors to issue additional ordinary shares from time to time as our board of directors shall determine, to the extent of available authorized but unissued shares. Our amended and restated memorandum and articles of association provides that, unless our company by special resolution directed otherwise, any new ordinary shares will be offered by our directors for subscription to the holders of the ordinary shares in such proportions as equal (as nearly as possible) the proportion of ordinary shares held by them respectively at that time.

Our amended and restated memorandum and articles of association also provides that, subject to the provisions of the Companies Act and our amended and restated memorandum and articles of association and to any special rights conferred on the holders of any shares or class of shares, any share in our company (whether forming part of the present capital or not) may be issued with or have attached thereto such rights or restrictions whether in regard to dividend, voting, return of capital or otherwise as our company may by ordinary resolution determine or, if there has not been any such determination or so far as the same shall not make specific provision, as our board of directors may determine.

Subject to the provisions of the Companies Act, the rules of any designated stock exchange and our amended and restated memorandum and articles of association, and to any special rights conferred on the holders of any shares or attaching to any class of shares, shares may be issued on the terms that they may be, or at the option of our company or the holder are, liable to be redeemed on such terms and in such manner, including out of capital, as our board of directors may deem fit.

Subject to the Companies Act, any preference shares may be issued or converted into shares that, at a determinable date or at the option of our company or the holder if so authorized by our amended and restated memorandum and articles of association, are liable to be redeemed on such terms and in such manner as our company before the issue or conversion may be ordinary resolution of the members determine.

Where our company purchases for redemption a redeemable share, purchases not made through the market or by tender shall be limited to a maximum price as may from time to time be determined by our company in general meeting, either generally or with regard to specific purchases. If purchases are by tender, tenders shall be available to all members alike.

Inspection of Books and Records

Our shareholders do not have a general right under the Companies Act to inspect or obtain copies of our list of shareholders or our corporate records. They will, however, have such rights as may be set out in our company's articles of association.

Anti-Takeover Provisions

Some provisions of our amended and restated memorandum and articles of association may discourage, delay or prevent a change of control of our company or management that shareholders may consider favorable, including provisions that limit the ability of shareholders to requisition and convene general meetings of shareholders. However, under Cayman Islands law, our directors may only exercise the rights and powers granted to them under our amended and restated memorandum and articles of association for a proper purpose and for what they believe in good faith to be in the best interests of our company.

General Meetings of Shareholders and Shareholder Proposals

Our shareholders' general meetings may be held in such time and place within or outside the Cayman Islands as our board of directors considers appropriate.

As a Cayman Islands exempted company, we are not obliged by the Companies Act to call shareholders' annual general meetings. Our amended and restated memorandum and articles of association provide that we shall in each year hold a general meeting as our annual general meeting. Our board of directors may whenever it thinks fit call extraordinary general meetings.

Cayman Islands law does not provide shareholders with an express right to put any proposal before a general meeting. However, these rights may be provided in a company's articles of association. Our amended and restated memorandum and articles of association allow our shareholders holding shares representing in aggregate not less than one-tenth of the paid up capital of our company carrying the right of voting at general meetings of our company shall at all times have the right, by written requisition to our board of directors or the secretary of our company, to require an extraordinary general meeting to be called by the board of directors for the transaction of any business specified in such requisition; however, our amended and restated memorandum and articles of association do not provide our shareholders with any right to put any proposals before annual general meetings or extraordinary general meetings not called by such shareholders.

Exempted Company

We are an exempted company with limited liability under the Companies Act. Any company that is registered in the Cayman Islands and the objects of which are to be carried out mainly outside of the Cayman Islands may apply to be registered as an exempted company.

Register of Members

Under the Companies Act, our company must keep a register of members and there should be entered therein:

- the names and addresses of the members, the number and class of shares held by each member, the amount paid or agreed to be considered as paid, on such shares, and whether for each relevant category of shares held by a member carries voting rights under the articles of association of the company, and if so, whether such voting rights are conditional; and

- the date on which the name of any person was entered on the register as a member; and the date on which any person ceased to be a member.

In accordance with Section 48 of the Companies Act, the register of members is prima facie evidence of the registered holder or member of shares of a company. Therefore, a person becomes a registered holder or member of shares of our company only upon entry being made in the register of members.

If the name of any person is, without sufficient cause, entered in or omitted from our register of members, or if default is made or unnecessary delay takes place in entering on the register the fact of any person having ceased to be a member of our company, the person or member aggrieved (or any member of our company or our company itself) may apply to the Cayman Islands Grand Court for an order that the register be rectified, and the Court may either refuse such application or it may, if satisfied of the justice of the case, make an order for the rectification of the register.

Differences in Corporate Law

The Companies Act is derived, to a large extent, from the older Companies Acts of England but does not follow recent U.K. statutory enactments, and accordingly there are significant differences between the Companies Act and the current Companies Act of England and Wales. In addition, the Companies Act differs from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of the significant differences between the provisions of the Companies Act applicable to our company and the laws applicable to companies incorporated in the United States and their shareholders.

Mergers and Similar Arrangements

The Companies Act permits mergers and consolidations between Cayman Islands companies and between Cayman Islands companies and non-Cayman Islands companies. For these purposes, (a) “merger” means the merging of two or more constituent companies and the vesting of their undertaking, property and liabilities in one of such companies as the surviving company and (b) a “consolidation” means the combination of two or more constituent companies into a consolidated company and the vesting of the undertaking, property and liabilities of such companies in the consolidated company. A merger of two or more constituent companies under Cayman Islands law requires a plan of merger or consolidation to be approved by the directors of each constituent company and (a) authorization by a special resolution of the members of each constituent company and (b) such other authorization, if any, as may be specified in such constituent company’s articles of association.

A merger between a Cayman Islands parent company and its Cayman Islands subsidiary or subsidiaries does not require authorization by a resolution of shareholders if a copy of the plan of merger is given to every member of each subsidiary company to be merged unless that member agrees otherwise. For this purpose, a subsidiary is a company of which at least 90% of the votes represented by issued shares of the subsidiary company are held by the parent company.

The consent of each holder of a fixed or floating security interest over a constituent company is required unless this requirement is waived by a court in the Cayman Islands.

Save in certain circumstances, a dissident shareholder of a Cayman Islands constituent company is entitled to payment of the fair value of his shares upon dissenting to a merger or consolidation. The exercise of appraisal rights will preclude the exercise of any other rights save for the right to seek relief on the grounds that the merger or consolidation is void or unlawful.

In addition, there are statutory provisions that facilitate the reconstruction and amalgamation of companies approved by (i) a majority in number representing seventy-five percent (75%) in value of creditors, or (ii) seventy-five percent (75%) in value of shareholders or class of shareholders, as the case may be, that are present and voting either in person or by proxy at a meeting, or meetings, convened for that purpose. The convening of the meetings and subsequently the arrangement must be sanctioned by the Grand Court of the Cayman Islands. While a dissenting shareholder has the right to express to the court the view that the transaction ought not to be approved, the Grand Court can be expected to approve the arrangement if it determines that:

- the statutory provisions as to the required majority vote have been met;

- the shareholders have been fairly represented at the meeting in question and the statutory majority are acting bona fide without coercion of the minority to promote interests adverse to those of the class;
- the arrangement is such that may be reasonably approved by an intelligent and honest man of that class acting in respect of his interest; and
- the arrangement is not one that would more properly be sanctioned under some other provision of the Companies Act.

The Companies Act also contains statutory provisions which provide that a company may present a petition to the Grand Court of the Cayman Islands for the appointment of a restructuring officer on the grounds that the company (a) is or is likely to become unable to pay its debts within the meaning of section 93 of the Companies Act; and (b) intends to present a compromise or arrangement to its creditors (or classes thereof) either, pursuant to the Companies Act, the law of a foreign country or by way of a consensual restructuring. The petition may be presented by a company acting by its directors, without a resolution of its shareholders or an express power in its articles of association. On hearing such a petition, the Grand Court of the Cayman Islands may, among other things, make an order appointing a restructuring officer or make any other order as the Court thinks fit.

When a takeover offer is made and accepted by holders of 90% in value of the shares affected within four months, the offeror may, within a two-month period commencing on the expiration of such four month period, require the holders of the remaining shares to transfer such shares on the terms of the offer. An objection can be made to the Grand Court of the Cayman Islands but this is unlikely to succeed in the case of an offer which has been so approved unless there is evidence of fraud or bad faith.

Shareholders' Suits

The Cayman Islands Grand Court Rules allow shareholders to seek leave to continue derivative actions in the name of the company against wrongdoers. In principle, we will normally be the proper plaintiff and a derivative action may not be brought by a minority shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority in the Cayman Islands, exceptions to the foregoing principle apply in circumstances in which:

- a company is acting or proposing to act illegally or beyond the scope of its authority;
- the act complained of, although not beyond the scope of the company's authority, could be effected if authorized by more than a simple majority vote which has not been obtained; or
- those who control the company are perpetrating a "fraud on the minority."

Indemnification of Directors and Executive Officers and Limitation of Liability

Cayman Islands law does not limit the extent to which a company's memorandum and articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our amended and restated memorandum and articles of association require us to indemnify our officers and directors for losses, damages, costs and expenses incurred in their capacities as such unless such losses or damages arise from dishonesty or fraud of such directors or officers. This standard of conduct is generally the same as permitted under the Delaware General Corporation Law for a Delaware corporation.

In addition, we have entered into indemnification agreements with our directors and executive officers that provide such persons with additional indemnification beyond that provided in our amended and restated memorandum and articles of association to the fullest extent permitted by applicable law.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act may be permitted to our directors, officers or persons controlling us under the foregoing provisions, we have been informed that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Duties of Directors

Under Cayman Islands law, our directors have a fiduciary duty to act honestly, in good faith, with skill and care and with a view to our best interests. Our directors also have a duty to exercise skills they actually possess and such care and diligence that a reasonably prudent person would exercise in comparable circumstances. In fulfilling their duty of care to us, our directors must ensure compliance with our amended and restated memorandum and articles of association, as amended and restated from time to time. Our company has the right to seek damages if a duty owed by our directors is breached. Our board of directors has all the powers necessary for managing, and for directing and supervising, our business affairs. The functions and powers of our board of directors include, among others:

- convening shareholders' annual general meetings and reporting its work to shareholders at such meetings; declaring dividends and distributions;
- appointing officers and determining the term of office of the officers;
- exercising the borrowing powers of our company and mortgaging the property of our company; and approving the transfer of shares in our company, including the registration of such shares in our share register.

A director who is in any way, whether directly or indirectly, interested in a contract or proposed contract with our company shall declare the nature of his or her interest at a meeting of the directors in accordance with the Companies Act and our articles of association. Subject to the Hong Kong Listing Rules and save as provided in the amended and restated memorandum and articles of association of our company, a director shall not vote on any resolution of our board approving any contract, arrangement, transaction or any other proposal whatsoever in which he or any of his or her close associates is materially interested otherwise than by virtue of his or her interests in shares or debentures or other securities of or otherwise in or through our company. A director of our company may not be counted in the quorum at a meeting in relation to any resolution on which that director is prohibited from voting. Our directors may exercise all the powers of our company to borrow money, mortgage our undertaking, property and uncalled capital and issue debentures or other securities whether outright or as collateral security for any debt, liability or obligation of our company or of any third party.

Under Delaware corporate law, a director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: the duty of care and the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director acts in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, the director must prove the procedural fairness of the transaction, and that the transaction was of fair value to the corporation.

Cayman Islands laws do not restrict transactions with directors but a director of a Cayman Islands company is in the position of a fiduciary with respect to the company and a director is required to exercise a duty of care, a duty to act bona fide in the best interests of the company, a duty not to make a profit based on his or her position as director (unless the company permits him to do so) and a duty not to put himself in a position where the interests of the company conflict with his or her personal interest or his or her duty to a third party. A director of a Cayman Islands company also owes to the company a duty to act with skill and care.

Shareholder Action by Written Consent

Under the Delaware General Corporation Law, a corporation may eliminate the right of shareholders to act by written consent by amendment to its certificate of incorporation. Cayman Islands laws and our articles of association provide that shareholders may approve corporate matters by way of a unanimous written resolution signed by or on behalf of each shareholder who would have been entitled to vote on such matter at a general meeting without a meeting being held.

Shareholder Proposals

The Delaware General Corporation Law does not provide shareholders an express right to put any proposal before the annual meeting of shareholders, but in keeping with common law, Delaware corporations generally afford shareholders an opportunity to make proposals and nominations provided that they comply with the notice provisions in the certificate of incorporation or bylaws. The Companies Act does not provide shareholders with an express right to put forth any proposal before the annual general meeting of the shareholders. However, depending on what is stipulated in a company's articles of association, shareholders in an exempted Cayman Islands company may make proposals in accordance with the relevant shareholder requisition provisions. For shares that are represented by ADSs, the depositary in many cases may be the only shareholder. In such cases, only the depositary has the direct right to requisition a shareholders' meeting. However, unless otherwise provided in the deposit agreement, the holders of the ADSs generally do not have the right to petition the depositary to requisition a shareholders' meeting or to put forth shareholder proposals through the depositary.

Cumulative Voting

Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Cumulative voting potentially facilitates the representation of minority shareholders on a board of directors since it permits the minority shareholder to cast all the votes to which the shareholder is entitled on a single director, which increases the shareholder's voting power with respect to electing such director. There are no prohibitions in relation to cumulative voting under the laws of the Cayman Islands, but our articles of association do not provide for cumulative voting. As a result, our shareholders are not afforded any less protections or rights on this issue than shareholders of a Delaware corporation.

Removal of Directors

Under the Delaware General Corporation Law, a director of a corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. Under our amended and restated memorandum and articles of association, directors may be removed by ordinary resolution of our shareholders.

Transactions with Interested Shareholders

The Delaware General Corporation Law contains a business combination statute applicable to Delaware corporations whereby, unless the corporation has specifically elected not to be governed by such statute by amendment to its certificate of incorporation, it is prohibited from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or a group who or which owns or owned 15% or more of the target's outstanding voting share within the past three years. This has the effect of limiting the ability of a potential acquirer to make a two-tiered bid for the target in which all shareholders would not be treated equally. The statute does not apply if, among other things, prior to the date on which such shareholder becomes an interested shareholder, the board of directors approves either the business combination or the transaction which resulted in the person becoming an interested shareholder. This encourages any potential acquirer of a Delaware corporation to negotiate the terms of any acquisition transaction with the target's board of directors.

Cayman Islands law has no comparable statute. As a result, we cannot avail ourselves of the types of protections afforded by the Delaware business combination statute.

Dissolution; Winding up

Under the Delaware General Corporation Law, unless the board of directors approves the proposal to dissolve, dissolution must be approved by shareholders holding 100% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.

A Cayman Islands company may be wound up compulsorily by order of the Court of the Cayman Islands, voluntarily or under supervision of the Court of the Cayman Islands. The Court of the Cayman Islands has authority to order winding up in a number of specified circumstances including where it is, in the opinion of the Court, just and equitable to do so.

A company may be wound up voluntarily when the members so resolve in general meeting by special resolution, or, in the case of a limited duration company, when the period fixed for the duration of the company by its memorandum expires, or the event occurs on the occurrence of which the memorandum provides that the company is to be dissolved, or, the company does not commence business for a year from its incorporation (or suspends its business for a year), or, the company is unable to pay its debts. In the case of a voluntary winding up, such company is obliged to cease to carry on its business from the time of passing the resolution for voluntary winding up or upon the expiry of the period or the occurrence of the event referred to above.

Variation of Rights of Shares

Under the Delaware General Corporation Law, a corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise. Cayman Islands law has no comparable statute.

Amendment of Governing Documents

Under the Delaware General Corporation Law, a corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. Under Cayman Islands law, our amended and restated memorandum and articles of association may only be amended with a special resolution of our shareholders.

Exhibit 4.16

THE SYMBOL “[***]” DENOTES PLACES WHERE CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THE EXHIBIT BECAUSE IT IS BOTH (i) NOT MATERIAL AND (ii) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

EXECUTION VERSION

LICENSE AGREEMENT

by and among

HUTCHMED LIMITED (和记黄埔医药（上海）有限公司)

and

TAKEDA PHARMACEUTICALS INTERNATIONAL AG

and

HUTCHMED (CHINA) LIMITED (和黄医药（中国）有限公司)

January 23, 2023

TABLE OF CONTENTS

TABLE OF CONTENTS (CONTINUED)

TABLE OF CONTENTS (CONTINUED)

TABLE OF CONTENTS (CONTINUED)

LICENSE AGREEMENT

This LICENSE AGREEMENT (the "**Agreement**") is entered into on this 23rd day of January, 2023 (the "**Execution Date**"), by and among HUTCHMED Limited (和记黄埔医药（上海）有限公司), a company organized under the laws of the People's Republic of China, having its registered office at Building 4, 720 Cailun Road, China (Shanghai) Pilot Free Trade Zone, Shanghai 201203, P. R. China ("**HUTCHMED**"), and **Takeda Pharmaceuticals International AG**, a company organized under the laws of Switzerland, having its principal place of business located at Thurgauerstrasse 130, 8152 Glattpark (Opfikon), Switzerland ("**Company**") and, solely for the purposes of Section 11.18 (Guarantees), HUTCHMED (China) Limited (和黄医药（中国）有限公司), a company organized and existing under the laws of the Cayman Islands with its principal offices at PO Box 309, Ugland House, Grand Cayman, KY1-1104, Cayman Islands ("**HUTCHMED GUARANTOR**"). HUTCHMED and Company may each be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, HUTCHMED is a biopharmaceutical company focused on discovering, developing and commercializing therapeutics for the treatment of oncology and immunological diseases;

WHEREAS, Company is a pharmaceutical company with experience and expertise in the research, development and commercialization of pharmaceutical products in the Territory; and

WHEREAS, subject to the terms of this Agreement, HUTCHMED wishes to grant to Company, and Company wishes to receive from HUTCHMED, a license under the Licensed Technology (as defined below) to Develop, Manufacture, Commercialize and otherwise exploit the Licensed Compound and Licensed Products in the Field in the Territory.

AGREEMENT

NOW THEREFORE, in consideration of the mutual promises and covenants set forth below and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

1. DEFINITIONS.

1.1. [***]

1.2. [***]

1.3. "**Abbreviated New Drug Application**" or "**ANDA**" means an Abbreviated New Drug Application as defined in the FD&C Act and the regulations promulgated thereunder which references an NDA or the equivalent application or filing in another country (as applicable).

1.4. "**Acquired Person**" has the meaning set forth in Section 1.22 (Change of Control).

1.5. "**Acquisition Transaction**" has the meaning set forth in Section 2.7.3 (Acquisition of a Competing Product).

1.6. "**Actions**" has the meaning set forth in Section 11.1.2 (Jurisdiction; Venue; Service of Process).

1.7. "**Additional Third Party License**" has the meaning set forth in Section 5.3.3(a) (Third Party Patents).

1.8. "**Adverse Event**" means any adverse medical occurrence in a patient or clinical investigation subject that is administered a pharmaceutical product and which event does not necessarily have to have a causal relationship with the treatment.

1.9. "**Affiliate(s)**" means any entity directly or indirectly controlled by, controlling, or under common control with, a Person, but only for so long as such control exists. For purposes of this definition, "control" (including, with correlative meanings, "controlled by", "controlling" and "under common control with") means (a) possession, direct or indirect, of the power to direct or cause direction of the management or policies of an entity (whether through ownership of securities or other ownership interests, by contract or otherwise), or (b) beneficial ownership of more than fifty percent (50%) (or the maximum ownership interest permitted by Applicable Law) of the voting securities or other ownership or general partnership interest (whether directly or pursuant to any option, warrant or other similar arrangement) or other comparable equity interests of an entity; *provided*, *however*, that where an entity owns a majority of the voting power necessary to elect a majority of the board of directors or other governing board of another entity, but is restricted from electing such majority by contract or otherwise, such entity will not be considered to be in control of such other entity until such time as such restrictions are no longer in effect.

1.10. "**Agreement**" has the meaning set forth in the preamble.

1.11. "**Alliance Manager**" has the meaning set forth in Section 3.3 (Alliance Managers).

1.12. "**Annual Net Sales**" has the meaning set forth in Section 5.3.1 (Royalty Payments).

1.13. "**Antitrust Clearance**" means (a) with respect to an HSR Filing, the date on which the Parties have actual knowledge that all applicable waiting periods under the HSR Act have expired or have been terminated and (b) with respect to any other Antitrust Filings, the date on which the Parties have actual knowledge that all applicable waiting periods have expired or been terminated or all applicable consents have been received with respect to such Antitrust Filings as necessary to permit Company to consummate the transactions contemplated under this Agreement.

1.14. "**Antitrust Filing**" means (a) the HSR Filing, (b) the Austrian filing under Austrian Cartel and Competition Law Amendment Act 2021, (c) the German filing under the Act Against Restraints of Competition (as amended), and (d) any other filing that may arise out of a formal or informal inquiry from a Governmental Authority with respect to the antitrust clearance process.

1.15. "**Applicable Laws**" means all applicable laws, statutes, rules, regulations, treaties (including Tax treaties), orders, judgments or ordinances having the effect of law of any national, multinational, federal, state, provincial, county, city or other political subdivision, including, to the extent applicable, GCP, GLP and cGMP, as well as all applicable data protection and privacy laws, rules and regulations, in each case that may be in effect from time to time during the Term. For the avoidance of doubt, any specific references to any Applicable Law or any portion thereof, will be deemed to include all amendments thereto or any replacement or successor thereto.

1.16. "**BeiGene**" means BeiGene, Ltd., a corporation organized under the laws of the Cayman Islands.

1.17. "**BeiGene Collaboration Agreement**" means that certain clinical collaboration and drug supply agreement, dated May 22, 2020, by and between HUTCHMED and BeiGene, as amended subject to and in accordance with the terms of this Agreement.

1.18. "**Business Day**" means a day other than Saturday, Sunday or any day on which commercial banks located in New York, New York, Tokyo, Japan or Hong Kong, are authorized or obligated by Applicable Laws to close.

1.19. "**Calendar Quarter**" means each of the three (3) consecutive month periods ending on March 31, June 30, September 30, and December 31; *provided* that the first Calendar Quarter during the Term shall begin on the Effective Date and the last Calendar Quarter during the Term shall end on the date of this Agreement's termination or expiration.

1.20. "**Calendar Year**" means each twelve (12) month period beginning on January 1st and ending on the next subsequent December 31st; *provided* that the first Calendar Year during the Term shall begin on the Effective Date and the last Calendar Year during the Term shall end on the date of this Agreement's termination or expiration.

1.21. "**cGMP**" means all applicable current Good Manufacturing Practices, including, as applicable, (a) the principles detailed in the U.S. Current Good Manufacturing Practices, 21 C.F.R. Parts 4, 210, 211, 601, 610 and 820, (b) European Directive 2003/94/EC and Eudralex 4, (c) the principles detailed in the ICH Q7 of ICH

Guidelines, and (d) the equivalent Applicable Laws in the Territory, each as may be amended and applicable from time to time.

1.22. "**Change of Control**" means, with respect to a Person (an "**Acquired Person**"), the occurrence of any of the following events from and after the Effective Date: (a) any Person or group of Persons becomes the beneficial owner (directly or indirectly) of more than fifty percent (50%) of the voting shares of such Acquired Person; (b) such Acquired Person consolidates with or merges into or with another Person pursuant to a transaction in which more than fifty percent (50%) of the voting shares of the acquiring or resulting entity outstanding immediately after such consolidation or merger is not held by the holders of the outstanding voting shares of such Acquired Person immediately preceding such consolidation or merger; or (c) such Acquired Person sells or transfers to a Person other than an Affiliate of such Acquired Person all or substantially all of such Acquired Person's assets. Notwithstanding the foregoing, the following will not constitute a Change of Control: (i) a sale of capital stock to underwriters in an underwritten public offering of a Party's capital stock solely for the purpose of financing, (ii) the acquisition of securities of the Acquired Person by any Person or group of Persons that acquires the Acquired Person's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Acquired Person through the issuance of equity securities, (iii) a transaction solely to change the domicile of a Party; or (iv) a transaction or series of related transactions involving solely the Acquired Person and one or more Affiliates of the Acquired Person.

1.23. "**Clinical Trial**" means any human clinical study of a Licensed Product, including such clinical studies designed to (a) establish that a pharmaceutical product is reasonably safe for continued testing, (b) investigate the safety and efficacy of the pharmaceutical product for its intended use, and to define warnings, precautions and adverse reactions that may be associated with the pharmaceutical product in the dosage range to be prescribed or (c) support Regulatory Approval of such pharmaceutical product or label expansion of such pharmaceutical product.

1.24. "**Combination Licensed Product**" means a Licensed Product that is (a) sold in the form of a combination that contains or comprises the Licensed Compound and one or more other therapeutically active pharmaceutical or biological agents (whether coformulated or copackaged or otherwise sold for a single price) (each of the therapeutically active pharmaceutical or biological agents other than the Licensed Compound, an "**Other Component**") or (b) defined as a "combination product" by the FDA pursuant to 21 C.F.R. §3.2(e) or its foreign equivalent, where such "combination product" is sold for a single price.

1.25. "**Commercial Sales Milestone**" has the meaning set forth in Section 5.2.2 (Commercial Sales Milestones).

1.26. "**Commercial Sales Milestone Event**" has the meaning set forth in Section 5.2.2 (Commercial Sales Milestones).

1.27. "**Commercialization**" means any and all activities of using, importing (other than with respect to investigational or expanded access use), marketing, promoting, distributing, offering for sale or selling a Licensed Product including pre-commercial launch market activities conducted in anticipation of Regulatory Approval of a Licensed Product, seeking Pricing Approvals and reimbursement approvals for a Licensed Product, if applicable, preparing advertising and promotional materials, and sales force training and all activities required to fulfill regulatory obligations relating to Commercialization, including Adverse Event reporting. Commercialization shall not include Development, Manufacturing, or conducting Medical Affairs activities. When used as a verb, "Commercialize" means to engage in Commercialization.

1.28. "**Commercialization Plan**" has the meaning set forth in Section 4.4.4 (Reports of Commercialization Activities).

1.29. "**Commercially Reasonable Efforts**" means:

1.29.1 with respect to the efforts to be expended, or considerations to be undertaken, by Company or its Affiliate with respect to any objective, activity or decision to be undertaken hereunder, reasonable, good faith efforts to accomplish such objective, activity or decision as Company or its Affiliates would normally use to accomplish a similar objective, activity or decision under similar circumstances, it being understood and agreed that with respect to the Development, Manufacture, seeking and obtaining Regulatory Approval, or Commercialization of the Licensed Compound or Licensed Products, such efforts and resources shall be consistent with those efforts and resources commonly used by Company or its Affiliates under similar circumstances for similar compounds or products owned by it or to which it has similar rights, which compound or product, as applicable, is at a similar stage in its development or product life and is of similar market potential, taking into account: (a) issues of efficacy, safety, and expected and actual approved labeling, (b) the expected and actual competitiveness of alternative products sold by Third Parties in the marketplace, (c) the expected and actual product profile, (d) the expected and actual patent and other proprietary position, (e) the likelihood of Regulatory Approval given the regulatory structure involved, including regulatory or data exclusivity, (f) the expected and actual profitability and return on investment of the Licensed Compound or Licensed Product, or other compounds or products in Company's or its Affiliates' portfolio of compounds or products, taking into consideration, among other factors, expected and actual (i) payments to Third Parties and HUTCHMED for services or goods provided in connection with the activities contemplated, (ii) royalty, milestone and other payments to Third Parties and HUTCHMED, and (iii) the pricing and reimbursement relating to the product(s). Commercially Reasonable Efforts shall be determined on a country-by-country and Indication-by-Indication basis for the Licensed Compound or Licensed

Products, as applicable, and it is anticipated that the level of effort and resources that constitute "Commercially Reasonable Efforts" with respect to a particular country or Indication will change over time, reflecting changes in the status of the Licensed Compound or the Licensed Products, as applicable, and the country(ies) involved. Notwithstanding the foregoing, (i) Company or its Affiliates shall not be obligated to Develop, seek Regulatory Approval for, or Commercialize any Licensed Compound or Licensed Product in the Territory: (x) which, in Company's or its Affiliates' reasonable opinion after discussion with HUTCHMED, caused or is likely to cause an unacceptable risk for harm in humans that is reasonably expected based upon then available data, to preclude obtaining Regulatory Approval for such Licensed Product, or, if Regulatory Approval of such Licensed Product has already been obtained, to preclude continued marketing of such Licensed Product; or (y) in a manner inconsistent with Applicable Laws; and (ii) without limiting Company's obligations to use Commercially Reasonable Efforts to seek Pricing Approvals pursuant to Section 4.5.2 (Diligence Obligations), Company or its Affiliates shall not be obligated to Commercialize a Licensed Product in any jurisdiction where such Licensed Product has not received a Pricing Approval applicable to such jurisdiction; and

1.29.2 with respect to the efforts to be expended, or considerations to be undertaken, by HUTCHMED or its Affiliate with respect to any objective, activity or decision to be undertaken hereunder, reasonable, diligent and good faith efforts that HUTCHMED or its Affiliates would normally use to accomplish a similar objective, activity or decision under similar circumstances, for similar compounds or products owned by it or to which it has similar rights, which compound or product, as applicable, is at a similar stage in its development or product life and is of similar market potential, taking into account: (a) issues of efficacy, safety, and expected and actual approved labeling, (b) the expected and actual competitiveness of alternative products sold by Third Parties in the marketplace, (c) the expected and actual product profile, (d) the expected and actual patent and other proprietary position, and (e) the likelihood of Regulatory Approval given the regulatory structure involved, including regulatory or data exclusivity.

1.30. "**Company**" has the meaning set forth in the preamble.

1.31. "**Company Antitrust Clearance Notice**" means the earlier of the date upon which Company notifies HUTCHMED that (a) Company has determined that no ex-U.S. Antitrust Filings are required, and (b) all required Antitrust Filings have received Antitrust Clearance.

1.32. "**Company Combination Product Technology**" means any Know-How or Patent Rights Controlled by Company on the Effective Date or during the Term that is necessary or useful to exploit a Combination Licensed Product.

1.33. "**Company Indemnified Party**" has the meaning set forth in Section 10.1 (Indemnification by HUTCHMED).

1.34. "**Company Know-How**" means all Know-How that (a) is generated by or on behalf of Company, its Affiliates or Sublicensees as a result of the Development, Manufacture, Commercialization or other exploitation of the Licensed Compound or Licensed Products in the Field under this Agreement and (b) is actually used by Company, its Affiliates or Sublicensees in the Development, Manufacture, Commercialization or other exploitation of the Licensed Compound or the Licensed Products in the Field; *provided* that, Company Know-How will not include any Know-How that is not necessary or useful to exploit a Licensed Compound or a Licensed Product containing a Licensed Compound as the sole active ingredient but is necessary or useful to exploit another active ingredient of a Licensed Product other than a Licensed Compound.

1.35. "**Company Patent Rights**" means all Patent Rights that Cover the Company Know-How; *provided* that, Company Patent Rights will not include any intellectual property rights that are not necessary or useful to exploit a Licensed Compound or a Licensed Product containing a Licensed Compound as the sole active ingredient but are necessary or useful to exploit another active ingredient of a Licensed Product other than a Licensed Compound.

1.36. "**Company Technology**" means the Company Patent Rights and the Company Know-How.

1.37. "**Competing Infringement**" has the meaning set forth in Section 8.3.1 (Third Party Infringement).

1.38. "**Competing Product**" means, with respect to a Party, [***].

1.39. "**Confidential Information**" means, with respect to each Party, all Know-How or other information, including proprietary information and materials (whether or not patentable) regarding or embodying such Party's or its Representatives' technology, products, business information or objectives, that is communicated by or on behalf of the Disclosing Party to the Receiving Party or its permitted recipients before, before, on or after the Effective Date. Confidential Information does not include any Know-How or other information that (a) was already known by the Receiving Party (other than under an obligation of confidentiality to the Disclosing Party) at the time of disclosure by or on behalf of the Disclosing Party, (b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party, (c) became generally available to the public or otherwise part of the public domain after its disclosure to the Receiving Party, other than through any act or omission of the Receiving Party in breach of its obligations under this Agreement, (d) was disclosed to the Receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party not to disclose such information to the Receiving Party or (e) was independently discovered or developed by or on behalf of the Receiving Party without the use of any Confidential Information belonging to the Disclosing Party. The terms and conditions of this Agreement will be considered Confidential Information of both Parties.

1.40. “**Control**” **or** “**Controlled**” means, with respect to any intellectual property right, information, documents or materials of a Party, the ability to grant a license, sublicense or other right (including a right of reference) to or under such intellectual property right, information, documents or materials as provided for herein without (a) violating the terms of any agreement with any Third Party, or (b) violating any Applicable Law. Notwithstanding the foregoing, a Party will be deemed not to “Control” any intellectual property rights or rights of reference that are owned or in-licensed by a Third Party (or any Affiliates of such Third Party in existence prior to the Change of Control, other than such Party or its Affiliates) that becomes an Affiliate of such Party (or that merges or consolidates with such Party) after the Effective Date as a result of a Change of Control of such Party unless (i) prior to the consummation of such Change of Control, the Acquired Person or any of its Affiliates also Controlled such intellectual property rights or rights of reference, or (ii) after the consummation of such Change of Control, the Acquired Person or any of its Affiliates uses any such intellectual property rights or rights of reference in the performance of its obligations or exercise of its rights under this Agreement or in connection with the Development, Manufacture, Commercialization or other exploitation of any Licensed Compound or Licensed Product, in each case of clauses (i) and (ii), such intellectual property rights and rights of reference will be “Controlled” by such Party for purposes of this Agreement.

1.41. “**Cover**” means, with respect to a product, that, in the absence of ownership of or a license granted under a particular Patent Right, the Manufacture, use, offer for sale, sale or importation of such product would infringe a claim of such Patent Right or, in the case of a claim of a Patent Right that has not yet issued, would infringe such claim if it were to issue without change. “Covering” will have correlative meaning.

1.42. “**Data Protection Agreement**” has the meaning set forth in Section 4.2.6 (Data Protection Agreement).

1.43. “**Defaulting Party**” has the meaning set forth in Section 9.4.1(a) (Termination for Material Breach).

1.44. “**Development**” means all activities related to research, preclinical testing, test method development and stability testing, toxicology, formulation, Clinical Trials, seeking Regulatory Approval and otherwise handling regulatory affairs (including all interactions and correspondence with a Regulatory Authority in connection therewith, but excluding activities required to fulfill regulatory obligations relating to Commercialization, such as Adverse Event reporting), statistical analysis and report writing, in each case with respect to Licensed Products. Development shall not include Manufacturing, Commercialization or the performance of Medical Affairs activities. When used as a verb, “Develop” means to engage in Development.

1.45. "**Development Costs**" means all direct costs allocable to Development of a Licensed Product in the Field in the Territory and actually incurred by HUTCHMED or its Affiliates in accordance with the HUTCHMED Development Plan, including FTE Costs, reasonable costs of supplies and materials, including clinical supply of Licensed Product, and reasonable amounts paid to Third Parties performing activities on behalf of HUTCHMED or its Affiliates, it being understood that "direct costs" exclude overhead other than as included in the FTE Rate used to calculate FTE Costs.

1.46. "**Development Milestone Event**" has the meaning set forth in Section 5.2.1 (Development Milestones).

1.47. "**Development Milestone Payment**" has the meaning set forth in Section 5.2.1 (Development Milestones).

1.48. "**Development Plan**" has the meaning set forth in Section 4.1.3 (Development Plan).

1.49. "**Disclosing Party**" has the meaning set forth in Section 6.1.1 (Confidential Information).

1.50. "**Divest**" means, with respect to a Competing Product of a Party, the sale, exclusive license or other transfer by such Party and its Affiliates of all of their research, development, manufacturing and commercialization rights with respect to such Competing Product to a Third Party without the retention or reservation of any research, development, manufacturing or commercialization obligation, interest or participation rights (other than solely an economic interest or the right to enforce customary terms contained in the relevant agreements effectuating such transaction).

1.51. "**DOJ**" means the Antitrust Division of the Department of Justice.

1.52. "**Effective Date**" means[***].

1.53. "**European Union**" or "**E.U.**" means the economic, scientific and political organization of member states of the European Union as it may be constituted from time to time, which as of the Execution Date consists of Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and that certain portion of Cyprus included in such organization.

1.54. "**Execution Date**" means the date of this Agreement first set forth above.

1.55. "**Executive Officers**" means the Chief Executive Officer of HUTCHMED, initially Dr. Weiguo Su, or such officer's designee, and the President of Global Oncology Business Unit of Company, initially Teresa Bitetti, or such officer's designee.

1.56. **“Extended Cure Breach”** has the meaning set forth in Section 9.4.1(a) (Termination for Material Breach).

1.57. “**FD&C Act**” means the United States of America Federal Food, Drug, and Cosmetic Act, as amended, and the regulations promulgated thereunder.

1.58. “**FDA**” means the United States of America Food and Drug Administration or any successor agency thereto.

1.59. “**Field**” means all uses and indications.

1.60. “**Financial Records**” has the meaning set forth in Section 5.4.5 (Record Keeping).

1.61. “**First Commercial Sale**” means, with respect to a Licensed Product and any country, the first sale of such Licensed Product under this Agreement for use in the Field in the Territory to a Third Party in an arm’s length transaction in such country, after such Licensed Product has been granted Regulatory Approval for distribution, marketing and sale in the Field in the Territory by the competent Regulatory Authorities in such country. For clarity, the First Commercial Sale will not include distribution or other sale solely for Clinical Trials or under patient assistance, named patient use, compassionate use, or other patient access programs or for charitable or other promotional purposes, in each case, where the Licensed Product is supplied without charge or at or below the costs of goods therefor.

1.62. “**Force Majeure**” has the meaning set forth in Section 11.2 (Force Majeure).

1.63. [***]

1.64. “**FRESCO Clinical Trial**” means a Phase III Clinical Trial in respect of the Licensed Compound conducted by or on behalf of HUTCHMED in patients with locally advanced or metastatic colorectal cancer in the People’s Republic of China, which Clinical Trial is assigned NCT # 02314819 on ClinicalTrials.gov.

1.65. “**FRESCO II Clinical Trial**” means a global Phase III Clinical Trial in respect of the Licensed Compound conducted by or on behalf of HUTCHMED in patients with locally advanced or metastatic colorectal cancer, which Clinical Trial is assigned NCT # 04322539 on ClinicalTrials.gov.

1.66. “**Fruquintinib**” has the meaning set forth in Section 1.110(a) (Licensed Compound).

1.67. “**FTC**” means the Federal Trade Commission.

1.68. “**FTE**” means a full-time scientific or technical person, or in the case of less than a full-time scientific or technical person, a full-time equivalent scientific or technical person year, where “full-time” is based upon a total of 1,800 working hours per Calendar Year of scientific or technical work carried out by an appropriately qualified employee of HUTCHMED or its Affiliates.

1.69. "**FTE Cap**" means [***]

1.70. "**FTE Costs**" means the actual FTEs employed by HUTCHMED or its Affiliates in the conduct of Development activities under the HUTCHMED Development Plan pursuant to Section 4.3.3 (Manufacturing Technology Transfer) multiplied by the FTE Rate.

1.71. "**FTE Rate**" means, [***]

1.72. "**GAAP**" means United States generally accepted accounting principles, as in effect from time to time.

1.73. "**GCP**" means good clinical practices, which are the then-current standards for Clinical Trials for pharmaceuticals, as set forth in the FD&C Act or other Applicable Law, and such standards of good clinical practice as are required by the Regulatory Authorities of the European Union, Japan and other organizations and Governmental Authorities in countries for which the applicable Licensed Product is intended to be Developed, to the extent such standards are not less stringent than United States standards.

1.74. "**Generic Competition**" means [***]

1.75. "**Generic Product**" means, on a country-by-country basis, any pharmaceutical product that (a) is sold in the Territory by a Third Party that is not an Affiliate or Sublicensee of Company under a Regulatory Approval granted by a Regulatory Authority to a Third Party, (b) contains the identical active ingredient(s) (including an active moiety) as an approved Licensed Product and (c) is approved under an ANDA or under 505(b)(2) of the FD&C Act, is approved pursuant to Article 10.1 of Directive 2001/83/EC of the European Parliament and Council of 6 November 2001, or any enabling legislation thereof, or pursuant to any equivalent and comparable Regulatory Authority in other countries or any similar abbreviated route of approval in any other countries.

1.76. "**GLP**" means the then-current good laboratory practice standards promulgated or endorsed by the FDA as defined in 21 C.F.R. Part 58 or the successor thereto, or comparable regulatory standards in jurisdictions outside of the United States, to the extent such standards are not less stringent than United States standards.

1.77. "**Governmental Authority**" means any court, agency, department, authority or other instrumentality of any nation, state, county, city or other political subdivision.

1.78. "**HSR**" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the rules and regulations promulgated thereunder.

1.79. "**HSR Filing**" means a filing by Company and HUTCHMED or their ultimate parent entities as that term is defined in the HSR with the FTC and the DOJ of a Notification and Report Form for Certain Mergers and Acquisitions (as that term is defined in the HSR) with respect to the transactions contemplated under this Agreement together with all required documentary attachments thereto.

1.80. "**HUTCHMED**" has the meaning set forth in the preamble.

1.81. "**HUTCHMED Copyright**" means any copyright Controlled by HUTCHMED or any of its Affiliates as of the Execution Date or thereafter during the Term that are used in the Development, Manufacture, Commercialization or other exploitation of the Licensed Compound and/or the Licensed Products in the Field in the Territory by HUTCHMED or any of its Affiliates.

1.82. "**HUTCHMED Development Costs**" means all Development Costs incurred by HUTCHMED and its Affiliates.

1.83. "**HUTCHMED Development Plan**" has the meaning set forth in Section 4.1.2 (HUTCHMED Development Plan).

1.84. "**HUTCHMED Indemnified Party**" has the meaning set forth in Section 10.2 (Indemnification by Company).

1.85. "**HUTCHMED Manufacturing Know-How**" has the meaning set forth in Section 4.3.3 (Manufacturing Technology Transfer).

1.86. "**HUTCHMED Trademark**" means the Trademarks listed on Schedule 1.86 (HUTCHMED Trademarks).

1.87. "**ICH Guidelines**" mean the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Harmonized Tripartite Guideline.

1.88. "**Identified Licensed Patents**" means (a) the Patent Rights listed in Schedule 1.112 (Licensed Patent Rights), including the PCT or original direct national filing in any country, in each case, claiming priority to an application(s) listed in Schedule 1.112 (Licensed Patent Rights) that are filed on such application(s)); (b) provisional applications not listed in Schedule 1.112 (Licensed Patent Rights) but to which a nonprovisional application identified in clause (a) claims priority; (c) any patent or patent application that is a continuation or divisional or that is a reissue, renewal, reexamination, substitution or extension of any patent application identified in (a); (d) any patents issuing on any patent application identified in (a) or (c), including any reissues, renewals, reexaminations, substitutions or extensions thereof; (e) any continuation-in-part application or resulting patent (including any reissues, renewals, reexaminations, substitutions or extensions thereof) that is entitled to the priority date of, and is directed specifically to subject matter specifically described in, at least one of the patents or patent applications identified in (a); (f) any counterpart in another country or jurisdiction in the Territory (including PCTs) of any patent or patent application identified in (a) or (c) or of the claims identified in (e); and (g) any supplementary protection certificates, pediatric exclusivity periods, and other patent term extensions and exclusivity periods and the like of or based on any patents and patent applications identified in any of (a) through (f).

1.89. "**IFRS**" means International Financial Reporting Standards, as promulgated by the International Accounting Standards Board.

1.90. "**Indemnified Party**" has the meaning set forth in Section 10.3 (Procedure).

1.91. "**Indemnifying Party**" has the meaning set forth in Section 10.3 (Procedure).

1.92. "**Indication**" means a disease, condition, disorder or syndrome. For the avoidance of doubt, different lines of treatment or different subpopulations of patients with a particular disease shall be considered different Indications.

1.93. "**Infringement**" has the meaning set forth in Section 8.3.1 (Third Party Infringement).

1.94. "**Infringement Action**" has the meaning set forth in Section 8.3.2 (Infringement Actions).

1.95. "**Initiating Party**" has the meaning set forth in Section 8.3.2(b) (Procedures).

1.96. "**Innovent**" means Innovent Biologics (Suzhou) Co. Ltd., a company organized under the laws of the People's Republic of China.

1.97. "**Innovent Collaboration Agreement**" means that certain collaboration agreement, dated November 29, 2018, by and between HUTCHMED and Innovent, as amended subject to and in accordance with the terms of this Agreement.

1.98. "**Insolvency Event**" has the meaning set forth in Section 9.4.2 (Termination for Bankruptcy).

1.100. "**Interim Manufacturing Services**" has the meaning set forth in Section 4.3.2 (Interim Manufacturing).

1.101. "**Joint Know-How**" has the meaning set forth in Section 8.1.1 (Inventions).

1.102. "**Joint Patent Rights**" has the meaning set forth in Section 8.1.1 (Inventions).

1.103. "**Joint Technology**" means Joint Know-How, Joint Patent Rights, and all other intellectual property rights in the Joint Know-How.

1.104. "**JSC**" has the meaning set forth in Section 3.1 (Joint Steering Committee).

1.105. "**Know-How**" means all inventions, discoveries, data, information (including scientific, technical or regulatory information), trade secrets, processes, methods, techniques, materials, technology, results, analyses, laboratory data, data arising from Clinical Trials, and other know-how, whether or not patentable, including pharmacology, toxicology, drug stability, manufacturing and formulation data, methodologies and techniques, clinical and non-clinical safety and efficacy studies, marketing studies, absorption, distribution, metabolism and excretion studies.

1.106. "**Knowledge**" means, with respect to HUTCHMED, the actual knowledge that the officers of HUTCHMED after due inquiry of the officers, employees or agents of HUTCHMED or its Affiliates primarily responsible for, and having expertise in, the applicable subject matter(s).

1.107. "**Label Expansion Indication**" means with respect to a Licensed Product that has previously received Regulatory Approval by the FDA, an Indication that would require an additional Regulatory Approval from the FDA in order to permit the commercial marketing and sale of such Licensed Product in such Indication, which Regulatory Approval would result in a modification to the approved labeling of such Licensed Product in the United States to reflect such additional Indication; provided, however, that no Indication consisting solely of a pediatric population or subpopulation shall constitute a Label Expansion Indication.

1.108. "**Lead Indication**" means colorectal cancer, as more particularly defined in the initial Development Plan.

1.109. "**Liability**" has the meaning set forth in Section 10.1 (Indemnification by HUTCHMED).

1.110. "**Licensed Compound**" means (a) the compound identified by HUTCHMED on the Effective Date as fruquintinib, as more fully described in Schedule 1.110(a) ("**Fruquintinib**"), (b) [***].

1.111. "**Licensed Know-How**" means any and all Know-How Controlled by HUTCHMED or any of its Affiliates as of the Effective Date or during the Term that is necessary or reasonably useful to Develop, Manufacture, Commercialize and otherwise exploit any Licensed Compound or Licensed Product in the Territory; *provided* that, Licensed Know-How will not include any intellectual property rights Controlled by HUTCHMED or its Affiliates that are not necessary or useful to exploit a Licensed Compound or a Licensed Product containing a Licensed Compound as the sole active ingredient but are necessary or useful to exploit another active ingredient of a Licensed Product other than a Licensed Compound.

1.112. "**Licensed Patent Rights**" means any and all Patent Rights that are Controlled by HUTCHMED or any of its Affiliates as of the Effective Date or at any time during the Term that (a) Cover the Licensed Know-How or (b) are otherwise necessary or reasonably useful to Develop, Manufacture, Commercialize and otherwise exploit any Licensed Compound or Licensed Product in the Field in the Territory; *provided* that, Licensed Patent Rights will not include any intellectual property rights Controlled by HUTCHMED or its Affiliates that are not necessary or useful to exploit a Licensed Compound or a Licensed Product containing a Licensed Compound as the sole active ingredient but are necessary or useful to exploit another active ingredient of a Licensed Product other than a Licensed Compound. As of the Execution Date, the Licensed Patent Rights are as set forth on Schedule 1.112 (Licensed Patent Rights).

1.113. "**Licensed Product**" means any therapeutic product for any Indication that contains the Licensed Compound, either as the sole active ingredient or in combination with one or more other active ingredients, in all forms, presentations, doses and formulations.

1.114. "**Licensed Product Trademarks**" means the Trademark(s) Controlled or owned by Company, its Affiliates or Sublicensees and used for the Commercialization of Licensed Products in the Territory, and any registrations thereof or any pending applications relating thereto with any Governmental Authority; *provided* that in no event will any HUTCHMED Trademark or any other Trademark owned or Controlled by HUTCHMED or its Affiliates, including Trademarks used by HUTCHMED or its Affiliates to generally identify their respective companies be considered a Licensed Product Trademark.

1.115. "**Licensed Technology**" means the Licensed Know-How and the Licensed Patent Rights.

1.116. "**Life Cycle Indications**" means those Indications identified as "Life Cycle Indications" in accordance with the initial Development Plan.

1.117. "**Major Market Countries**" means [***].

1.118. "**Manufacture,**" "**Manufactured**" **or** "**Manufacturing**" means all activities associated with the production, manufacture, processing, filling, finishing, packaging, labeling, shipping and storage of Licensed Products to be Developed or Commercialized in the Territory under this Agreement (or, solely in relation to HUTCHMED's reporting and other obligations regarding its Development, Commercialization and Medical Affairs activities in the Restricted Territory, in the Restricted Territory), whether such activities are conducted by a Party, its Affiliates or a Third Party contractor of such Party. Manufacture shall not include Development, Commercialization or the performance of Medical Affairs activities. When used as a verb, "Manufacture" means to engage in Manufacturing.

1.119. "**Manufacturing Technology Transfer Agreement**" has the meaning set forth in Section 4.3.3 (Manufacturing Technology Transfer).

1.120. "**Marginal Royalty Rates**" has the meaning set forth in Section 5.3.1 (Royalty Payments).

1.121. "**Maximum FTE Charge**" means, with respect to particular FTE Cost subject to a FTE Cap, the FTE Rate multiplied by the number of FTEs set out in the FTE Cap applicable to such FTE Costs.

1.122. "**Medical Affairs**" means, with respect to a Licensed Product in the Field in the Territory (or, solely in relation to HUTCHMED's reporting and other obligations regarding its Development, Commercialization and Medical Affairs activities in the Restricted Territory, the Restricted Territory), any and all activities performed by or on behalf of a Company's (or, solely in relation to HUTCHMED's reporting and other obligations regarding its Development, Commercialization and Medical Affairs activities in the Restricted Territory, HUTCHMED's) or its Affiliates' medical affairs departments interacting with physicians or other healthcare professionals who utilize or conduct research related to a drug or biological product, including: supporting continuing medical education and other medical programs and communications; development, publication, and dissemination of publications; development and fulfillment of medical information responses; development and execution of disease awareness education including symposia and digital education initiatives; sponsorship and booth exhibition at key congresses; conducting health economic, burden of illness/disease, natural history and real world evidence studies; supporting educational fellowships and research grants, supporting external research efforts such as scientific research agreements and investigator initiated trials (following Regulatory Approval); medical resourcing, training and allocation; medical and scientific platform, content development, publications, and communications; conducting appropriate activities involving opinion leaders, including communications and engagement; conducting medical science liaison activities; advisory boards (to the extent related to medical affairs or clinical guidance) and conducting advisory board meetings or other consultant programs; establishing patient registries and expanded access programs; post-approval investigator initiated trials or scientific research agreements; life cycle management activities and clinical research. Medical Affairs activities shall not include Development, Manufacturing or Commercialization activities.

1.123. **"Medical Journals"** has the meaning set forth in Section 6.1.7(b) (Publication of Results).

1.124. "**Net Sales**" means, with respect to a Licensed Product, the gross amount invoiced in a country in the Territory by or on behalf of a Party or its Affiliates or, with respect to the Territory only, Sublicensees (each of the foregoing Persons, a "**Selling Party**") for the sale or other disposition of such Licensed Product in such country to Third Parties (including Third Party distributors), *less* the following deductions calculated in accordance with IFRS, consistently applied throughout the Territory by the relevant Selling Party, to the extent reasonably allocated to such Licensed Product and actually taken, paid, allowed, or allocated, in the gross sales price with respect to such sales, and not otherwise recovered by or reimbursed to the Selling Party, as set forth below:

1.124.1 cash, trade, or quantity discounts, charge-back payments, and rebates actually granted to trade customers, managed health care organizations, pharmaceutical benefit managers, group purchasing organizations, and national, state, or local Governmental Authorities;

1.124.2 credits, rebates, or allowances actually allowed upon prompt payment or on account of claims, damaged goods, rejections, or returns of such Licensed Product, including in connection with recalls and retroactive price reductions;

1.124.3 the actual amount of any write-offs for bad debt, except any amounts recovered or received will be included;

1.124.4 packaging, freight, postage, shipping, transportation, warehousing, handling and insurance charges, in each case, actually allowed or paid for delivery of such Licensed Product, and any customary payments with respect to such Licensed Product actually made to wholesalers or other distributors, in each case, actually allowed or paid for distribution and delivery of Licensed Product, to the extent billed or recognized;

1.124.5 Taxes to the extent included in the gross amount invoiced (excluding income or franchise Taxes of any kind), duties, tariffs, mandated contribution, or other governmental charges levied on the sale of such Licensed Product, including VAT (net of reimbursement of any VAT actually received), excise Taxes and sales Taxes, that the Selling Party allocates to sales of such Licensed Product in accordance with its standard policies and procedures consistently applied across its products, as applicable; and

1.124.6 any sales, credits, or allowances given or made with respect to Licensed Products for wastage replacement.

All allocations of discounts, allowance, credits, rebates and other deductions must be reasonable. Notwithstanding the foregoing, amounts received or invoiced by Company, its Affiliates, or their respective Sublicensees for the sale of such Licensed Product among Company, its Affiliates, or their respective Sublicensees, for resale will not be included in the computation of Net Sales hereunder. In any event, any amounts received or invoiced by Company, its Affiliates, or their respective Sublicensees, will be accounted for only once. For purposes of determining Net Sales, a Licensed Product will be deemed to be sold when recorded as a sale by Company, its Affiliates, or their respective Sublicensees, in accordance with standard accounting practices, as practiced by Company or such Affiliate or Sublicensee (as the case may be) in the relevant country in the Territory. For clarity, a particular deduction may only be accounted for once in the calculation of Net Sales. Net Sales will exclude any samples of

Licensed Product transferred or disposed of for Clinical Trials or at or below costs of goods therefor for any so-called treatment investigational new drug sales, named patient sales, expanded access program, compassionate or emergency use sales or pre-license sales made for non-commercial, compassionate purpose, or any indigent program or promotional or educational purposes, in all cases if such sale or disposition is at or below costs of goods therefor. For the avoidance of doubt, and for all purposes under this Agreement, Net Sales will be accounted for in accordance with standard accounting practices, as practiced by Company and its Affiliates and Sublicensees in the relevant country in the Territory, but in any event in accordance with IFRS, as consistently applied in such country in the Territory.

In the case of any Combination Licensed Product sold in a given country in the Territory, Net Sales for the purpose of determining royalties and Commercial Sales Milestone Events with respect to the Combination Licensed Product in such country will be calculated by multiplying actual Net Sales of such Combination Licensed Product in such country by the fraction A/(A+B), where A is the invoice price of the Single Active Licensed Product included in such Combination Licensed Product if sold separately as a stand-alone Single Active Licensed Product in such country, and B is the total invoice price of the Other Components in the Combination Licensed Product, if sold separately in such country.

If, on a country-by-country basis, the Single Active Licensed Product included in such Combination Licensed Product is sold separately as a stand-alone Single Active Licensed Product in a country, but the Other Components in the Combination Licensed Product are not sold separately in such country, then Net Sales for the purpose of determining royalties and sales milestone events of the Combination Licensed Product for such country will be calculated by multiplying actual Net Sales of the Combination Licensed Product in such country by the fraction A/C, where A is the invoice price of the Single Active Licensed Product if sold separately as a stand-alone Single Active Licensed Product in such country, and C is the invoice price of the Combination Licensed Product in such country.

If, on a country-by-country basis, the Single Active Licensed Product included in the Combination Licensed Product is not sold separately as a stand-alone Single Active Licensed Product in such country, but the Other Components included in the Combination Licensed Product are sold separately in such country, then Net Sales for the purpose of determining royalties and sales milestone events of the Combination Licensed Product for such country will be calculated by multiplying actual Net Sales of the Combination Licensed Product in such country by the fraction (C-B)/C, where B is the invoice price of the Other Components included in such Combination Licensed Product if sold separately in such country, and C is the invoice price of the Combination Licensed Product in such country.

If neither the Single Active Licensed Product nor the Other Components included in the Combination Licensed Product are sold separately in a given country, then

Net Sales for the purpose of determining royalties and Commercial Sales Milestone Events in such country will be determined by agreement of the Parties based on the relative contribution of the Single Active Licensed Product and the Other Components in the Combination Licensed Product.

1.125. "**New Drug Application**" **or** "**NDA**" means a New Drug Application or, with respect to a subsequent Indication for a Licensed Product in respect of which a New Drug Application was previously approved, a supplemental New Drug Application, filed with the FDA as described in 21 CFR § 314, or any corresponding application for Regulatory Approval (not including pricing and reimbursement approval) in any country or regulatory jurisdiction other than the U.S.

1.126. "**New In-License Agreement**" has the meaning set forth in Section 2.9.1(c) (New In-License Agreements).

1.127. "**Non-Defaulting Party**" has the meaning set forth in Section 9.4.1(a) (Termination for Material Breach).

1.128. "**Ongoing Clinical Trials**" has the meaning set forth in Section 4.1.2 (HUTCHMED Development Plan; Ongoing Clinical Trials).

1.129. "**Other Component**" has the meaning set forth in Section 1.24 (Combination Licensed Product).

1.130. "**Other Safety Information**" means all emerging and known information about the Licensed Products involving known or potential risks to humans including, misuse, abuse, overdose, off-label use, medication error, lack of effect, suspected transmission of an infectious agent, occupational exposure, pregnancy exposure or any use of a falsified product.

1.131. "**Party**" has the meaning set forth in the preamble.

1.132. "**Patent Challenge**" means any action that contests anywhere in the world the scope, validity, or enforceability of a Patent Right in any court, arbitration proceeding, tribunal, or administrative agency, including the U.S. Patent and Trademark Office, European Patent Office, a national court in any country or jurisdiction and the Unified Patent Court (as applicable if and when in force). For clarity, a Patent Challenge shall not include arguments made by a Party that distinguishes the inventions claimed in Patent Rights owned or Controlled by such Party from those claimed in another Patent Right. As used in this definition the term "contest" includes (a) filing an action seeking a determination of invalidity or unenforceability of any such Patent Right; (b) filing, or joining in, a post-grant proceeding, including (i) a petition under 35 U.S.C. § 311 to institute inter partes review of any such Patent Right or (ii) a petition under 35 U.S.C. § 321 to institute post-grant review of any such Patent Right or any portion thereof; (c) filing, or joining in, any opposition, nullity, or similar proceedings challenging the validity of any such Patent Right in any country, (d) filing, or joining in, any derivation proceedings before an administrative agency, interferences, inventorship challenges or any other proceeding that challenges the inventorship or ownership of any such Patent Right, and (e) any foreign equivalent of clauses (a), (b), (c), or (d).

1.133. "**Patent Right**" means any and all (a) patent applications filed under Applicable Law in any jurisdiction, including all provisional applications, substitutions, continuations, continuations-in-part, divisions, renewals, and all patents granted thereon, (b) all patents, reissues, reexaminations and extensions or restorations by existing or future extension or restoration mechanisms, including supplementary protection certificates or the equivalent thereof, and (c) any other form of government-issued right substantially similar to any of the foregoing.

1.134. "**Patient Enrollment (FPD)**" means the first patient receiving the first dose in a Registrational Clinical Trial.

1.135. "**Payments**" has the meaning set forth in Section 5.4.2(a) (General).

1.136. "**Person**" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture, or similar entity or organization, including a government or political subdivision or department or agency of a government.

1.137. "**Pharmacovigilance Agreement**" has the meaning set forth in Section 4.2.5 (Adverse Events).

1.138. "**Potential In-License Notice**" has the meaning set forth in Section 2.9.1(a) (New In-License Agreements).

1.139. "**Pricing Approval**" means any approval, agreement, determination, or decision establishing prices that can be charged to consumers for a pharmaceutical product or that will be reimbursed by Governmental Authorities or other payers for a biopharmaceutical product, in each case, in a country where Regulatory Authorities approve or determine pricing for pharmaceutical products for reimbursement or otherwise.

1.140. **"Publications and Communications Charter"** has the meaning set forth in Section 6.1.7(a) (Publications Committee).

1.141. **"Publications Committee"** has the meaning set forth in Section 6.1.7(a) (Publications Committee).

1.142. "**Quality Agreement**" has the meaning set forth in Section 4.3.4 (Quality Agreement).

1.143. "**Receiving Party**" has the meaning set forth in Section 6.1.1 (Confidential Information).

1.144. "**Recipients**" has the meaning set forth in Section 6.1.1 (Confidential Information).

1.145. "**Registrational Clinical Trial**" means (a) a Clinical Trial that is intended to obtain sufficient data and results to support the filing of a Regulatory Submission and (b) each Clinical Trial as described in 21 C.F.R. §312.21(b) or (c) or, with respect to a jurisdiction other than the United States, a similar Clinical Trial.

1.146. "**Regulatory Approval**" means, with respect to a Licensed Product in a country or jurisdiction in the Territory (or, solely in relation to HUTCHMED's reporting and other obligations regarding its Development, Commercialization and Medical Affairs activities in the Restricted Territory, the Restricted Territory), those approval(s) (including regular or accelerated approval of an NDA), licenses, registrations or authorizations of a Regulatory Authority that are necessary for the commercial marketing and sale of such Licensed Product. Regulatory Approval does not include Pricing Approval.

1.147. "**Regulatory Authority**" means any national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity in each country of the world involved in the granting of Regulatory Approval for a Licensed Product.

1.148. "**Regulatory Exclusivity**" means, with respect to a Licensed Product in a country, any data exclusivity rights or other exclusive right, other than a Patent Right, granted, conferred, or afforded by any Regulatory Authority in such country or otherwise under Applicable Law with respect to such Licensed Product in such country, which either confers exclusive marketing rights with respect to a product or prevents another party from using or otherwise relying on the data supporting the approval of the Regulatory Approval for a product without the prior written authorization of the Regulatory Approval holder, as applicable, such as new chemical entity exclusivity, exclusivity associated with new Clinical Trials necessary to approval of a change (e.g., new indication or use), orphan drug exclusivity, non-patent-related pediatric exclusivity, or any other applicable marketing or data exclusivity, including any such periods under national implementations in the EU of Article 10 of Directive 2001/83/EC, Article 14(11) of Parliament and Council Regulation (EC) No 726/2004, Parliament and Council Regulation (EC) No 141/2000 on orphan medicines, Parliament and Council Regulation (EC) No 1901/2006 on medicinal products for pediatric use and all international equivalents.

1.149. "**Regulatory Submission Transfer Date**" has the meaning set forth in Section 4.2.1 (Transfer of Regulatory Submissions).

1.150. "**Regulatory Submissions**" means applications for Regulatory Approval, notification and other submissions made to or with a Regulatory Authority that are necessary or reasonably desirable to Develop, Manufacture or Commercialize a Licensed Product in the Field in a particular country, whether obtained before or after a Regulatory Approval in the country. Regulatory Submissions include, without limitation, investigative new drug applications and NDAs, and amendments and supplements to any of the foregoing and their foreign counterparts, applications for Pricing Approvals and reimbursement approvals, and all proposed labels, labeling, package inserts, monographs, promotional materials and packaging for a Licensed Product in a particular country.

1.151. "**Regulatory Transition Plan**" has the meaning set forth in Section 4.2.1 (Transfer of Regulatory Submissions).

1.152. "**Representatives**" means (a) with respect to Company, Company, its Affiliates, its Sublicensees and each of their respective officers, directors, employees, consultants, contractors and agents and (b) with respect to HUTCHMED, HUTCHMED, its Affiliates, its licensees and each of their respective officers, directors, employees, consultants, contractors and agents.

1.153. "**Restricted Territory**" means mainland People's Republic of China, Hong Kong and Macau.

1.154. "**Right of Reference**" has the meaning set forth in Section 2.4 (Right of Reference).

1.155. "**Royalty Term**" has the meaning set forth in Section 5.3.2 (Royalty Term).

1.156. "**Scientific Meeting**" has the meaning set forth in 6.1.8 (Presentation at Scientific Meetings).

1.157. "**Scientific Paper**" has the meaning set forth in 6.1.7(b) (Publication in Medical Journals).

1.158. [***]

1.159. "**Selling Party**" has the meaning set forth in Section 1.124 (Net Sales).

1.160. "**Single Active Licensed Product**" means a Licensed Product that contains the Licensed Compound as the sole active ingredient.

1.161. "**Standard Product Cost**" means, [***].

1.162. "**Sublicense**" means an agreement or arrangement pursuant to which a license, sublicense, covenant not to sue or other comparable grant of rights under the licenses granted pursuant to Section 2.1 (License to Company) of this Agreement has been granted to a Sublicensee.

1.163. "**Sublicensee**" means an Affiliate or Third Party that is granted a license, sublicense, covenant not to sue or other comparable grant of rights under the licenses granted pursuant to Section 2.1 (License to Company) of this Agreement.

1.164. "**Sublicensee Material Breach**" has the meaning set forth in Section 2.3.2 (Breach of Sublicense).

1.165. "**Supply Agreement**" has the meaning set forth in Section 4.3.2 (Interim Manufacturing).

1.166. "**Supply Price**" means, with respect to any particular Licensed Compound or Licensed Product, the applicable Standard Product Cost, plus [***].

1.167. "**Tax**" or "**Taxes**" means any form of tax or taxation, levy, duty, charge, social security charge, contribution or withholding of whatever nature (including any related fine, penalty, surcharge or interest) imposed by, or payable to, any Governmental Authority in the Territory.

1.168. "**Term**" has the meaning set forth in Section 9.1 (Term).

1.169. "**Terminated Country**" means (a) any country in the Territory with respect to which this Agreement is terminated pursuant to Article 9 (Term and Termination), and (b) in the event of termination of this Agreement in its entirety, all countries in the Territory.

1.170. "**Territory**" means all the countries throughout the world, except for the Restricted Territory.

1.171. [***]

1.172. "**Third Party**" means any Person other than HUTCHMED and its Affiliates and Company and its Affiliates.

1.173. "**Trademark**" means trademarks, trade dress and trade names.

1.174. "**United Kingdom**" or "**U.K.**" means England, Scotland, Wales and Northern Ireland.

1.175. "**United States**" or "**U.S.**" means the United States of America.

1.176. "**Valid Claim**" means claim of (a) any issued and unexpired Identified Licensed Patent that has not been (i) revoked or held unenforceable, unpatentable or invalid by a Governmental Authority of competent jurisdiction in a decision that is not appealable or that has not been appealed within the time allowed for appeal or (ii) abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise, or (b) any patent application that is an Identified Licensed Patent that has not been (i) cancelled, withdrawn or abandoned without being refiled in another application in the applicable jurisdiction or (ii) finally rejected by an administrative agency or Governmental Authority of competent jurisdiction in a decision that is not appealable or that has not been appealed within the time allowed for appeal, provided that, on a country-by-country basis, a patent application pending for [***] from the priority date of such application shall not be considered to have any Valid Claim for purposes of this Agreement [***].

1.177. "**VAT**" means (a) in relation to any jurisdiction within the European Union, the Tax imposed by the EC Council Directive on the common system of value added Tax (2006/112/EC) and any successor or equivalent legislation and any national legislation implementing that directive together with legislation supplemental thereto and the equivalent Tax (if any) in that jurisdiction; and (b) in any other jurisdiction, any other value added, goods and services, consumption or similar Tax chargeable on the supply or deemed supply of goods or services under applicable legislation or regulation but, in each case, excluding any U.S. sales Tax.

1.178. "**VEGFRs**" has the meaning set forth in Section 1.38 (Competing Product).

2. GRANTS OF LICENSES.

2.1. License to Company. Subject to the terms and conditions of this Agreement, HUTCHMED hereby grants to Company (a) an exclusive (including as to HUTCHMED, but subject to Section 2.6 (No Other Rights and Retained Rights)), royalty-bearing, non-transferable (except in accordance with Section 11.8 (Assignment)) license, with the right to grant sublicenses through multiple tiers (solely in accordance with Section 2.3 (Right to Sublicense)), under the Licensed Technology and under HUTCHMED's right, title and interest in the Joint Technology, to Develop, Manufacture, Commercialize, perform Medical Affairs activities, and otherwise exploit the Licensed Compound and Licensed Products in the Field in the Territory and (b) a non-exclusive royalty-bearing, non-transferable (except in accordance with Section 11.8 (Assignment)) license, with the right to grant sublicenses through multiple tiers (solely in accordance with Section 2.3 (Right to Sublicense)), under the Licensed Technology to Manufacture the Licensed Compound and Licensed Products in the Restricted Territory for the purposes of supporting Development, Manufacturing and Commercialization of the Licensed Compound and Licensed Products in the Territory.

2.2. License to HUTCHMED. Company hereby grants to HUTCHMED a non-exclusive, perpetual, fully-paid, irrevocable license, with the right to grant sublicenses through multiple tiers, under the Company Technology, to (a) Manufacture the Licensed Compound and Licensed Products in the Territory for the sole purposes of supporting Development (including obtaining regulatory approval), Manufacturing and Commercialization of the Licensed Compound and Licensed Product in the Restricted Territory, (b) conduct HUTCHMED's other obligations under this Agreement and (c) Develop, Manufacture, Commercialize and otherwise exploit the Licensed Compound and Licensed Products in the Restricted Territory.

2.2.1. In the event that Company or its Affiliate pursues any material Development or Commercialization activities with respect to a particular Combination Product, then, upon HUTCHMED's written request, Company will discuss with HUTCHMED in good faith for a period of up to [***] the possibility of HUTCHMED obtaining a license under any Company Combination Product Technology relating to such Combination Product solely to exploit the same in the Restricted Territory.

2.3. Right to Sublicense.

2.3.1. Company Right to Sublicense.

(a) Company shall have the right to grant Sublicenses through multiple tiers under the rights granted to Company in this Section 2.1 (License to Company), in Section 4.4.2(b) (License to HUTCHMED Trademarks for Commercialization) and in Section 4.4.2(c) (Copyright License), to its Affiliates and to Third Parties for the Development, Manufacture, Commercialization, performance of Medical Affairs activities, and other exploitation of the Licensed Compound and Licensed Products in the Field without HUTCHMED's consent. Notwithstanding any Sublicense, Company will remain liable and responsible for all of Company's duties and obligations contained in this Agreement (including all payments due hereunder), and any act or omission of a Sublicensee which would be a breach of this Agreement if performed (or not performed) by Company shall be deemed a breach by Company of this Agreement.

(b) Each Sublicense (i) shall be consistent with, the terms and conditions of this Agreement; (ii) shall not diminish, reduce or eliminate any of Company's obligations under this Agreement; (iii) shall require the Sublicensee(s) to comply with all applicable terms of this Agreement (except for the payment obligations, for which Company shall remain financially responsible); (iv) shall, if applicable, require that any Sublicensee grant to HUTCHMED a right of reference to the same extent of the right of reference granted to HUTCHMED pursuant to Section 2.4.2 (HUTCHMED Right of Reference); and (v) shall prohibit further sublicensing except on terms consistent with this Section 2.3.1 (Company Right to Sublicense).

2.3.2. Breach of Sublicense. In the event of an uncured material breach by any Sublicensee under a Sublicense that would constitute a material breach of Company's obligations under this Agreement (a "**Sublicensee Material Breach**"), Company shall use Commercially Reasonable Efforts to remedy such Sublicensee Material Breach; *provided*, *however*, that if Company is unable to cure such Sublicensee Material Breach in accordance with Section 9.4.1 (Termination for Material Breach) of this Agreement, such Sublicensee Material Breach shall be deemed to be an uncured material breach by the Company under this Agreement.

2.4. Right of Reference.

2.4.1. Company Right of Reference. HUTCHMED hereby grants to Company and its Sublicensees a "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b) (or any analogous Applicable Law recognized outside of the United States) to (a) subject to the terms of the Data Protection Agreement, all clinical data generated by or on behalf of HUTCHMED in respect of the Licensed Compound or Licensed Products and Controlled by HUTCHMED or its Affiliates and (b) all regulatory materials included in the Regulatory Submissions and Regulatory Approvals Controlled by HUTCHMED or its Affiliates relating to the Licensed Compound or Licensed Products, in each case (a)-(b), to the extent necessary or reasonably useful for Company to make Regulatory Submissions and obtain Regulatory Approval of any Licensed Product in the Field in the Territory and solely for the purpose of making Regulatory Submissions with respect to and obtaining Regulatory Approval of any Licensed Product in the Field in the Territory.

HUTCHMED shall provide a signed statement to this effect, if requested by Company, in accordance with 21 C.F.R. § 314.50(g)(3) (or any analogous Applicable Law recognized outside of the United States).

2.4.2. HUTCHMED Right of Reference. Company hereby grants, and, to the extent requested by HUTCHMED in writing, will cause its applicable Sublicensees to grant, to HUTCHMED and its licensees and sublicensees in respect of the Licensed Compound a "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b) (or any analogous Applicable Law recognized outside of the United States) to (a) subject to the terms of the Data Protection Agreement, all clinical data generated by or on behalf of Company, its Affiliates or Sublicensees in respect of the Licensed Compound or Licensed Products, and (b) all regulatory materials included in the Regulatory Submissions and Regulatory Approvals Controlled by Company, its Affiliates or Sublicensees relating to the Licensed Compound or Licensed Products, in each case ((a)-(b)), to the extent necessary or reasonably useful to make Regulatory Submissions for the Licensed Compound or Licensed Products and obtain Regulatory Approval of any Licensed Product outside of the Territory, and solely for the purpose of making Regulatory Submissions for the Licensed Compound or Licensed Products and obtaining Regulatory Approval of any Licensed Product in the Field outside of the Territory. To the extent necessary or reasonably useful for the foregoing purpose, Company shall provide a signed statement to this effect, if requested by HUTCHMED, in accordance with 21 C.F.R. § 314.50(g)(3) (or any analogous Applicable Law recognized outside of the United States).

2.5. Delivery of Licensed Know-How. Within [***] (in the case of materials and information existing as of the Effective Date), and thereafter during the Term as may be reasonably requested by Company HUTCHMED shall transfer to Company true and complete copies, in English, of all Licensed Know-How necessary, or believed by HUTCHMED in good faith to be reasonably useful to, exploiting the Licensed Compound and Licensed Products (in electronic or hard copy format where applicable); *provided* that, subject to Section 11.3 (Additional Approvals), HUTCHMED will not be required to transfer any Licensed Know-How to the extent any such transfer would violate Applicable Laws applicable as of the time of the intended transfer, in which case HUTCHMED shall notify Company of the scope of the Licensed Know-How so impacted and the details of such Applicable Laws.

2.6. No Other Rights and Retained Rights. No rights, other than those expressly set forth in this Agreement are granted to either Party hereunder, and no additional rights shall be deemed granted to either Party by implication, estoppel or otherwise, with respect to any intellectual property rights. All rights not expressly granted by either Party to the other hereunder are reserved. Without limiting the foregoing, HUTCHMED hereby expressly retains the right (on behalf of itself, its Affiliates and licensees) (a) to perform Manufacturing activities for the Licensed Compound and Licensed Products in the Territory for the purposes of supporting Development (including obtain Regulatory Approval), Manufacturing and Commercialization of the Licensed Compound and Licensed Product in the Restricted Territory, (b) to perform HUTCHMED's other obligations under this Agreement in accordance with the terms and conditions hereof, including under the HUTCHMED Development Plan, and (c) for BeiGene to complete the Clinical Trial currently being conducted in the Republic of Korea pursuant to the BeiGene Collaboration Agreement, as described on Section 7.2.19 of Schedule 7.2 (HUTCHMED Disclosures), subject to and in accordance with Section 4.1.2 hereof.

2.7. Exclusivity.

2.7.1. Exclusivity. Subject to Section 2.7.2 (Development Exclusivity in the European Union and the United Kingdom), 2.7.3 (Acquisition of a Competing Product) and Section 2.8 (Change of Control), during the period from the Effective Date until [***], each Party will not, and will cause its Affiliates to not, directly or indirectly, either itself or in collaboration with a Third Party, Develop (including submitting any applications for Regulatory Approval), Manufacture or Commercialize any Competing Product in the Territory.

2.7.2. Development Exclusivity in the European Union and the United Kingdom. Solely with respect to the European Union and the United Kingdom, each Party's obligation not to directly or indirectly, either itself or in collaboration with a Third Party, Develop (including submitting any applications for Regulatory Approval) any Competing Product will only be effective from the Effective Date until [***].

2.7.3. Acquisition of a Competing Product. Notwithstanding Section 2.7.1 (Exclusivity), if a Party or any of its Affiliates acquires rights to a Competing Product as the result of a merger or acquisition with or of a Third Party other than a Change of Control where such Party or any of its Affiliates is the acquired entity (each, an "**Acquisition Transaction**"), such Party or such Affiliate will, [***] notify the other Party in writing of such acquisition and that such Party or its Affiliate will Divest its rights to such Competing Product, in which case, within [***], such Party or its Affiliate will Divest such Competing Product. Prior to the time of divestiture, the applicable Party and its Affiliates will segregate all research, development, manufacturing or commercialization activities relating to the Competing Product from Development, Manufacture and Commercialization activities with respect to Licensed Compounds or Licensed Products under this Agreement, including ensuring that (a) no personnel involved in performing research, development, manufacturing or commercialization activities with respect to such Competing Product have access to non-public plans or information relating to the Development, Manufacture or Commercialization of Licensed Compounds or Licensed Products under this Agreement and (b) no personnel involved in performing Development, Manufacture or Commercialization activities with respect to Licensed Compounds or Licensed Products under this Agreement have access to non-public plans or information relating to the discovery, research, development, manufacture or commercialization of such Competing Product.

2.8. Change of Control If there is a Change of Control involving a Party (where such Party is the acquired entity), the obligations of Section 2.7.1 (Exclusivity) will not apply to any product that is controlled by the relevant acquirer or its Affiliates and that exists prior to the closing of such Change of Control; provided that (a) the acquired Party and the acquirer and its Affiliates existing immediately prior to the effective date of such Change of Control establish and enforce internal processes, policies, procedures and systems to segregate information relating to any such program from any Confidential Information related to the Licensed Compounds and Licensed Products under this Agreement, (b) the acquirer and its Affiliates existing immediately prior to the effective date of such Change of Control do not use or practice, directly or indirectly, any Patent Rights, Know-How or Confidential Information of the acquired Party or its Affiliates (including any Patent Rights, Know-How or Confidential Information licensed or acquired from the other Party under this Agreement) in such program, and (c) no personnel who were employees or consultants of the acquired Party or its Affiliates at any time prior to or after the Change of Control will conduct any activities under such program.

2.9. Third Party In-Licenses.

2.9.1. <u>New In-License Agreements</u>.

(a) If, during the Term, HUTCHMED identifies any Third Party to any Patent Rights or Know-How that would, if Controlled by HUTCHMED, constitute Licensed Technology because such Patent Right or Know-How is necessary to Develop, Manufacture, Commercialize and otherwise exploit any Licensed Compound or Licensed Product in the Territory in HUTCHMED's reasonable opinion, then HUTCHMED will promptly notify Company thereof in writing, including by providing a summary description of such Patent Rights or Know-How (such notice, a "**Potential In-License Notice**").

(b) After the receipt of a Potential In-License Notice, [***] with such Third Party to obtain rights under or in respect of such Patent Rights or Know-How for exploitation of Licensed Products and Licensed Compounds solely in the Field in the Territory (or any part thereof, in Company's discretion, and *provided* that any license to such Patent Rights or Know-How solely related to the Manufacture of the Licensed Compound or Licensed Product shall be non-exclusive unless otherwise agreed by HUTCHMED). In no event shall HUTCHMED obtain, or permit any of its Affiliates to obtain, any rights under any Patent Right or Know-How that is necessary to Develop, Manufacture, Commercialize and otherwise exploit any Licensed Compound or Licensed Product in the Field in the Territory, including any Patent Right that Covers any Licensed Product or Licensed Compound in any part of the Territory, for the Development, Manufacture, Commercialization or exploitation of any Licensed Compound or Licensed Product in the Field in the Territory without Company's prior written consent; provided, however, that the foregoing shall not preclude HUTCHMED or its Affiliates from obtaining (i) [***].

(c) If Company enters into any such agreement or arrangement contemplated by Section 2.9.1(b) (a "**New In-License Agreement**"), [***] with whom such New In-License Agreement is entered into, subject to and without limitation of Company's rights under this Agreement, including Section 5.3.3(a) hereof.

2.10. Antitrust Filings; Effectiveness.

2.10.1. Each of Company and HUTCHMED (as applicable in each case) agrees to prepare and make the Antitrust Filings relating to this Agreement and the transactions contemplated hereby as soon as reasonably practicable after the Execution Date (but no later than [***] with respect to any HSR filing), and Company shall bear the filing fees associated with any HSR Filing, but each Party shall otherwise bear its own costs in connection with the Austrian and German filings. The Parties agree to cooperate in the antitrust clearance process and to furnish promptly to relevant Governmental Authorities, any information reasonably requested by them in connection with such filings or formal or informal inquiries. With respect to the Antitrust Filings, each of Company and HUTCHMED shall, to the extent practicable, and to the extent permitted by Applicable Laws: (a) promptly notify the other Party of any material communication to that Party from any Governmental Authority and discuss with and permit the other Party to review in advance any proposed written communication to any of the foregoing; (b) not agree to participate in any substantive meeting or discussion with any Governmental Authority in respect of any filings, investigation or inquiry concerning this Agreement unless it consults with the other Party in advance and give the other Party the opportunity to attend and participate thereat; and (c) furnish the other Party with copies of all correspondence and communications (and memoranda setting forth the substance thereof) between them and their Affiliates and their respective Representatives on the one hand, and any Governmental Authority or members of their respective staffs on the other hand, with respect to this Agreement. HUTCHMED and Company, as each deems advisable and necessary, may reasonably designate any competitively sensitive material to be provided to the other under this Section 2.10.1 as "Antitrust Counsel Only Material." Such materials and the information contained therein shall be given only to the outside antitrust counsel of the recipient and shall not be disclosed by such outside counsel to employees, officers, or directors of the recipient Party unless express permission is obtained in advance from the source of the materials or the applicable Party's legal counsel.

2.10.2. In furtherance of obtaining the Antitrust Clearances, HUTCHMED and Company will use their respective Commercially Reasonable Efforts to resolve as promptly as practicable any objections that may be asserted with respect to this Agreement or the transactions contemplated by this Agreement under any antitrust, competition or trade regulatory law. In connection with obtaining such clearance from the FTC, the DOJ or any other Governmental Authority, Company and its Affiliates will not be required to (a) sell, divest (including through a license or a reversion of licensed or assigned rights), hold separate, transfer or dispose of any assets, operations, rights, product lines, businesses or interest therein of Company or any of its Affiliates (or consent to any of the foregoing actions); or (b) litigate or otherwise formally oppose any determination (whether judicial or administrative in nature) by a Governmental Authority seeking to impose any of the restrictions referenced in clause (a) above.

2.10.3. Other than the provisions of this Section 2.10 (Antitrust Filings; Effectiveness), Section 4.1.2(b) (HUTCHMED Development Plan; Ongoing Clinical Trials), Section 4.2.2(e) (Responsibility for Regulatory Interactions), Section 4.2.6 (Data Protection Agreement), Section 4.3.5 (Negotiation of Agreements), Article 6 (Covenants), Section 7.1 (Representations and Warranties of Each Party), Section 7.2 (Additional Representations and Warranties of HUTCHMED), Section 7.3 (Bring Down of HUTCHMED Representations and Warranties), Section 7.4 (Covenants of HUTCHMED), Section 9.2 (Termination for Failure to Obtain Antitrust Clearance), Section 11.1 (Governing Law), Section 11.3 (Additional Approvals), Section 11.5 (Notices), Section 11.7 (Amendment), Section 11.8 (Assignment), Section 11.13 (Publicity), and all definitions necessary to give effect to the foregoing provisions, each of which shall each become effective on the Execution Date, the rights and obligations of the Parties under this Agreement shall not become effective until the Effective Date.

3. DECISION MAKING AND DISPUTE RESOLUTION.

3.1. Joint Steering Committee. Within [***], the Parties shall establish a joint steering committee (the "**JSC**") that will be responsible for receiving status updates, facilitating the exchange of information regarding activities with respect to the Development, Manufacturing, Commercialization and conduct of Medical Affairs activities of or in respect of Licensed Products in the Territory and taking any other actions specifically ascribed to the JSC pursuant to the terms of this Agreement.

3.1.1. Membership. The JSC will consist of an equal number of representatives from each Party and no fewer than two (2) senior representatives from each Party. Company will designate the initial chairperson of the JSC for the period of time ending at the end of the first full Calendar Year of the Term and then the Party designating the chairperson of the JSC shall alternate thereafter on an annual basis. The chairperson will be responsible for calling meetings and setting the agenda (which shall include a list of all participants expected at a meeting) and circulating such agenda at least [***] prior to each meeting and distributing minutes of the meetings for review by the Parties within [***] following such meeting, but will not otherwise have any greater power or authority than any other member of the JSC. JSC members shall have such expertise as appropriate to the activities of the JSC from time to time and the JSC may invite personnel of the Parties having relevant expertise to participate in discussions of the JSC from time to time as appropriate to assist in the activities of the JSC.

3.1.2. Responsibilities. The JSC may discharge its responsibilities through one or more subcommittees. The JSC's responsibilities will include, without limitation:

(a) providing a forum for the discussion of the Parties' activities under this Agreement;

(b) reviewing progress under the HUTCHMED Development Plan and the Development Plan on a semi-annual basis;

(c) reviewing and discussing proposed amendments to the HUTCHMED Development Plan and the Development Plan;

(d) reviewing and commenting on Company's strategy with respect to Regulatory Submissions relating to Licensed Products in the Field in the Territory;

(e) reviewing and discussing the Regulatory Submission Transition Plan set forth on Schedule 4.2.1 (Key Terms of Regulatory Transition Plan);

(f) facilitating the exchange of all data, information, material or results relating to Development of Licensed Products in the Field in the Territory;

(g) discussing the procedures regarding the collection, sharing and reporting of Adverse Event information related to Licensed Products consistent with the Pharmacovigilance Agreement to be entered into in accordance with Section 4.2.5 (Adverse Events);

(h) reviewing and discussing the Commercialization Plan;

(i) discussing matters relevant to coordination between the Parties on matters relevant to the Licensed Compound and Licensed Products in both the Territory and the Restricted Territory;

(j) facilitating the transfer of Know-How pursuant to this Agreement and the Manufacturing Technology Transfer Agreement, including the HUTCHMED Manufacturing Know-How;

(k) establishing the Publications Committee and reviewing and discussing the Publications and Communications Charter; and

(l) performing such other activities as are specifically ascribed to the JSC pursuant to the terms of this Agreement or that the Parties mutually agree in writing shall be the responsibility of the JSC.

3.1.3. Meetings. So long as activities are being performed under the HUTCHMED Development Plan or the Development Plan, the JSC will meet at such frequency as shall be established by the Parties (but not less frequently than [***] per year, unless otherwise agreed between the Parties or requested by HUTCHMED (which requests by HUTCHMED shall not result in the JSC meeting more than [***] per year)). All meetings will be conducted in English. Meetings shall be held telephonically or by video conference. Meetings of the JSC shall be effective only if at least one representative of each Party is in attendance or participating in the meeting. Members of the JSC shall have the right to participate in and vote at meetings by telephone or video conference. Each Party shall be responsible for expenses incurred by its employees and its members of the JSC in attending or otherwise participating in JSC meetings. Each Party shall use reasonable efforts to cause its representatives to attend the meetings of the JSC. If a representative of a Party is unable to attend a meeting, such Party may designate an alternate to attend such meeting in place of the absent representative.

3.1.4. Minutes and Agendas. The minutes of each JSC meeting shall provide a description in reasonable detail of the discussions held at the meeting and a list of any actions, decisions or determinations approved by the JSC. Minutes of each JSC meeting shall be approved or disapproved, and revised as necessary, no later than [***] after the meeting to which the minutes pertain.

3.1.5. Decision-Making. The JSC will not have any decision-making authority and will serve solely as a forum for discussion and guidance. For clarity, the JSC will not have the authority to: (a) modify or amend the terms and conditions of this Agreement; or (b) waive either Party's compliance with the terms of this Agreement. Each Party will retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers or discretion will be delegated to or vested in the JSC.

3.2. Other Committees. The JSC may establish other committees or sub-committees as the Parties mutually deem appropriate. Section 3.1.5 (Decision-Making) shall apply to any such other committee or sub-committee *mutatis mutandis*.

3.3. Alliance Managers. Within [***], each Party shall appoint a representative ("**Alliance Manager**") to facilitate communications between the Parties and to act as a liaison between the Parties with respect to activities to be conducted pursuant to this Agreement. Each Party may replace its Alliance Manager with an alternative representative at any time with prior written notice to the other Party. Each Party's Alliance Manager shall be entitled to attend all JSC and committee meetings. Each Alliance Manager may bring any matter to the attention of the JSC where such Alliance Manager reasonably believes that such matter requires attention of the JSC.

4. DEVELOPMENT, REGULATORY, MANUFACTURE AND COMMERCIALIZATION.

4.1. Development.

4.1.1. General Responsibilities. Subject to Section 4.1.2 (HUTCHMED Development Plan; Ongoing Clinical Trials), Company will have the sole right (including through its Affiliates or Sublicensees), at its own cost and expense, to manage and conduct all Development activities for the Licensed Compound and Licensed Products in the Territory. Company will undertake its Development activities in accordance with all Applicable Laws.

4.1.2. HUTCHMED Development Plan; Ongoing Clinical Trials.

(a) From the Effective Date and subject to the terms of this Agreement, HUTCHMED shall use Commercially Reasonable Efforts to continue or wind-down, as set forth in the HUTCHMED Development Plan, the conduct of Clinical Trials with respect to the Licensed Compound and Licensed Products in, or in respect of, the Territory, that are ongoing as of the Effective Date (such Clinical Trials, the "**Ongoing Clinical Trials**"). Attached hereto as Schedule 4.1.2 (HUTCHMED Development Plan) is a development plan setting out the Ongoing Clinical Trials and their status as of the Execution Date and the Development activities to be conducted by or on behalf of HUTCHMED or its Affiliates in the conduct of the Ongoing Clinical Trials, as well as a budget for such activities which shall be consistent with Section 4.1.4(b) (the "**HUTCHMED Development Plan**"), which HUTCHMED Development Plan may only be amended by mutual agreement of the Parties. Company will reimburse HUTCHMED for the Development Costs incurred by HUTCHMED and its Affiliates from the Effective Date to the extent set forth in the HUTCHMED Development Plan, in accordance with Section 4.1.4 (Development Costs). For clarity, Company shall not reimburse HUTCHMED for any costs and expenses incurred by HUTCHMED in connection with Ongoing Clinical Trials conducted pursuant to the BeiGene Collaboration Agreement. HUTCHMED shall provide all data and results obtained from such Ongoing Clinical Trials to Company promptly following receipt.

(b) HUTCHMED shall not (i) conduct, or permit, agree, or commit to the conduct of, any new Development, Manufacturing, Commercialization or other exploitation activities with respect to any Licensed Compound or Licensed Product in the Field in the Territory under the BeiGene Collaboration Agreement or Innovent Collaboration Agreement in connection with the Licensed Compound or any Licensed Product in the Territory, other than as expressly provided for in the HUTCHMED Development Plan, or (ii) agree to or enter into any amendment of, supplement to or other modification of the BeiGene Collaboration Agreement or Innovent Collaboration

Agreement that relates to the Territory and is not contemplated by the HUTCHMED Development Plan, or could reasonably be expected to, or does, adversely affect the rights granted by HUTCHMED to Company hereunder relating to or affecting the Licensed Compound or the Licensed Product in the Field in the Territory, or (iii) without limiting the foregoing, submit any Ex-China Exclusivity Request (as defined under the Innovent Collaboration Agreement) or consent or agree to any Ex-China Exclusivity Request received, in each case (clauses (i), (ii) and (iii)), other than at the written direction of Company. For clarity, HUTCHMED shall not be limited or restricted in any way from (x) conducting any further Development, Manufacturing, Commercialization or other exploitation activities with respect to any Licensed Compound or Licensed Product solely in the Restricted Territory under the BeiGene Collaboration Agreement or Innovent Collaboration Agreement in connection with the Licensed Compound or any Licensed Product in the Restricted Territory, or (y) agreeing to or entering into any amendment of, supplement to or other modification of the BeiGene Collaboration Agreement or Innovent Collaboration Agreement solely relating to or solely affecting the Licensed Compound or the Licensed Product in the Restricted Territory.

(c) For clarity, HUTCHMED shall not be entitled to expand any Ongoing Clinical Trial or initiate any new Clinical Trial within the Territory without the prior written consent of Company.

4.1.3. <u>Development Plan</u>. During the Term, Company will provide a development plan to HUTCHMED on an annual basis (each a "**Development Plan**"). The initial Development Plan is attached as Schedule 4.1.3 (Initial Development Plan). Each Development Plan will include a written report summarizing (a) except in the case of the initial Development Plan, Company's and its Affiliates' and Sublicensees' Development activities for the Licensed Compound and each Licensed Product since the prior report, including a reasonably detailed summary of all results and data, if any, obtained from such activities, and (b) any planned future Development activities, including those activities it anticipates to initiate or has initiated for the following Calendar Year.

4.1.4. <u>Development Costs</u>.

(a) <u>Company Development Activities</u>. As between the Parties, Company will be responsible for all costs and expenses of any Development activities conducted by Company, its Affiliates, its Sublicensees or its subcontractors hereunder with respect to the Territory.

(b) <u>HUTCHMED Development Costs</u>. Within [***] after each Calendar Quarter during which activities are conducted under the HUTCHMED Development Plan, HUTCHMED will invoice Company for the HUTCHMED Development Costs incurred during such Calendar Quarter that are associated with the conduct of the HUTCHMED Development Plan; *provided*, *however*, that in no event shall HUTCHMED invoice for, or be entitled to compensation for, FTE Costs in connection with such Development activities that exceed the applicable Maximum FTE Charge. Each such invoice shall include a description of the activities conducted, a calculation of the actual FTE Costs applicable to each such individual, and any reasonable out-of-pocket expenses incurred by HUTCHMED and its Affiliates (together with supporting documentation). Company shall reimburse HUTCHMED for such costs actually incurred by HUTCHMED and its Affiliates, up to the applicable Maximum FTE Charge with respect to FTE Costs, within [***] of invoice. For the avoidance of doubt, the FTE Cap and Maximum FTE Charges applicable to such Development Activities shall not limit HUTCHMED's obligation to perform its obligations under Section 4.1.2(a) (HUTCHMED Development Plan; Ongoing Clinical Trials).

4.2. Regulatory Matters.

4.2.1. Transfer of Regulatory Activities. Without limiting Section 2.5 (Delivery of Licensed Know-How), HUTCHMED shall transfer regulatory responsibilities, obligations and Regulatory Submissions (including supporting data and documentation underlying such Regulatory Submissions) in the Territory in respect of the Licensed Compound and Licensed Products to Company or its Third Party designee in accordance with a transition plan that the Parties will agree upon after the Execution Date, which plan shall be in accordance with terms set forth on Schedule 4.2.1 hereto and shall contain such other terms as the Parties shall mutually agree upon in good faith ("**Regulatory Transition Plan**"). The date of such complete transfer, with respect to a particular country in the Territory is referred to herein as the "**Regulatory Submission Transfer Date**".

4.2.2. Responsibility For Regulatory Interactions.

(a) The following shall apply with respect to each country within the Territory in which HUTCHMED or its Affiliate has made, or makes (in accordance with the Regulatory Transition Plan), one or more Regulatory Submissions, during the period from and after the Effective Date and until the Regulatory Submission Transfer Date for such country in the Territory:

(i) HUTCHMED will coordinate all communications with applicable Regulatory Authorities with respect to the Licensed Compound and Licensed Products in the Field in such country, acting in accordance with Company's directions to the extent such instructions do not conflict with Applicable Laws. Company will have the sole right to select the attendees at any meetings with applicable Regulatory Authorities relating to such Regulatory Submissions or otherwise relating to the Licensed Compound or Licensed Products in the Territory to the extent permitted by the applicable Regulatory Authority; *provided*, that Company will consult with HUTCHMED in good faith regarding Company's selection of attendees at such meetings, and HUTCHMED will be permitted to have at least two (2) Representatives in attendance at each such meeting; *provided*, *further*, that if the subject matter of such meeting also relates to other products of HUTCHMED or its Affiliates, Company will be permitted to participate in the portions of such meetings pertaining to such Regulatory Submissions, the Licensed Compound or Licensed Products in the Territory; *provided*, *further*, that HUTCHMED shall use its reasonable efforts to avoid scheduling such meetings that relate to such Regulatory Submissions, the Licensed Compound or Licensed Products in the Territory, on the one hand, and other products of HUTCHMED or its Affiliates, on the other hand.

(ii) Without limiting the foregoing clause (i), HUTCHMED will provide to Company for its review and comment drafts of all Regulatory Submissions to be submitted to Regulatory Authorities in such country for the Licensed Compound and/or any Licensed Products prior to submission within a reasonable amount of time (but not less than [***], unless such time period is not practicable, in which case the maximum amount of time practicable) to allow Company to review and comment thereon and will adhere to Company's directions regarding all such Regulatory Submissions, including with respect to the content thereof and when and if to file the same, to the extent such directions do not conflict with Applicable Law. In addition, HUTCHMED will notify Company of any comments or other correspondence related thereto submitted to or received from any Regulatory Authority in such country for the Licensed Compound or any Licensed Product as soon as practicable and in any event within [***] of such receipt or submission, and will provide Company with copies thereof promptly after its submission or receipt.

(iii) Within [***] after each Calendar Quarter during which activities are conducted by HUTCHMED under this Section 4.2.2(a) (Responsibility for Regulatory Interactions) and Section 4.2.3(a) (Regulatory Cooperation), HUTCHMED will invoice Company for all FTE Costs and reasonable out-of-pocket expenses incurred by HUTCHMED or its Affiliates during such Calendar Quarter that are associated with the coordination and conduct of activities under this Section 4.2.2(a) (Responsibility for Regulatory Interactions) and Section 4.2.3(a) (Regulatory Cooperation); *provided*, *however*, that in no event shall HUTCHMED invoice Company, or be entitled to compensation, for FTE Costs in connection with such activities that exceed the applicable Maximum FTE Charge. Each such invoice shall include a description of the activities conducted, a calculation of the actual FTE Costs applicable to each such individual, and any reasonable out-of-pocket expenses incurred by HUTCHMED and its Affiliates (together with supporting documentation). Company shall reimburse HUTCHMED for all such FTE Costs and reasonable out-of-pocket expenses actually incurred by HUTCHMED and its Affiliates pursuant to the coordination and conduct of activities under this Section 4.2.2(a) (Responsibility for Regulatory Interactions) and Section 4.2.3(a) (Regulatory Cooperation), up to the applicable Maximum FTE Charge with respect to FTE Costs, within [***] of invoice. For the avoidance of doubt, the FTE Cap and Maximum FTE Charges applicable to the activities contemplated by Section 4.2.2(a) (Responsibility for Regulatory Interactions) and Section 4.2.3(a) (Regulatory Cooperation) shall not limit HUTCHMED's obligation to perform its obligations under Section 4.2.2(a) (Responsibility for Regulatory Interactions) and Section 4.2.3(a) (Regulatory Cooperation).

(b) From and after the Regulatory Submission Transfer Date for each country in the Territory, at Company's sole cost and expense, Company will coordinate all communications with applicable Regulatory Authorities with respect to the Licensed Compound and Licensed Product in the Field in such country. Upon the written request of Company, HUTCHMED shall make up to two (2) appropriate Representatives having suitable experience available to participate in meetings (or portions of meetings pertaining to Licensed Products) with applicable Regulatory Authorities relating to Regulatory Submissions in the Territory.

(c) Subject to the roles and responsibilities of the Parties set out in Sections 4.2.2(a) and 4.2.2(b), and subject to the remaining terms and conditions of this Agreement, as between the Parties, Company shall have sole authority in the Territory with respect to (i) obtaining Regulatory Approvals and Pricing Approvals for Licensed Products and subsequently maintaining such Regulatory Approvals and Pricing Approvals, in each case in the Field in the Territory, (ii) communicating with Regulatory Authorities about Licensed Products in the Field in the Territory and (iii) preparing and submitting supplements, communications, annual reports, Adverse Event reports, manufacturing changes, supplier designations and other related regulatory filings and Regulatory Submissions, in each case with respect to the Licensed Product in the Field in the Territory.

(d) Each Party shall keep the JSC reasonably informed regarding the status and progress of its activities conducted pursuant to this Section 4.2.2 (Responsibility for Regulatory Interactions), including, to the extent practicable, providing the JSC with advance notice of all meetings scheduled with a Regulatory Authority (including notice promptly after a request for a meeting received from a Regulatory Authority) involving material Regulatory Submissions and providing summaries of the outcomes of such meetings and any material correspondence relating thereto.

(e) On and after the Execution Date until the Effective Date, HUTCHMED will provide to Company for its review and comment drafts of all material Regulatory Submissions to be submitted to Regulatory Authorities in the Territory for the Licensed Compound and/or any Licensed Products prior to submission within a reasonable amount of time (but not less than [***], unless such time period is not practicable, in which case the maximum amount of time practicable) to allow Company to review and comment thereon, and HUTCHMED will consider any reasonable comments received from Company with respect to such Regulatory Submissions; *provided*, that HUTCHMED shall have the right to make the final decision whether to include any such comments. In addition, HUTCHMED will notify Company of any comments or other correspondence related thereto submitted to or received from any Regulatory Authority in such country for the Licensed Compound and/or any Licensed Product as soon as practicable and in any event within [***] of such receipt or submission and will provide Company with copies thereof promptly after its submission or receipt. In addition, the Parties will negotiate in good faith and finalize the Regulatory Transition Plan as soon as practicable after the Execution Date and in any event within [***].

4.2.3. <u>Regulatory Cooperation</u>.

(a) HUTCHMED shall provide reasonably requested assistance to Company to assist Company in exercising its rights under Section 4.2.2 (Responsibility for Regulatory Interactions), and will otherwise cooperate with Company with respect to Company's Regulatory Submissions in respect of Licensed Products in the Territory and efforts to obtain and maintain Regulatory Approvals for, Licensed Products in the Territory pursuant to Section 4.2.2 (Responsibility for Regulatory Interactions); *provided* that in no event shall HUTCHMED be obligated to provide such assistance beyond the second anniversary of the Effective Date. Company will reimburse HUTCHMED for all such costs in accordance with Section 4.2.2(a)(iii) (Responsibility for Regulatory Interactions).

(b) Company shall provide reasonably requested assistance to HUTCHMED to assist HUTCHMED in performing its obligations under Section 4.2.2 (Responsibility for Regulatory Interactions) and Company will take such actions as are required on its part to complete the transition contemplated by Section 4.2.1 as soon as practicable after the Effective Date.

(c) Except to the extent prohibited under any agreement between HUTCHMED and any licensee in the Restricted Territory as of the Execution Date, if applicable, HUTCHMED shall keep the JSC reasonably informed regarding material communications with Governmental Authorities with respect to the Licensed Compound and Licensed Products in the Restricted Territory, including, to the extent practicable, providing the JSC with advance notice of all meetings scheduled with a Governmental Authority (including notice promptly after a request for a meeting received from a Governmental Authority) involving material regulatory submissions relating to a Licensed Compound or Licensed Product in the Restricted Territory and providing summaries of the outcomes of such meetings and any material correspondence relating thereto. Notwithstanding the foregoing, HUTCHMED will not be required to provide Company with translated versions of any such communications from the language in which they are received.

4.2.4. Regulatory Audits. If a Regulatory Authority desires to conduct an inspection or audit of a Party's facility, or a facility under contract with a Party, with regard to a Licensed Product in the Territory, then such Party shall promptly notify the other Party and permit and cooperate with such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which the audited Party will immediately provide to the other Party), the audited Party shall prepare the response to any such observations and shall provide a copy of such response to the other Party. Where HUTCHMED or its Affiliate, licensee or contract service provider is the audited Party, HUTCHMED shall permit Representatives of Company to observe such inspection or audit at such facility.

4.2.5. Adverse Events. Within [***], the Parties will enter into a customary pharmacovigilance agreement reasonably acceptable to both Parties (the "**Pharmacovigilance Agreement**"). The Pharmacovigilance Agreement will set forth guidelines and procedures for the receipt, investigation, recording, review, communication, reporting and exchange between the Parties of Adverse Event reports and Other Safety Information, that, for purposes of information exchange between the Parties, will include Adverse Events and serious Adverse Events, and any other information concerning or impacting the safety of any Licensed Product or Licensed Compound. Company shall maintain and will be the recognized holder of a global safety database for Adverse Event reports related to the Licensed Compound and Licensed Products received by either Party. Company will respond to safety inquiries regarding Licensed Products in the Field in all countries and territories in the Territory and HUTCHMED will respond to safety inquiries regarding Licensed Products in the Restricted Territory.

4.2.6. Data Protection Agreement. Within [***], the Parties will enter into a customary data protection agreement reasonably acceptable to both Parties containing customary and appropriate provisions in respect of the sharing of such data between the Parties (the "**Data Protection Agreement**"), which shall become effective upon the Effective Date.

4.2.7. Product Information; Labeling; Core Data Sheet. HUTCHMED will transfer ownership of the core data sheet in accordance with the Pharmacovigilance Agreement.

New efficacy, safety, manufacturing, or other emerging data will be incorporated into the core data sheet (by the then-current core data sheet owner), and local labeling updated, in accordance with Applicable Laws and the standard practices of Company. Each Party will notify the other Party of any local labeling changes, whether initiated by a Party or as a result of a request from a Regulatory Authority.

4.3. Manufacture.

4.3.1. General. During the Term, and without limiting the terms [***], Company will have the sole right (including through its Affiliates or Sublicensees), [***], to conduct all Manufacturing activities for the Licensed Compound and Licensed Products in the Territory. Company will undertake its Manufacturing activities in accordance with all Applicable Laws.

4.3.2. Interim Manufacturing. From the Effective Date and, [***], until Company is able to Manufacture and supply sufficient quantities of the Licensed Compound and Licensed Products to fully support its Development and Commercialization activities in the Territory under this Agreement, which Company will seek to be able to do as soon as reasonably practicable following the transfer of HUTCHMED Manufacturing Know-How pursuant to Section 4.3.3 (Manufacturing Technology Transfer), HUTCHMED, either itself or through its Affiliates or contractors, will Manufacture and supply the Licensed Compound and all Licensed Products to support the Development and Commercialization activities in the Territory under this Agreement (the "**Interim Manufacturing Services**"). Subject to and in accordance with the Supply Agreement, for the Licensed Compound and Licensed Products supplied pursuant to the Interim Manufacturing Services, HUTCHMED will charge to, and Company will pay [***]. Within [***], the Parties will negotiate in good faith and enter into a supply agreement, the terms of which shall include the terms set forth in the Supply term sheet attached hereto as Schedule 4.3.2 (Terms of Clinical and Commercial Supply Agreement) and such other terms and conditions as the Parties shall mutually agree upon ("**Supply Agreement**") and corresponding Quality Agreement as described in Section 4.3.4 (Quality Agreement) for the clinical and commercial supply of Licensed Product from HUTCHMED or its Affiliates to Company.

4.3.3. Manufacturing Technology Transfer. Within [***], the Parties will enter into a separate agreement setting forth the terms and conditions under which HUTCHMED will transfer, or have transferred by its contract manufacturing organizations, to Company or its designee, the Licensed Know-How and materials that are necessary or useful to Manufacture the Licensed Compound and Licensed Products in the Territory (the "**HUTCHMED Manufacturing Know-How**"), the terms of which agreement shall include the terms set forth in the Manufacturing Technology Transfer Term Sheet attached hereto as Schedule 4.3.3 (Terms of Manufacturing Technology Transfer) and such other terms and conditions as the Parties shall mutually agree upon (the "**Manufacturing Technology Transfer Agreement**"). Each Party will use reasonable efforts to effect such transfer as soon as reasonably practicable following the Parties entering into the Manufacturing Technology Transfer Agreement regarding such transfer and, in any event, within any timeline contemplated in Schedule 4.3.3 (Terms of Manufacturing Technology Transfer). Any materials provided by HUTCHMED in connection with the transfer of the HUTCHMED Manufacturing Know-How will remain the sole property of HUTCHMED, and Company will (a) use such HUTCHMED Manufacturing Know-How, including any materials transferred in connection therewith, only in the fulfillment of obligations or exercise of rights under this

Agreement, and (b) not use such HUTCHMED Manufacturing Know-How, including any materials received from HUTCHMED, or deliver the same to any Third Party, other than permitted Sublicensees, Subcontractors and Third Party consultants solely for the purpose of Manufacturing the Licensed Compound or Licensed Products in the Territory in accordance with this Agreement, without HUTCHMED's prior written consent. HUTCHMED will provide [***] of HUTCHMED Manufacturing Know-How transfer support free of charge. Within thirty (30) days after the end of each Calendar Quarter, HUTCHMED shall deliver a report to Company of the HUTCHMED Manufacturing Know-How transfer support provided pursuant to this Section 4.3.3 (Manufacturing Technology Transfer), which report shall include a description of activities conducted, the number of hours devoted by each individual performing such activities (regardless of whether or not 1,800 working hours of transfer support has been provided), a calculation of the actual FTE Costs applicable to each such individual (if applicable pursuant to the immediately following sentence), and any reasonable out-of-pocket expenses incurred (together with supporting documentation). Company will reimburse HUTCHMED for (x) the FTE Costs in excess of [***] (if any) and (y) all reasonable out-of-pocket costs, charges, and expenses, in each case clauses (x) and (y), incurred by HUTCHMED and its Affiliates in connection with any HUTCHMED Manufacturing Know-How transfer support. HUTCHMED will invoice Company for any costs, charges and expenses payable by Company pursuant to the immediately preceding sentence quarterly, and, subject to its receipt of the reports of the transfer support provided by HUTCHMED and the audit rights of Company contemplated in Schedule 4.3.3 (Terms of Manufacturing Technology Transfer), Company will pay all invoices submitted by HUTCHMED within [***] of the date of receipt of the invoice.

4.3.4. Quality Agreement. Within [***], and in any event before any Licensed Product may be distributed or Commercialized in the Territory by Company, its Affiliates or Sublicensees, the Parties will enter into a quality agreement, which upon such execution will be attached as a schedule hereto ("**Quality Agreement**") setting forth the Parties', their Affiliates', and their subcontractors' respective responsibilities and procedures regarding complaint handling, quality-specific audit rights (including with respect to compliance with cGMP, GCP and GLP), and other quality-related matters with respect to the Licensed Compound and Licensed Products in the Territory, the terms of which are hereby incorporated into this Agreement by reference, as applicable.

4.3.5. Negotiation of Agreements. The Parties shall negotiate in good faith the final terms of the Manufacturing Technology Transfer Agreement and the Supply Agreement as promptly as practicable after the Execution Date.

4.4. Commercialization and Medical Affairs Activities.

4.4.1. Commercialization Activities. Subject to the terms and conditions of this Agreement, Company and its Sublicensees shall have the sole right (including through its Affiliates or Sublicensees) to conduct Medical Affairs and Commercialization activities for the Licensed Products in the Field in the Territory, including full decision-making authority with respect to pricing, at Company's sole expense. Company shall undertake all such Commercialization and Medical Affairs activities in accordance with all Applicable Laws.

4.4.2. Trademarks for Commercialization; Copyrights.

(a) Licensed Product Trademarks. Company shall select, and will be the exclusive owner of, the Licensed Product Trademarks and shall be solely responsible for applying for, searching, registering, maintaining and defending the registrations for the Licensed Product Trademarks in the Territory, and all goodwill associated therewith will inure to the benefit of Company. Company shall bear all costs of applying for and maintaining registrations for the Licensed Product Trademarks.

(b) License to HUTCHMED Trademarks for Commercialization. HUTCHMED will, upon request by Company, grant (or cause its Affiliates to grant) Company an (with respect to Commercialization) exclusive or (with respect to the conduct of Medical Affairs activities) co-exclusive with HUTCHMED and its Affiliates, royalty-free, fully-paid up, revocable, non-transferable (except in accordance with Section 11.8 (Assignment)) license, with the right to grant Sublicenses through multiple tiers (solely in accordance with Section 2.3 (Right to Sublicense)) under the HUTCHMED Trademarks solely for the purpose of Commercializing, and conducting Medical Affairs activities in respect of the Licensed Products in the Territory. In the event this license is granted to Company, Company shall use the HUTCHMED Trademarks (a) with the Trademark designations set forth on Schedule 1.86 (HUTCHMED Trademarks), (b) in a manner consistent with HUTCHMED's reasonable branding strategy if, and as, communicated in writing to Company and (c) in a manner that will not knowingly interfere with or diminish HUTCHMED's or its Affiliates' rights in the HUTCHMED Trademarks. Company hereby acknowledges and agrees that all use of the HUTCHMED Trademarks will inure to the benefit of HUTCHMED or its Affiliates, as applicable. Company shall not apply for, register, have registered or use any Trademarks that are confusingly similar to the HUTCHMED Trademarks. Following termination of this Agreement, Company shall refrain from all further use of the HUTCHMED Trademarks in the Territory. HUTCHMED and its Affiliates reserve all rights not expressly granted herein to the HUTCHMED Trademarks and will exercise such rights in a manner that will not knowingly interfere with or diminish Company's or its Sublicensee's rights in the HUTCHMED Trademarks. Company will be solely responsible for, and shall use Commercially Reasonable Efforts in, applying for, registering, maintaining and defending the registrations for and enforcing the HUTCHMED Trademarks in the Territory. Company shall bear all costs of applying for, maintaining and defending registrations for and enforcing the HUTCHMED Trademarks in the Territory. HUTCHMED, upon request by Company, will provide (or cause its Affiliates to provide) all reasonable assistance required by Company in order to apply for, register, maintain and defend the registrations for and enforce the HUTCHMED Trademarks in the Territory including the timely execution of any documents relating thereto.

(c) Copyright License. Subject to the terms and conditions of this Agreement, HUTCHMED hereby grants to Company a non-exclusive license, with the right to grant sublicenses through multiple tiers, to use the HUTCHMED Copyrights (i) in connection with the Commercialization of, and conduct of Medical Affairs activities in respect of, the Licensed Compound and Licensed Products in accordance with this

Agreement in the Territory in the Field, and (ii) for carrying out Medical Affairs activities in accordance with this Agreement.

4.4.3. Branding. Company has the sole right to develop the brand, marketing and promotion strategy for the Licensed Products in the Territory.

4.4.4. Reports of Commercialization Activities. Company shall provide HUTCHMED via the JSC with annual reports of the activities it has undertaken with regard to Commercializing Licensed Products in the Field in the Territory. In addition, Company shall submit to the JSC a high level, non-binding, plan of the activities it intends to undertake with regard to Commercializing Licensed Products in the Field in the Territory, including the launch plan for Licensed Products in each Major Market Country for which Regulatory Approval is expected to be received in the following Calendar Year, and Company shall reasonably consider any comments provided by HUTCHMED's representatives on the JSC by Company ("**Commercialization Plan**"). Each Commercialization Plan will be provided to the JSC annually no later than [***] prior to the beginning of each Calendar Year, with the first Commercialization Plan provided no later than [***] prior to the first anticipated Regulatory Approval for a Licensed Product in any Major Market Country.

4.5. Diligence Obligations. During the Term, Company will use Commercially Reasonable Efforts to:

4.5.1. Develop and obtain Regulatory Approval for at least one Licensed Product in each Major Market Country;

4.5.2. Seek Pricing Approval for, if applicable, and Commercialize each Licensed Product in each Major Market Country in which Regulatory Approval for such Licensed Product has been obtained and, in each such Major Market Country in which Regulatory Approval has been obtained for a Licensed Product, Commercialize such Licensed Product in each Indication for which such Licensed Product has obtained Regulatory Approval in such Major Market Country; and

4.5.3. Without limiting Section 4.5.1, Develop and obtain Regulatory Approval for at least one (1) Licensed Product in the Lead Indication and each Life Cycle Indication in the Major Market Countries.

4.6. Audits.

4.6.1. Upon thirty (30) days' prior written notice from Company, HUTCHMED shall permit an independent certified public accounting firm of internationally recognized standing selected by Company and reasonably acceptable to HUTCHMED, to examine, at Company's sole expense, the relevant books and records of HUTCHMED and its Affiliates and subcontractors as may be reasonably necessary to verify the amounts reported by HUTCHMED in accordance with Sections 4.1.4(b) (HUTCHMED Development Costs), Section 4.2.2(a) (Responsibility for Regulatory Interactions) and 4.2.3(a) (Regulatory Cooperation). Company shall be entitled to conduct an audit in accordance with this Section 4.6 (Audits) not more than once in any Calendar Year and such audit shall be limited to the pertinent books and records from any Calendar Year ending not more than three (3) years prior to the date of the request. The accounting firm shall be provided access to such books and records at HUTCHMED's facility(ies) where such books and records are normally kept and such audit shall be conducted during HUTCHMED's normal business hours. Upon completion of the audit, the accounting firm shall provide both Parties with a written report disclosing any discrepancies in the reports submitted by HUTCHMED or payments made by Company, if any, and in each case, the specific details concerning any discrepancies. Any information provided by HUTCHMED to the accounting firm and the written report of the accounting firm shall be the Confidential Information of HUTCHMED.

4.6.2. If a report of an independent public accounting firm submitted to the Parties in accordance with Section 4.6.1 (Audits) shows any overpayment of amounts due under Sections 4.1.4(b) (HUTCHMED Development Costs), Section 4.2.2(a) (Responsibility for Regulatory Interactions) and 4.2.3(a) (Regulatory Cooperation), at Company's election, Company shall receive a credit equal to such overpayment against the other payments otherwise payable to HUTCHMED hereunder or HUTCHMED shall remit to Company within [***] after receipt of such report an amount equal to such overpayment. If such overpayment exceeds [***] of the total amount owed to HUTCHMED for the payments then being audited, HUTCHMED shall remit to Company within [***] after receipt of such report the reasonable fees and expenses of such independent public accounting firm performing the audit, subject to reasonable substantiation thereof.

4.7. HUTCHMED Activities in Restricted Territory. HUTCHMED shall provide the JSC with annual high-level reports of the activities it has undertaken with regard to Developing, Commercializing and conducting Medical Affairs activities with respect to the Licensed Compound and Licensed Products in the Restricted Territory. In addition, HUTCHMED shall submit to the JSC a high level, non-binding, plan of the activities it intends to undertake with respect to Developing, Commercializing and conducting Medical Affairs Activities with respect to the Licensed Compound and Licensed Products in the Restricted Territory in the following Calendar Year. Each such report and plan will be provided to the JSC annually no later than [***] prior to the beginning of each Calendar Year, except that the first such report and plan will be provided to the JSC within [***] after the formation of the JSC. Notwithstanding anything to the contrary in this Section 4.7 (HUTCHMED Activities in Restricted Territory), HUTCHMED will have no obligation to share any information with Company that is not permitted to be disclosed under an agreement between HUTCHMED or its Affiliate, on one hand, and a Third Party on the other hand; *provided* that, (a) for any such agreement entered into after Effective Date, HUTCHMED shall use reasonable efforts to avoid any such restriction in any such agreement and (b) HUTCHMED shall use Commercially Reasonable Efforts to obtain any consent required to share such information with Company.

5. CONSIDERATION.

5.1. Upfront Payment. Within [***], Company will pay to HUTCHMED a one-time, non-refundable, non-creditable payment of Four Hundred Million Dollars ($400,000,000).

5.2. Milestones.

5.2.1. Development Milestones. Company will make one-time milestone payments (each, a "**Development Milestone Payment**") to HUTCHMED upon the first occurrence of each of the development milestone events for a Licensed Product in the Field in the Territory by or on behalf of Company, its Affiliate or Sublicensee set forth below in this Section 5.2.1 (Development Milestones) (each, a "**Development Milestone Event**") for the first Licensed Product to achieve such Development Milestone Event under this Agreement; *provided* that, upon receipt of 3L CRC Approval for the first Licensed Product in the U.S., the E.U. or Japan, as the case may be, the Development Milestone Event with respect to the 4L CRC Approval in the same jurisdiction shall be deemed to have been achieved as well. Company will, as promptly as reasonably practicable, but in no event later than [***] after Company becomes aware of the achievement of a Development Milestone Event, notify HUTCHMED in writing that such Development Milestone Event has occurred, and HUTCHMED will provide Company with an invoice related to the respective Development Milestone Payment. Each of the Development Milestone Payments will be payable to HUTCHMED by Company within [***] of receipt of invoice. The maximum amount payable by Company under this Section 5.2.1 (Development Milestones) if all Development Milestone Events occur (regardless of the number of times they occur or the number of Licensed Products that trigger them) is [***].

EVENT	**MILESTONE PAYMENT**
[***]	
[***]	[***]
[***]	[***]
[***]	[***]
[***]	
[***]	[***]
[***]	[***]
[***]	[***]
[***]	
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

EVENT	MILESTONE PAYMENT
[***]	
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

Subject to the proviso in the first sentence of this Section 5.2.1, the Development Milestone Events above shall be successive.

5.2.2. Commercial Sales Milestones. Company will make a one-time commercial sales milestone payment (each, a "**Commercial Sales Milestone Payment**") to HUTCHMED upon the occurrence of each of the commercial sales-based milestones events (each, a "**Commercial Sales Milestone Event**") set forth below in this Section 5.2.2 (Commercial Sales Milestones). For the avoidance of doubt, each of the Commercial Sales Milestone Payments set forth below will be payable only one time for the first Calendar Year in which the corresponding Commercial Sales Milestone Event is achieved, *provided* that, if more than one Commercial Sales Milestone Event is achieved in a single Calendar Year, each of the payments for the Commercial Sales Milestone Events achieved in such Calendar Year will be paid. Each Commercial Sales Milestone Payment will be invoiced by HUTCHMED within [***] of the end of the Calendar Quarter in which such Commercial Sales Milestone Event is achieved, and will be payable to HUTCHMED by Company within [***] of receipt of invoice. The maximum amount payable by Company under this Section 5.2.2 (Commercial Sales Milestones) if all Commercial Milestone Events occur (regardless of the number of times they occur or the number of Licensed Products that trigger them) is [***].

COMMERCIAL SALES MILESTONE EVENT	COMMERCIAL SALES MILESTONE PAYMENT
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]
First Calendar Year in which aggregate annual Net Sales of Licensed Products in the Territory are [***] or more	[***]

5.3. Royalties. In addition to the payments under Sections 5.2.1 (Development Milestones), and 5.2.2 (Commercial Sales Milestones), in consideration for the rights granted to Company under this Agreement, Company shall pay to HUTCHMED the royalty payments set forth in, and subject to the terms of, this Section 5.3 (Royalties).

5.3.1. Royalty Payments. Subject to the provisions of Section 5.3.3 (Adjustments in Royalty Rates), Company will pay HUTCHMED royalties on a tiered marginal royalty rate basis as set forth below (the "**Marginal Royalty Rates**") based on the portion of the annual aggregate Net Sales in the United States and its territories and possessions, and in the Territory other than the United States and its territories and possessions, respectively, resulting from the sale of all Licensed Products during each Calendar Year of the applicable Royalty Term for each Licensed Product (the "**Annual Net Sales**").

ANNUAL NET SALES (ALL LICENSED PRODUCTS THROUGHOUT (A) THE U.S. AND ITS TERRITORIES AND POSSESSIONS OR (B) TERRITORY (OTHER THAN THE U.S. AND ITS TERRITORIES AND POSSESSIONS), AS APPLICABLE)	**MARGINAL ROYALTY RATE (% OF ANNUAL SUCH NET SALES)**	
	For Net Sales in the U.S. and its territories and possessions	**For Net Sales in the Territory (other than the U.S. and its territories and possessions)**
Less than or equal to [***]	[***]	[***]
More than [***] and less than or equal to [***]	[***]	[***]
More than [***] and less than or equal to [***]	[***]	[***]
More than [***]	[***]	[***]

5.3.2. Royalty Term. On a Licensed Product-by-Licensed Product and country-by-country basis, Company will pay royalties to HUTCHMED for a Licensed Product in a country in the Territory until the later of [***] (the "**Royalty Term**").

5.3.3. Adjustments in Royalty Rates.

(a) Third Party Patents. If Company determines in good faith that a license under one or more Patent Rights of one or more Third Parties is necessary in order to Commercialize any Licensed Product in a country in the Territory without infringing such Patent Right(s), then Company may, in its sole discretion, negotiate and obtain a license under such Patent Right(s) in such country (each such Third Party license referred to herein as an "**Additional Third Party License**"). Subject to Section 5.3.3(d) (Royalty Floor), any royalty otherwise payable to HUTCHMED under this Agreement with respect to Net Sales of any Licensed Product in a country in the Territory by Company, its Affiliates or Sublicensees will be reduced by [***] of the royalties payable to Third Parties pursuant to any Additional Third Party Licenses (to the extent such royalties payable to Third Parties are applicable to such Licensed Product in such country).

(b) No Patent Right Coverage. In the event that, with respect to any particular Licensed Product in a particular country in the Territory, such Licensed Product sold in such country is not covered by a Valid Claim of an Identified Licensed Patent, any royalty payable to HUTCHMED under this Agreement with respect to such Licensed Product in such country shall be, subject to Section 5.3.3(d) (Royalty Floor), reduced by [***] for so long as such lack of Valid Claim coverage exists.

(c) Generic Competition. Subject to Section 5.3.3(d) (Royalty Floor), (i) if, in any Calendar Quarter during the Royalty Term for a given Licensed Product in a given country, the Generic Competition for such Licensed Product in such country is [***].

(d) Royalty Floor. In no event shall the cumulative reduction in royalties under Section 5.3.3(a) (Third Party Patents) through 5.3.3(c) (Generic Competition) reduce the royalties payable to HUTCHMED under Section 5.3.1 for any Licensed Product in any country during any Calendar Quarter by [***] in the aggregate; *provided*, *however*, that in the event that Company is precluded from applying the full amount it would otherwise be entitled to apply in reducing its royalty payments in any Calendar Quarter by virtue of this Section 5.3.3(d) (Royalty Floor), with any reduction in Section 5.3.3(b) (No Patent Right Coverage) or Section 5.3.3(c) (Generic Competition) being applied first, then it shall be permitted to apply such unapplied portion of reductions under Section 5.3.3(a) (Third Party Patents) through 5.3.3(c) (Generic Competition) to reduce its royalty obligations in the next subsequent Calendar Quarter(s).

5.3.4. Fully Paid-Up, Royalty Free License. Following the expiration of the Royalty Term for any Licensed Product in a given country in the Territory, no further royalties shall be payable in respect of sales of such Licensed Product in such country and, thereafter, the license granted to Company under Section 2.1 (License to Company) with respect to such Licensed Product in such country shall automatically become fully paid-up, perpetual, irrevocable, non-terminable and royalty-free.

5.4. Reports and Payments.

5.4.1. Royalty Reports. Within [***] after the end of each Calendar Quarter beginning with the Calendar Quarter in which the First Commercial Sale is made in a country following receipt of Regulatory Approval in such country, Company shall deliver to HUTCHMED a report setting forth for such Calendar Quarter the following information on a Licensed Product-by-Licensed Product basis for such country: (a) the gross sales and Net Sales of each Licensed Product in such country, (b) the number of units sold by Company, its Affiliates or Sublicensees, (c) the basis for any adjustments to the royalty payable for the sale of each Licensed Product, (d) the royalty due hereunder for the Net Sales of each Licensed Product, and (e) the applicable exchange rate as determined in accordance with this Agreement. HUTCHMED will provide Company with an invoice related to the total royalty due for the sale of Licensed Products during such Calendar Quarter set forth in such report and Company will pay the total royalty due for such Calendar Quarter within [***] of receipt of such invoice. No such reports shall be due for any Licensed Product after the relevant Royalty Term for such Licensed Product has expired.

5.4.2. Taxes and Withholding.

(a) General. Any and all amounts payable pursuant to this Agreement ("**Payments**") will be paid without deduction or withholding for any Taxes, except as required by Applicable Law. [***].

(b) VAT and Sales Tax. All Payments, whether monetary or non-monetary are exclusive of VAT and sales Tax and their equivalents. Any Party receiving a supply in connection with the transactions contemplated by this Agreement hereby covenants that it will pay any such VAT or sales Tax correctly charged in addition to any amounts due under this Agreement or a Supply Agreement. Where the prevailing legislation requires a VAT or sales Tax reverse charge, then the receiving Party covenants that it shall correctly account for VAT and sales Tax in respect of the services received. The supplying Party agrees that it will provide a Tax invoice (or equivalent document), compliant with relevant legal and fiscal regulations, to support the charge to VAT or sales Tax. For the purposes of VAT, the services, rights and licenses provided by HUTCHMED under this Agreement shall be considered to be Taxed under by Art 44 of Council Directive 2006/112/EC or any equivalent provision in the country of performance if performed outside the European Union and as such will be considered to be Taxed for VAT and sales Taxes purposes in the country of the recipient. Any supply of goods in connection with the transactions contemplated by this Agreement shall be Taxed (where applicable) in accordance with the prevailing VAT or sales Tax legislation. All Parties agree that they will reasonably cooperate to ensure the use of any VAT or sales Tax exemptions, suspensions or other reliefs if applicable. In the event that the local competent Tax authority determines that VAT or sales Tax is chargeable, HUTCHMED in the first instance shall undertake in close cooperation with Company all reasonable steps to refuse any such assertions by the local Tax authority. Only once this process is completed should HUTCHMED provide valid Tax invoices for the additional VAT or sales Tax liability.

(c) Redomicile or Assignment. [***].

(d) Tax Cooperation. To the extent Company is required to deduct and withhold Taxes on any payments to HUTCHMED, Company will pay the amounts of such Taxes to the proper Governmental Authority in a timely manner and promptly transmit to HUTCHMED an official Tax certificate or other evidence of such withholding sufficient to enable HUTCHMED to claim such payments of Taxes. HUTCHMED will provide to Company any Tax forms that may be necessary in order for Company not to withhold Tax or to withhold Tax at a reduced rate under an applicable bilateral income Tax treaty. [***].

5.4.3. Currency. All amounts payable and calculations hereunder shall be in United States dollars. If, due to restrictions or prohibitions imposed by national or international authority, payments cannot be made as provided in this Section 5, the Parties shall consult with a view to finding a prompt and acceptable solution, and the paying Party shall deal with such monies as the other Party may lawfully direct at no additional out-of-pocket expense to the paying Party.

5.4.4. Method of Payment. Except as permitted pursuant to Section 5.4.3 (Currency), each payment hereunder shall be made by electronic transfer in immediately available funds via a bank wire transfer, an automated clearing house (ACH) mechanism or any other means of electronic funds transfer, at the paying Party's election, to the bank account designated by the Party receiving payments under this Article 5 (Consideration) in writing to the paying Party at least [***] before the payment is due.

5.4.5. Record Keeping. Company shall keep, and shall causes its Affiliates and Sublicensees to keep, books and accounts of record in connection with the sale of Licensed Products, including records of gross invoiced sales, Net Sales, exchange rates and royalty payments (collectively, the "**Financial Records**"), in accordance with IFRS or GAAP (as applicable based on the Company's or its applicable Sublicensees' standard accounting practices) and in sufficient detail to permit accurate determination of all figures necessary for verification of royalties and Commercial Sales Milestone payments to be made by Company under this Article 5.

Company and its Affiliates and Sublicensees shall maintain such records for a period of at least [***] after the end of the Calendar Quarter in which they are generated.

5.4.6. Audits. Upon thirty (30) days prior written notice from HUTCHMED, Company shall permit an independent certified public accounting firm of internationally recognized standing selected by HUTCHMED and reasonably acceptable to Company, to examine, at HUTCHMED's sole expense, the relevant Financial Records of Company and its Affiliates and Sublicensees as may be reasonably necessary to verify the amounts reported by Company in accordance with Section 5.4.1 (Royalty Reports) and the royalties and Commercial Sales Milestone payments made by Company in accordance with this Article 5 (Consideration). HUTCHMED shall be entitled to conduct an audit in accordance with this Section 5.4.6 (Audits) not more than once in any Calendar Year and such audit shall be limited to the pertinent Financial Records from any Calendar Year ending not more than three (3) years prior to the date of the request. The accounting firm shall be provided access to such Financial Records at Company's facility(ies) where such Financial Records are normally kept and such audit shall be conducted during Company's normal business hours. Upon completion of the audit, the accounting firm shall provide both Parties with a written report disclosing any discrepancies in the reports submitted by Company or payments made by Company, if any, and in each case, the specific details concerning such discrepancies. Any information provided by Company to the accounting firm and the written report of the accounting firm shall be the Confidential Information of Company.

5.4.7. Underpayments/Overpayments. If a report of an independent public accounting firm submitted to the Parties in accordance with Section 5.4.6 (Audits) shows any underpayment of royalties or Commercial Sales Milestone payments due under this Article 5 (Consideration), Company shall remit to HUTCHMED within [***] after receipt of such report by Company, (a) the amount of such underpayment and (b) if such underpayment exceeds [***] of the total amount owed to HUTCHMED for the Calendar Year then being audited, the reasonable fees and expenses of such independent public accounting firm performing the audit, subject to reasonable substantiation thereof. If such independent public accounting firm's written report shows any overpayment of royalties and Commercial Sales Milestone payments due under this Article 5 (Consideration), at Company's election, Company shall receive a credit equal to such overpayment against the royalties and Commercial Sales Milestone payments due under this Article 5 (Consideration) otherwise payable to HUTCHMED or HUTCHMED shall pay to Company an amount equal to such overpayment.

5.4.8. Interest. Any payment under this Agreement that is past due shall be subject to interest at an annual percentage rate of the Secured Overnight Financing Rate (as published in the "Money Rates" table of the Eastern Edition of *The Wall Street Journal* during period such amount is overdue) [***].

5.4.9. Exchange Rate. For the purposes of calculating any sums due under this Agreement, Company will convert any amount expressed in a foreign currency into U.S. dollar equivalents, calculated using the applicable currency conversion rate notified by Company to the JSC in each Calendar Quarter in accordance with Company's customary and usual currency conversion procedures. As applicable, Net Sales and any royalty deductions shall be translated into U.S. dollars in accordance with Company's customary and usual currency conversion procedures, consistently applied in accordance with IFRS. Periodically upon HUTCHMED's written request, Company will either (a) provide its current currency conversion procedures to HUTCHMED or (b) confirm to HUTCHMED that such procedures have not changed from the procedures most recently provided to HUTCHMED. If there is a variance of [***] or greater between the currency conversion rate applied by Company's currency conversion procedures and the applicable currency conversion fixing (BFIX) rate for the last working day in London, United Kingdom of the applicable calendar month that is published by Bloomberg at 10:00 a.m. London, United Kingdom, time, the Parties will use the applicable currency conversion rate as published by Bloomberg or, in the event that the "applicable currency conversion rate" as published by Bloomberg is discontinued or is not available, an alternate currency conversion index as agreed by the Parties.

6. COVENANTS.

6.1. Confidentiality.

6.1.1. Confidential Information. Except to the extent expressly permitted by this Agreement and subject to the provisions of Section 6.1.2 (Authorized Disclosure), at all times during the Term and for [***] following the expiration or termination thereof, each Party (the "**Receiving Party**") receiving any Confidential Information of the other Party (the "**Disclosing Party**") in connection with this Agreement shall: (a) keep confidential and shall not publish or otherwise disclose any Confidential Information furnished to it by the Disclosing Party, except to those of the Receiving Party's Representatives who have a need to know such information (collectively, "**Recipients**") to perform such Party's obligations or exercising its rights hereunder and (b) shall not use Confidential Information of the Disclosing Party directly or indirectly for any purpose other than performing its obligations or exercising its rights hereunder. The Receiving Party shall be liable for any breach by any of its Recipients of the restrictions set forth in this Agreement.

6.1.2. Authorized Disclosure. Notwithstanding the provisions of Section 6.1.1 (Confidential Information), the Receiving Party and its Recipients may disclose Confidential Information belonging to the Disclosing Party to the extent that such disclosure is reasonably necessary to:

(a) Subject to the proviso of Section 6.1.5(b), comply with Applicable Laws (including the rules, regulations or requirements of the U.S. Securities and Exchange Commission or a national securities exchange or another similar regulatory body) or any judicial or administrative process or court or governmental order (including in connection with the prosecution or defense of litigation), if in the reasonable opinion of the Receiving Party's counsel, such disclosure is so required; *provided*, that Confidential Information disclosed shall be limited to that information which the Receiving Party is advised by legal counsel is legally required under the relevant Applicable Law, rule, regulation, requirement, judicial or administrative process or court or governmental order;

(b) Make filings and submissions to, or correspond or communicate with, any Governmental Authority reasonably necessary for the filing, prosecuting, defending or enforcing Patent Rights, for obtaining or maintaining approval to conduct Clinical Trials, or for Developing, Manufacturing or Commercializing, or conducting Medical Affairs activities in respect of, the Licensed Compound or the Licensed Products, in each case, as contemplated by and in accordance with this Agreement; provided that such disclosure is only to the extent reasonably necessary for the foregoing; or

(c) Disclose pharmacovigilance information originating from a Party, its Affiliates, or the other Party to Governmental Authorities, investigators, ethical committees and internal review boards, and any other Third Parties that have a need to know such information according to each Party's risk management and Adverse Event reporting policies and requirements.

In the event that the Receiving Party or its Recipients, as applicable, deem it reasonably necessary to disclose Confidential Information belonging to the Disclosing Party pursuant to this Section 6.1.2 (Authorized Disclosure), the Receiving Party shall, to the extent possible, provide the Disclosing Party with reasonable advance notice of such disclosure and take reasonable measures to ensure confidential treatment of such information. In addition, the Receiving Party may disclose Confidential Information belonging to the Disclosing Party to any Third Party who is performing diligence in connection with a transaction with the Receiving Party (including potential Sublicensees and licensees), and any Third Party (including licensees) who need to know for the purposes of compliance with an existing agreement; *provided* that, each such Third Party has signed a written confidentiality agreement with the Receiving Party that is no less restrictive than the terms hereof.

6.1.3. Notification. The Receiving Party shall notify the Disclosing Party immediately, and cooperate with the Disclosing Party as the Disclosing Party may reasonably request, upon the Receiving Party's discovery of any loss or unauthorized disclosure of the Disclosing Party's Confidential Information.

6.1.4. Destruction of Confidential Information. Upon the termination of this Agreement pursuant to Section 9.2 (Termination for Failure to Obtain Antitrust Clearance), 9.3 (Termination for Convenience) or 9.4 (Termination for Cause), the Receiving Party shall (a) destroy all tangible embodiments of Confidential Information of the Disclosing Party, including any and all copies thereof, and those portions of any documents, memoranda, notes, studies and analyses prepared by the Receiving Party or its Recipients that contain, incorporate or are derived from such Confidential Information and provide written certification of such destruction to the Disclosing Party in a form reasonably acceptable to the Disclosing Party, *provided* that the legal department of the Receiving Party shall have the right to retain one (1) copy of any such tangible embodiments for archival purposes or compliance with Applicable Laws, *provided* such copy shall continue to be maintained on a confidential basis subject to the terms of this Agreement, and (b) immediately cease, and shall cause its Recipients to cease, use of such Confidential Information as well as any information or materials that contain, incorporate or are derived from such Confidential Information.

6.1.5. Use of Name and Disclosure of Terms.

(a) Each Party shall keep the existence of, the terms of and the transactions covered by this Agreement confidential and shall not disclose such information to any Third Party through a press release or otherwise, or mention or otherwise use the name, insignia, symbol, trademark, trade name or logotype of the other Party or its Affiliates in any manner without the prior written consent of the other Party in each instance (which shall not be unreasonably withheld); *provided*, *however*, that a Receiving Party may disclose such information without the prior consent of the Disclosing Party to any Third Party who has a need to know the same for the purposes of performing diligence in connection with a bona fide transaction with such Receiving Party (including potential Sublicensees and licensees) so long as each such Third Party has signed a written confidentiality agreement with such Receiving Party no less restrictive than the terms hereof with respect to confidentiality, non-disclosure and non-use.

(b) The restrictions imposed by this Section 6.1.5 (Use of Name and Disclosure of Terms) shall not prohibit either Party from making any disclosure that is required by Applicable Law, rule or regulation or the requirements of a national securities exchange or another similar regulatory body, if in the reasonable opinion of the Receiving Party's counsel, such disclosure is so required; *provided* that (a) the disclosing Party shall provide the other Party with a copy of relevant portions of the proposed disclosure not less than ten (10) Business Days (or such shorter period of time as may be required, under the circumstances, to comply with Applicable Law, rule or regulation or the requirements of a national securities exchange or another similar regulatory body, but in no event less than three (3) Business Days) prior to such disclosure (and any revisions to such portions of the proposed disclosure a reasonable time prior to the filing thereof), including any exhibits thereto relating to the terms and conditions of this Agreement, (b) Confidential Information disclosed shall be limited to that information which the disclosing Party is advised by legal counsel is legally required under the relevant Applicable Law, rule, regulation or requirement, and (c) the disclosing Party shall use diligent efforts to obtain confidential treatment of the terms and conditions of this Agreement that the other Party requests be kept confidential.

(c) Further, the restrictions imposed on each Party under this Section 6.1.5 (Use of Name and Disclosure of Terms) are not intended, and shall not be construed, to prohibit a Party from identifying the other Party in its internal business communications, *provided* that any Confidential Information in such communications remains subject to this Section 6.1.5 (Use of Name and Disclosure of Terms).

6.1.6. Remedies. The Parties acknowledge and agree that the restrictions set forth in Section 6.1 (Confidentiality) are reasonable and necessary to protect the legitimate interests of the Parties and that neither Party would have entered into this Agreement in the absence of such restrictions, and that any breach or threatened breach of any provision of Section 6.1 (Confidentiality) will result in irreparable injury to the other Party for which there will be no adequate remedy at law. In the event of a breach or threatened breach of any provision of Section 6.1 (Confidentiality) by a Party, the other Party shall be authorized and entitled to obtain from any court of competent jurisdiction injunctive relief, whether preliminary or permanent, specific performance and an equitable accounting of all earnings, profits and other benefits arising from such breach, which rights shall be cumulative and in addition to any other rights or remedies to which such Party may be entitled in law or equity. The breaching Party agrees to waive any requirement that the non-breaching Party (a) post a bond or other security as a condition for obtaining any such relief and (b) show irreparable harm, balancing of harms, consideration of the public interest or inadequacy of monetary damages as a remedy. Nothing in this Section 6.1.6 is intended, or shall be construed, to limit the Parties' rights to equitable relief or any other remedy for a breach of any provision of this Agreement.

6.1.7. Publication of Results.

(a) Publications Committee. Neither Party nor its Affiliates nor Sublicensees may develop any publications or presentations with respect to the results of the Development of the Licensed Compound or Licensed Products without prior consultation with the other Party via a publications and medical and scientific communications committee (the "**Publications Committee**") to be nominated by the JSC promptly after formation of the JSC. The Publications Committee will discuss and issue a joint publications and medical and scientific communications charter (the "**Publications and Communications Charter**") to set out the principles and procedures for review of all such publications concepts and drafts, with the objective of protecting each Party's Confidential Information and providing at least [***] notice for patent prosecution prior to submission, while facilitating publication activities by the Parties as are customary for companies that develop and commercialize proprietary therapeutic products.

(b) Publication in Medical Journals. Unless otherwise set forth in the Publications and Communications Charter, each Party with at least [***] prior notice to the other Party may submit for publication in medical or scientific journals ("**Medical Journals**") articles and papers, including primary reports of clinical data, secondary or pooled analyses, and review papers concerning a Licensed Compound or Licensed Product which have been prepared by or on behalf of such Party, for publication in the Territory (in the case of Company) or in the Restricted Territory (in the case of HUTCHMED) and related to studies conducted concerning a Licensed Compound or Licensed Product (each a "**Scientific Paper**"); *provided*, that, the Party proposing to submit such Scientific Paper shall have provided a copy of such Scientific Paper to the other Party concurrently with such [***] notice and otherwise complied with the Publications and Communications Charter with respect to such Scientific Paper. Commencing with the receipt of any such Scientific Paper, the receiving Party shall have [***] to inform the sending Party of its observations and suggestions with respect thereto; it being understood that, during such [***] period, no submission or publication thereof shall take place and the Parties shall discuss these suggestions, if requested by either Party. The Party proposing to submit such Scientific Paper for publication shall, in good faith, consider the comments made by the other Party, particularly if disclosure may be prejudicial to the other Party's opportunity to obtain any Patent Rights. A Party will not submit any Scientific Paper containing any Confidential Information of the other Party without such other Party's prior written consent. The sending Party shall provide to the receiving Party copies of all final Scientific Papers as submitted no later than [***] after submission.

(c) Abstracts and Posters. Each Party shall provide to the other, at least [***] prior to submission of an abstract or presentation of a poster or oral presentation, as the case may be, copies of such abstracts, posters and other materials (such as slides) that will be submitted to or presented at any Scientific Meeting, in each case, related to the use of a Licensed Compound or Licensed Product, which have been prepared by or on behalf of one of the Parties. Commencing with the receipt of any such abstract or poster or oral presentation materials, the receiving Party shall have [***] to inform the sending Party of its observations and suggestions with respect thereto; it being understood that, during such [***] period, no submission or presentation thereof shall take place and the Parties shall discuss these suggestions, if requested by either Party. The Party proposing to publish such an abstract or make such a presentation shall, in good faith, consider the comments made by the other Party, particularly if disclosure may be prejudicial to the other Party's opportunity to obtain any Patent Rights. A Party will not submit in any abstract or present in any poster, other written materials or oral presentation any Confidential Information of the other Party without such other Party's prior written consent. The sending Party shall provide to the receiving Party copies of all final abstracts as submitted and all final posters as presented no later than [***] after submission or presentation.

6.1.8. Presentations at Scientific Meetings. Unless otherwise set forth in the Publications and Communications Charter, with at least [***] prior notice to the other Party, each Party may present findings with respect to the Licensed Compound or Licensed Products at symposia and other meetings of healthcare professionals, and congresses, conferences or meetings organized by a professional society or organization (any such occasion, a "**Scientific Meeting**"); *provided*, that, unless otherwise agreed by the Parties, that (a) the Party presenting at any such Scientific Meeting shall have complied with the Publications and Communications Charter with respect to such presentation, and, with respect to any such Scientific Meeting at which a Party is presenting, such presenting Party shall inform the other Party of such Scientific Meeting and where invitation is required, invite the other Party to attend such Scientific Meeting; and (b) a Party shall not organize or sponsor any satellite symposia in a country outside the Territory (in the case of Company) or the Restricted Territory (in the case of HUTCHMED) without the other Party's prior written consent, not to be unreasonably withheld.

6.1.9. Disclosure of Clinical Data. Unless otherwise set forth in the Publications and Communications Charter, each Party may disclose any clinical data generated by such Party concerning a Licensed Compound or Licensed Product in Clinical Trial registries; *provided*, that, the Party proposing to make such disclosure shall have provided the other Party with at least [***] notice to the other Party prior to such disclosure, a detailed description of the proposed disclosure and shall have, in good faith, considered the comments made by the other Party.

6.2. Compliance with Law. Each Party hereby covenants and agrees to comply with all Applicable Law in performing its activities in connection with the Development, Manufacture, Commercialization and Medical Affairs activities (as applicable) of the Licensed Compound and Licensed Products. Without limiting the generality of the foregoing:

6.2.1. Patient Information. Each Party agrees to abide by all laws, rules, regulations, and orders of all applicable supranational, national, federal, state, provincial, and local governmental entities concerning the confidentiality or protection of patient identifiable information or patients' protected health information in the course of their performance under this Agreement. [***].

6.2.2. Export Controls. This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States or other countries which may be imposed upon or related to HUTCHMED or Company from time to time. Each Party agrees that it shall not export, directly or indirectly, any technical information acquired from the other Party pursuant to this Agreement or any Licensed Products using such technical information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate agency or other Governmental Authority. The Parties agree to use Commercially Reasonable Efforts to obtain any such licenses, or approvals as may be necessary or useful in connection with the activities contemplated by this Agreement. Without limiting the foregoing, HUTCHMED shall use Commercially Reasonable Efforts to obtain the export registration certificate described in Section 7.1(g)(ii) of Schedule 7.2 (HUTCHMED Disclosures) as soon as reasonably practicable after the Execution Date.

6.2.3. Anti-Bribery. Company (a) will comply with all Applicable Laws concerning bribery, money laundering, or corrupt practices or which in any manner prohibit the giving of anything of value to any official, agent, or employee of any government, political party, or public international organization, candidate for public office, health care professional, or to any officer, director, employee, or representative of any other organization specifically including the U.S. Foreign Corrupt Practices Act, and the U.K. Bribery Act, in each case, in connection with the activities conducted pursuant to this Agreement, and will require any contractors, subcontractors, distributors, or other Person that provide services to Company in connection with this Agreement to comply with Company's obligations under this Section 6.2.3(a); and (b) will not, with respect to any activities conducted under this Agreement, (i) commit an act, (ii) make a statement, or (iii) fail to act or make a statement, in any case ((i), (ii), or (iii)), that (A) would be or create an untrue statement of material fact or fraudulent statement to the FDA or any other Regulatory Authority with respect to the exercise of the rights granted to Company under the Licensed Technology or the Development, Manufacture, Commercialization or Medical Affairs activities (as applicable) of any Licensed Compound or Licensed Products, or (B) could reasonably be expected to provide a basis for the FDA to invoke its policy respecting "Fraud, Untrue Statements of Material Facts, Bribery and Illegal Gratuities," set forth in 56 Fed. Reg. 46191 (September 10, 1991) and any amendments thereto or any analogous laws or policies in any country in the Territory, with respect to the exercise of the rights granted to Company under the Licensed Technology or the Development, Manufacture, Commercialization or Medical Affairs activities (as applicable) of any Licensed Compound or Licensed Products.

6.2.4. Debarment. Each Party agrees that it shall not knowingly use, in any capacity, in connection with any of its obligations to be performed under this Agreement any individual who has been disqualified or debarred by the United States Food and Drug Administration, pursuant to 21 U.S.C. §§ 335(a) or (b), or been charged with or convicted under United States law for conduct relating to the development or approval, or otherwise relating to the regulation of Licensed Product under the Generic Drug Enforcement Act of 1992, or any other relevant law, rule, or regulation or been disbarred, disqualified, or convicted under or for any equivalent or similar applicable foreign law, rule, or regulation.

6.2.5. Non-Solicitation. During the Term, neither Company nor any of its Affiliates shall, without HUTCHMED's prior written consent, directly or indirectly, anywhere in the world employ, solicit for employment, or recommend for employment any person engaged in the Development, Manufacture or Commercialization of the Licensed Compound or Licensed Products and employed by HUTCHMED or any Affiliate of HUTCHMED, during the period such Person is so employed. Notwithstanding the foregoing, nothing in this Section 6.2.5 shall prohibit Company or any of its Affiliates from (a) making general employment solicitations, not specifically directed at such employees of HUTCHMED or its Affiliates or (b) soliciting, recruiting, or hiring any individual who is not employed by HUTCHMED or its Affiliate at the time of such solicitation, recruitment or hire, so long as neither Company nor its Affiliates had any contact with such individual in violation of the first sentence of this Section 6.2.5 (Non-Solicitation) prior to the end of such individual's employment with HUTCHMED or its Affiliate.

7. REPRESENTATIONS, WARRANTIES AND COVENANTS.

7.1. Representations and Warranties of Each Party. Each Party represents and warrants to the other as of the Execution Date and the Effective Date that: (a) it is duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization; (b) the execution, delivery and performance of this Agreement by such Party has been duly authorized by all requisite action under the provisions of its charter, bylaws and other organizational documents, and does not require any action or approval by any of its shareholders or other holders of its voting securities or voting interests; (c) it has the power and authority to execute, deliver and perform each of this Agreement and (in accordance with the terms set forth in Schedule 4.3.2 (Terms of Clinical and Commercial Supply Agreement) and Schedule 4.3.3 (Terms of Manufacturing Technology Transfer), respectively) the Manufacturing Technology Transfer Agreement and the Supply Agreement; (d) this Agreement has been duly executed and is a legal, valid and binding obligation on each Party, enforceable against such Party in accordance with its terms; (e) the execution, delivery and performance by such Party of each of this Agreement and (on the basis of the terms set forth in Schedule 4.3.2 (Terms of Clinical and Commercial Supply Agreement) and Schedule 4.3.3 (Terms of Manufacturing Technology Transfer), respectively) the Manufacturing Technology Transfer Agreement and the Supply Agreement and its compliance with the terms and provisions hereof and thereof, does not and will not conflict with or result in a breach of or default under any binding arrangement or agreement with a Third Party existing as of the Execution Date or the Effective Date; (f) the execution, delivery, and performance of each of this Agreement and (in accordance with the terms set forth in Schedule 4.3.2 (Terms of Clinical and Commercial Supply Agreement) and Schedule 4.3.3 (Terms of Manufacturing Technology Transfer), respectively) the Manufacturing Technology Transfer Agreement and the Supply Agreement by such Party does not and will not violate any Applicable Laws of any Governmental Authority having jurisdiction over such Party (or any of its Affiliates); and (g) no government authorization, consent, approval, license, exemption of or filing or registration with any Governmental Authority under any Applicable Law currently in effect, is or shall be necessary for, or in connection with, the transactions contemplated by this Agreement and (on the basis of the terms set forth in Schedule 4.3.2 (Terms of Clinical and Commercial Supply Agreement) and Schedule 4.3.3 (Terms of Manufacturing Technology Transfer), respectively) the Manufacturing Technology Transfer Agreement or the Supply Agreement, or for the performance by it of its obligations hereunder or thereunder pursuant to the terms thereof, except: (i) as may be required to conduct Clinical Trials or to seek or obtain Regulatory Approvals; or (ii) as set forth in Section 7.1 of Schedule 7.2 (HUTCHMED Disclosures).

7.2. Additional Representations and Warranties of HUTCHMED. HUTCHMED hereby represents and warrants to Company that as of the Execution Date and as of the Effective Date, except as set forth in the applicable Section of Schedule 7.2 (HUTCHMED Disclosures):

7.2.1. Except as set forth on Section 7.2.1 of Schedule 7.2 (HUTCHMED Disclosures), HUTCHMED has the full right, power and authority to grant all of the right, title and interest in the licenses granted to Company pursuant to Section 2.1 (License to Company), Section 4.4.2(b) (License to HUTCHMED Trademarks for Commercialization) and Section 4.4.2(c) (Copyright License) and neither such right, title, or interest, nor any other provision of this Agreement are subject to any in-license, option, assignment or other similar agreements with another Person regarding any licenses or rights granted in the Territory hereunder;

7.2.2. Except as set forth on Section 7.2.2 of Schedule 7.2 (HUTCHMED Disclosures), HUTCHMED has obtained or made all necessary authorizations, consents, approvals, licenses, exemptions of or filings or registrations with any Third Party (including Governmental Authorities) required for, and no Applicable Laws prohibit or restrict, the transfer of the Licensed Know-How, including the transfer of the HUTCHMED Manufacturing Know-How to Company and all data generated pursuant to all Clinical Trials conducted or being conducted by or on behalf of HUTCHMED or its Affiliates or, to HUTCHMED's Knowledge, Third Parties, in respect of the Licensed Compound and Licensed Products prior to the Execution Date, and the performance of the other obligations of HUTCHMED hereunder (disregarding, for purposes of this Section 7.2.2, Section 6.2.2 (Export Controls) and the proviso set forth in Section 2.5 (Delivery of Licensed Know-How));

7.2.3. The transfer of the HUTCHMED Manufacturing Know-How contemplated by the terms of the Manufacturing Technology Transfer Agreement set forth on Schedule 4.3.3 (Terms of Manufacturing Technology Transfer), upon the completion thereof, will be a complete and accurate transfer to Company and its designees of the HUTCHMED Manufacturing Know-How, such that the HUTCHMED Manufacturing Know-How will be sufficient for Company and its designees to Manufacture the Licensed Compound, the Licensed Products and related packaging in the manner in which the Licensed Compound, the Licensed Products and related packaging are manufactured;

7.2.4. Except as set forth on Section 7.2.4 of Schedule 7.2 (HUTCHMED Disclosures), HUTCHMED has not granted any Third Party rights that would otherwise interfere or be inconsistent with Company's rights hereunder, and there are no agreements or arrangements to which HUTCHMED or any of its Affiliates is a party relating to the Licensed Compound, Licensed Products, Licensed Patent Rights, or Licensed Know-How that would limit the rights granted to Company under this Agreement or that restrict or will result in a restriction on Company's ability to Develop, Manufacture, use or Commercialize the Licensed Compound or Licensed Products;

7.2.5. Except as set forth on Section 7.2.5 of Schedule 7.2 (HUTCHMED Disclosures), HUTCHMED (a) does not own or Control any Patent Rights, other than the Licensed Patent Rights, that are necessary or reasonably useful to Develop, Manufacture, or Commercialize the Licensed Products or Licensed Compound; (b) is the sole and exclusive owner of all of the Licensed Patent Rights free from encumbrances and is listed in the records of the appropriate

Governmental Authorities as the sole and exclusive owner of record for each registration, grant, and application included in the Licensed Patent Rights in the Territory; and (c) there is no Know-How (i) owned by HUTCHMED or (ii) being used in a material manner by HUTCHMED as of the Execution Date in the Development, Manufacture or Commercialization of the Licensed Compound or Licensed Products in the Field, that, in either case (clauses (i) and (ii)), would be Licensed Know-How, but for HUTCHMED's failure to Control such Know-How;

7.2.6. HUTCHMED has taken all reasonable precautions to preserve the confidentiality and trade secret protections under Applicable Law of the Licensed Know-How;

7.2.7. to the Knowledge of HUTCHMED, the issued patents in the Licensed Patent Rights are valid and enforceable;

7.2.8. HUTCHMED has (a) filed and prosecuted the patent applications within the Licensed Patent Rights in good faith and complied with all duties of disclosure with respect thereto; (b) not committed any act, or omitted to commit any act, that may cause the Licensed Patent Rights to expire prematurely or be declared invalid or unenforceable; (c) paid all application, registration, maintenance, and renewal fees in respect of the Licensed Patent Rights; and (d) filed all necessary documents and certificates with the relevant agencies for the purpose of maintaining the Licensed Patent Rights;

7.2.9. other than routine patent prosecution, (a) there is no pending, or to HUTCHMED's Knowledge, threatened, litigation, challenges, oppositions, nullity actions, interferences, inter-partes reexaminations, inter-partes reviews, post-grant reviews, derivation proceedings, or other proceedings relating to it or any Affiliate that seeks to invalidate or challenge the enforceability of any of the Licensed Patent Rights set forth on Schedule 1.112 (Licensed Patent Rights), and (b) no Third Party has challenged, or, to the Knowledge of HUTCHMED, has threatened in writing to challenge, HUTCHMED's right to use and license the Licensed Know-How, and (c) there are no claims asserted in writing, judgments, or settlements in effect against HUTCHMED relating to the Licensed Patent Rights;

7.2.10. to HUTCHMED's Knowledge, no Third Party is infringing or misappropriating the Licensed Know-How or Licensed Patent Rights in the Territory in derogation of the rights granted to Company in this Agreement and HUTCHMED has not initiated or been involved in any proceedings or other claims in which it alleges that any Third Party is or was infringing or misappropriating any Licensed Technology, nor have any such proceedings been threatened by HUTCHMED, nor does HUTCHMED know of any valid basis for any such proceedings;

7.2.11. there are no material investigations, inquiries, actions, or other proceedings pending before or, to HUTCHMED's Knowledge, threatened by any Regulatory Authority or other Governmental Authority in the Territory with respect to any Licensed Product in the Territory arising from any violation of Applicable Law by HUTCHMED or a Third Party acting on behalf of HUTCHMED in the Development or Manufacturing of a Licensed Compound or Licensed Product, and HUTCHMED has not received written notice threatening any such investigation, inquiry, action, or other proceeding;

7.2.12. there are no material claims or litigation pending or, to the Knowledge of HUTCHMED, threatened in writing alleging that the exploitation of the Licensed Products in the Territory in the manner contemplated in this Agreement, infringes or would infringe any issued patent or misappropriate the know-how of any Third Party, and to HUTCHMED's Knowledge, there is no basis for any such allegations;

7.2.13. HUTCHMED has obtained from all individuals who participated in any respect in the invention or Development of any Licensed Compound or Licensed Products or authorship or invention of any Licensed Technology effective assignments of all ownership rights of such individuals in intellectual property generated by such individuals in the course of such work, either pursuant to written agreement or by operation of Applicable Law;

7.2.14. all of HUTCHMED's and its Affiliates' employees, officers, and consultants have executed agreements or have existing obligations under Applicable Law requiring assignment to HUTCHMED of all inventions made during the course of and as the result of their association with HUTCHMED or its Affiliate and obligating the individual to maintain as confidential HUTCHMED's Confidential Information as well as confidential information of other parties that such individual may receive, to the extent required to support HUTCHMED's obligations under this Agreement;

7.2.15. no officer or employee of HUTCHMED is subject to any agreement with any other Third Party that requires such officer or employee to assign any interest in any Licensed Technology relating to the Licensed Compound or Licensed Products to any Third Party;

7.2.16. HUTCHMED has not entered into a funding relationship with a Governmental Authority that would result in rights to any Licensed Compound or Licensed Products residing in the United States Government, National Institutes of Health, National Institute for Drug Abuse or other Governmental Authority (including counterparts of such agencies in any other countries), and the licenses granted hereunder are not subject to overriding obligations to the United States Government as set forth in Public Law 96 517 (35 U.S.C. 200 204) or any similar obligations under the Applicable Laws of any other country with respect to other Governmental Authorities;

7.2.17. HUTCHMED has disclosed to Company all material information and data and all material correspondence to or from any Regulatory Authority, in each case related to the Licensed Compound and Licensed Products, regardless of whether such data and information would have a positive, negative or neutral impact on the potential commercial, scientific, or strategic value or attractiveness of such Licensed Compound or Licensed Products;

7.2.18. HUTCHMED and its contractors, and consultants, have complied in all material respects with all Applicable Law, including cGMP, GLP and GCP, in the Development, Manufacture, Commercialization and other exploitation of the Licensed Compound and the Licensed Products. HUTCHMED has obtained or made all necessary authorizations, consents, approvals, licenses, exemptions of or filings or registrations with any Third Party (including Governmental Authorities) for the performance of its obligations with respect to the Interim Manufacturing Services and Supply Agreement. The facility(ies) to be utilized for the supply of Licensed Compound and Licensed Product to Company in connection with the Interim

Manufacturing Services have each received approval from the appropriate Regulatory Authorities to Manufacture the Licensed Compound and Licensed Product and have sufficient Manufacturing capacity to supply Company with its reasonably anticipated requirements of the Licensed Compound and Licensed Products pursuant to the Interim Manufacturing Services, and to otherwise satisfy the obligations of HUTCHMED with respect to the Interim Manufacturing Services and Supply Agreement, as contemplated by the terms set forth on Schedule 4.3.2 (Terms of Clinical and Commercial Supply Agreement);

7.2.19. Section 7.2.19 of Schedule 7.2 (HUTCHMED Disclosures) contains a true and correct summary of all Clinical Trials and other Development activities in respect of the Licensed Compound or Licensed Products being conducted by HUTCHMED and any Third Parties in the Territory and the status thereof;

7.2.20. HUTCHMED Controls (subject to (a) HUTCHMED undertaking Commercially Reasonable Efforts to provide the notices to living data subjects as set forth on Section 7.2.2 of Schedule 7.2 (HUTCHMED Disclosures), and (b) the Parties entering the Data Protection Agreement promptly following the Execution Date) all data generated pursuant to all Clinical Trials conducted or being conducted by HUTCHMED, its Affiliates or Third Parties in respect of the Licensed Compound and Licensed Products prior to the Execution Date;

7.2.21. Except as set forth in Section 7.2.21 of Schedule 7.2 (HUTCHMED Disclosures), HUTCHMED Controls all Regulatory Submissions in the Restricted Territory in respect of the Development, Manufacturing and Commercialization of the Licensed Compound and Licensed Products, HUTCHMED receives all correspondence from Regulatory Authorities in relation to such Regulatory Submissions, and HUTCHMED is not precluded by Applicable Laws or any obligation to any Third Party from disclosing any such correspondence to Company or granting to Company the rights contemplated by Section 2.4.1 (Company Right of Reference);

7.2.22. Except as set forth in Section 7.2.22 of Schedule 7.2 (HUTCHMED Disclosures), all Licensed Know-How existing as of the Execution Date constitutes technology allowed to be exported freely (自由出口的技术) pursuant to the Administrative Regulations of the People’s Republic of China on Import and Export of Technologies（中华人民共和国技术进出口管理条例, as amended; and

7.2.23. The data generated pursuant to the FRESCO Clinical Trial does not contain genetic data, metabolic data or biomarker data.

7.3. **[***]**

7.4. Covenants of HUTCHMED. HUTCHMED covenants and agrees that:

7.4.1. it will not (a) grant any interest in the Licensed Patent Rights or Licensed Know-How that is inconsistent with the terms and conditions of this Agreement, nor shall HUTCHMED assign its right, title or interest in or to the Licensed Patent Rights or Licensed Know-How to any Third Party other than in connection with an assignment under Section 11.8 (Assignment), and will use all reasonable precautions to preserve the confidentiality of the

Licensed Know-How or (b) incur or permit to exist any lien, security interest or other encumbrance, other than liens, security interests or other encumbrances entered into in the ordinary course of business, on the Licensed Patent Rights or Licensed Know-How unless, in each case, such lien, security interest or other encumbrance is subject to the terms of this Agreement (including Company's licenses hereunder);

7.4.2. with respect to any Affiliate of HUTCHMED that Controls any Licensed Technology, prior to such time as such Affiliate ceases to be an Affiliate of HUTCHMED, HUTCHMED shall cause such Person to transfer such Licensed Technology to HUTCHMED or another Affiliate of HUTCHMED;

7.4.3. HUTCHMED shall make any and all payments owing by HUTCHMED or any of its Affiliates to any inventor of any Licensed Know-How or Licensed Patent Rights (other than Joint Technology and Joint Patent Rights) owned by HUTCHMED or such Affiliate that is required in connection with the creation or exploitation of or transfer of rights to such Licensed Know-How or Licensed Patent Rights;

7.4.4. if, at any time after the Execution Date, it becomes aware that it or any employee, agent or subcontractor of HUTCHMED who participated, or is participating, in the performance of any activities hereunder is on, or is being added to the FDA Debarment List or any FDA Clinical Investigator Restriction List, each as maintained and published by the FDA, it will provide written notice of this to Company within five (5) Business Days of its becoming aware of this fact;

7.4.5. except as otherwise expressly permitted under this Agreement, HUTCHMED will maintain Control of the Patent Rights and Know-How purported to be included in the Licensed Technology as of the Execution Date, and will not, and will cause its Affiliates not to assign, transfer, license or grant to any Third Party, or agree to assign, transfer, license or grant to any Third Party, any rights to such intellectual property or any Licensed Compound or Licensed Products if such license or grant would conflict with, in any respect, any of the rights or licenses contemplated to be granted to Company hereunder;

7.4.6. HUTCHMED shall maintain sufficient security systems and intellectual property protection guidelines within its organization equivalent to industry standards and qualified to avoid any unauthorized disclosure of intellectual property rights, including Know-How, to any Third Party; and

7.4.7. HUTCHMED shall not, without the prior written consent of Company, perform its obligations with respect to the Interim Manufacturing Services and Supply Agreement at any facility other than the facility(ies) referenced in Section 7.2.18.

7.5. Representation by Legal Counsel. Each Party hereto represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption shall exist or be implied against the Party which drafted such terms and provisions.

7.6. Disclaimer. NEITHER PARTY MAKES ANY EXPRESS OR IMPLIED REPRESENTATION OR WARRANTY EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, ALL OTHER REPRESENTATIONS AND WARRANTIES WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE ARE EXPRESSLY DISCLAIMED, INCLUDING ANY REPRESENTATION OR WARRANTY REGARDING THE VALIDITY OR SCOPE OF ITS PATENT RIGHTS, THAT THE MANUFACTURE, USE OR SALE OF THE LICENSED COMPOUND OR LICENSED PRODUCTS WILL NOT INFRINGE THE PATENT RIGHTS OF THIRD PARTIES, OR ANY REPRESENTATION OR WARRANTY AS TO THE VALUE, ADEQUACY, FREEDOM FROM FAULT OF, OR QUALITY, EFFICIENCY, CHARACTERISTICS OR USEFULNESS OF, OR MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OF ANY LICENSED COMPOUND OR LICENSED PRODUCT.

8. INTELLECTUAL PROPERTY.

8.1. Ownership.

8.1.1. Inventions. (a) Each Party will own all rights, title, and interests in and to (i) any and all Know-How developed or invented solely by or on behalf of such Party or its Affiliates in connection with the performance of such Party's activities under this Agreement and (ii) any and all Patent Rights claiming any such Know-How described in clause (a)(i) of this Section 8.1.1 (Inventions), and (b) the Parties will jointly own any and all (i) Know-How developed or invented jointly by or behalf of the Parties or their Affiliates in connection with the performance of the Parties' activities under this Agreement ("**Joint Know-How**") and (ii) Patent Rights claiming any such Know-How described in clause (b)(i) of this Section 8.1.1 ("**Joint Patent Rights**"). All determinations of inventorship under this Agreement will be made in accordance with U.S. patent law.

8.1.2. Disclosure. (a) HUTCHMED will promptly disclose to Company all Joint Know-How, and (b) Company will promptly disclose to HUTCHMED all Joint Know-How, in each case ((a) and (b)), that it develops or invents, whether solely or jointly with others (in any event, prior to the filing of any patent application with respect to such Know-How), including all invention disclosures or other similar documents submitted to such Party by its or its Affiliates' employees, agents, or independent contractors relating thereto. Each Party will also promptly respond to reasonable requests from the other Party for additional information relating thereto.

8.1.3. Licensed Technology. Subject to the license grants under Article 2 (Grant of License) of this Agreement, as between the Parties, HUTCHMED shall own all Licensed Technology.

8.1.4. Joint Technology. Subject to Section 2.1 (License to Company) and the other terms and conditions set forth in this Agreement, the Parties will jointly own all Joint Technology and each Party is entitled to practice the Joint Technology on a worldwide basis and to license such Joint Technology through multiple tiers without consent of the other Party (where consent is required by Applicable Law, such consent is deemed hereby granted) and without a duty of accounting to the other Party. For the avoidance of doubt, unless this Agreement is terminated in accordance with Section 9.3 or 9.4, HUTCHMED has no rights in the Joint Technology to

Develop, Manufacture, Commercialize and otherwise exploit the Licensed Compound and Licensed Products in the Field in the Territory, other than in connection with the performance of its obligations hereunder and in connection with its retained rights under Section 2.6 (No Other Rights and Retained Rights). Subject to the foregoing, each Party will grant and hereby does grant to the other Party all further permissions, consents, and waivers with respect to, and all licenses under, the Joint Technology, throughout the world, necessary to provide the other Party with full rights of use and exploitation of the Joint Technology. Without limitation, each Party will cooperate with the other Party if the Parties determine to apply for U.S. or foreign patent protection for any Joint Technology and will obtain the cooperation of the individual inventors of any such Joint Technology.

8.2. Filing, Prosecution and Maintenance of Patent Rights.

8.2.1. Right to File and Prosecute Licensed Patent Rights and Joint Patent Rights. Following the Effective Date, Company will have the first right, but not the obligation, to control of the filing, prosecuting (including in connection with any reexaminations, oppositions, and the like), and maintaining the Licensed Patent Rights and Joint Patent Rights in the Territory. Company will file, prosecute, and maintain such Licensed Patent Rights and Joint Patent Rights using qualified outside patent counsel and foreign patent associates selected by Company. Company will be responsible for all costs and expenses in connection with such filing, prosecution, and maintenance. Company will provide HUTCHMED an opportunity to review and provide comment on any filing, maintenance or prosecution documentation with respect to a Licensed Patent Rights and Joint Patent Rights in the Territory no less than [***] before submission, and will reasonably consider HUTCHMED's comment on such filing, maintenance or prosecution documentation. If Company determines to abandon, or not file a patent application included in, any of the Licensed Patent Rights or Joint Patent Rights in the Territory, then at least [***] in advance of the relevant deadline: (a) Company will notify HUTCHMED of its determination in writing; (b) HUTCHMED may, or may allow a Third Party to, file, prosecute, and maintain (in its sole discretion) such Licensed Patent Right or Joint Patent Rights; (c) upon HUTCHMED's request, Company will promptly provide all files related to filing, prosecuting, and maintaining such Licensed Patent Right or Joint Patent Rights to counsel designated by HUTCHMED; (d) the term "Licensed Patent Rights" or "Joint Patent Rights" (as applicable) will automatically exclude such patent or patent application as of the date Company provides such written request to HUTCHMED and Company will assign to HUTCHMED all of Company's rights, title, and interests in and to such abandoned Joint Patent Right; and (e) Company will no longer be responsible for such costs and expenses relating to filing, prosecuting, and maintaining (as applicable) such Licensed Patent Right or Joint Patent Rights.

8.2.2. Coordination and Cooperation. Company will keep HUTCHMED reasonably informed as to material developments with respect to the preparation, filing, prosecution, issuance, and maintenance of the Licensed Patent Rights and Joint Patent Rights in the Territory, and will provide HUTCHMED a reasonable opportunity to review and comment on substantive communications from any patent authority in the Territory regarding the Licensed Patent Rights or Joint Patent Rights, as well as drafts of any substantive filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Company will consider and implement HUTCHMED's reasonable comments regarding such communications and drafts in good faith. On at least a yearly basis, or more frequently upon HUTCHMED's written request, but no more than once per quarter, Company will provide to HUTCHMED a report detailing the status of all Licensed Patent Rights and Joint Patent Rights in the Territory, including any patent term extensions, and the anticipated expiration dates of any issued patents.

8.2.3. Patent Term Extensions. As between the Parties, Company shall determine whether and how (and for which Joint Patent Rights and Licensed Patent Rights) it will apply to seek patent term restoration (including under the Drug Price Competition and Patent Term Restoration Act) as it relates to the Licensed Products, supplemental protection certificates or their equivalents, and patent term extensions that are now or become available in the future with respect to the Joint Patent Rights or Licensed Patent Rights in any jurisdiction. Company will provide HUTCHMED an opportunity to review and provide comment on obtaining patent term extensions in the Territory no less than fifteen (15) days before submission, and will reasonably consider HUTCHMED's comment. HUTCHMED shall provide all reasonable assistance requested by Company in obtaining such extensions, including by permitting Company to proceed with applications for such in the name of HUTCHMED, if deemed appropriate by Company, and executing documents and providing any relevant information to Company. Company shall be responsible for making the filings in respect of such patent term extensions.

8.2.4. Orange Book Listing. HUTCHMED shall, at Company's expense and upon Company's reasonable request, provide all necessary information to enable Company to make filings with Regulatory Authorities with respect to Licensed Patent Rights or Joint Patent Rights as required (a) in the United States for the FDA's Orange Book and (b) in the Territory outside the United States under other international equivalents.

8.2.5. Defense of Patent Rights. As between the Parties, the Party controlling the preparation, filing, prosecution, and maintenance of any Patent Right under this Section 8.2 (Filing, Prosecution and Maintenance of Patent Rights) will have the first right, but not the obligation, to defend against a declaratory judgment action, inter partes review, opposition proceeding, interference, or other action challenging any such patent, other than with respect to (a) any counter claims or defenses in any Infringement Action brought by the other Party pursuant to Section 8.3.2 (Infringement Actions), or (b) any action by a Third Party in response to an Infringement Action brought by the other Party, which, in both cases ((a) and (b)), will be controlled by such other Party.

8.3. Patent Enforcement.

8.3.1. Third Party Infringement. During the Term, the Parties will promptly inform each other in writing if either Party becomes aware of any suspected, threatened, or actual infringement by any Third Party of any Licensed Patent Rights or Joint Patent Rights (an "**Infringement**"), and in any case no less than ten (10) days after becoming aware of such Infringement, including any Infringement that arises as a result of the making, using, offering to sell, selling, or importing of a product that is or would be competitive with a Licensed Product in the Territory (a "**Competing Infringement**"). In addition, each Party will promptly notify the other in the event such Party becomes aware of any action by a Third Party for a declaration that any of the Licensed Patent Rights or Joint Patent Rights are not infringed or are invalid, or unenforceable. In all cases, each Party will provide any available evidence of such Infringement or other conduct with such notification.

8.3.2. Infringement Actions.

(a) Infringement Actions for Competing Infringements.

(i) Company Rights. During the Term, Company will have the first right, but not the obligation, to initiate an infringement, misappropriation, or other appropriate suit (an "**Infringement Action**") against a Competing Infringement with respect to any Licensed Patent Rights or Joint Patent Rights of which Company is responsible for the prosecution and maintenance under Section 8.2 (Filing, Prosecution and Maintenance of Patent Rights**)**, at Company's sole discretion and at Company's sole cost and expense. Prior to commencing involvement in any such Infringement Action, Company will consult with HUTCHMED and will consider HUTCHMED's reasonable recommendations regarding the proposed Infringement Action.

(ii) HUTCHMED Rights. If Company (A) provides written notice to HUTCHMED that it does not intend to initiate an Infringement Action, or (B) fails to initiate an Infringement Action with respect to such Competing Infringement upon the earlier of: (1) expiration of the 45-day period following first receipt by either Party of notice from the other Party of such Competing Infringement under Section 8.3.1 (Third Party Infringement); or (2) 5 days prior to the deadline for initiating such Infringement Action, then HUTCHMED will have the right (but not the obligation) to initiate and control an Infringement Action against such Competing Infringement by counsel of its choice, at its own discretion and at HUTCHMED's sole cost and expense. Company will have the right, at its own expense, to be represented in any such Infringement Action by counsel of its own choice.

(b) Procedures. If the Party having the right to initiate an Infringement Action under this Section 8.3.2 (the "**Initiating Party**") desires to initiate such Infringement Action but may not do so due to Applicable Law or regulation (even as the assignee or exclusive licensee of such infringed Patent Right), then such Initiating Party may require that the other Party join as a named party in such action or itself initiate such Infringement Action, at the Initiating Party's sole cost and expense. The Initiating Party will take the lead in the control and conduct of any such Infringement Action under this Section 8.3.2 (Infringement Actions) and will keep the other Party reasonably informed of any such Infringement Action, and the other Party will reasonably assist the Initiating Party in any such Infringement Action under this Section 8.3.2 (Infringement Actions) at the Initiating Party's expense. In no event may the Initiating Party settle any such Infringement Action in a manner that would limit the rights of the other Party or impose any obligation on the other Party, in each case, without the other Party's prior written consent, which consent will not be unreasonably withheld, delayed, or conditioned.

(c) Recoveries. Any amount recovered in any Infringement Action under this Section 8.3.2 (Infringement Actions), including any amount recovered in any settlement of such Infringement Action, will first be used to reimburse each Party's costs and expenses with respect to such Infringement Action (which reimbursement will be on a pro rata basis to the extent such costs and expenses exceed such recovered amount). Any remaining recoveries will be shared as follows: (i) if Company is the enforcing Party, such remaining recoveries will be deemed Net Sales earned in the country to which such

Infringement Action primarily relates during the Calendar Quarter in which such recoveries are received solely for the purpose of calculating royalties owing in respect of such Net Sales pursuant to Section 5.3.1 (Royalty Payments) (and not, for clarity, for purposes of determining whether any Commercial Sales Milestone has been met or any other purpose) and (ii) if HUTCHMED is the enforcing Party, any remaining amounts will be shared equally (50/50) between the Parties.

8.4. Infringement of Third Party Rights.

8.4.1. Notice. If any Licensed Product becomes the subject of a Third Party's claim or assertion of infringement of a Patent Right within the Territory, the Party first having notice of the claim or assertion will promptly notify the other Party.

8.4.2. Defense. Except as otherwise provided in Article 10 (Product Liability, Indemnification and Insurance), Company will have the first right, but not the obligation to defend any such Third Party claim or assertion of infringement of a Third Party Patent Right with respect to any Licensed Product, or pursue any invalidation proceedings against a Third Party Patent Right with respect to any Licensed Product, at Company's expense. HUTCHMED will reasonably cooperate with Company, including if required to conduct such defense or invalidation proceedings, furnishing a power of attorney.

8.4.3. Settlement; Licenses. Except as otherwise provided in Article 10 (Product Liability, Indemnification and Insurance), neither Party will, without the consent of the other Party, enter into any settlement of any claim described in this Section 8.4 (Infringement of Third Party Rights) that (a) imposes any liability or obligation on such other Party, (b) includes the grant of any license, covenant or other rights to any Third Party that would conflict with or reduce the scope of the subject matter included under the rights and licenses granted to such other Party under this Agreement, or (c) otherwise materially affect the licenses or other rights granted to such other Party hereunder adversely in any respect.

8.5. Summary of Activities. Upon HUTCHMED's request, Company will provide to HUTCHMED, no more frequently than on an annual basis, a written report summarizing all material activities undertaken by Company in the preceding Calendar Year with respect to the enforcement and defense of the Licensed Patent Rights and Joint Patent Rights in the exercise of the rights granted to Company under this Article 8 (Intellectual Property).

9. TERM AND TERMINATION; RIGHTS IN LIEU OF TERMINATION.

9.1. Term. Except as set forth in Section 2.10.3 (Antitrust Filings; Effectiveness), this Agreement will be effective as of the Effective Date, and will continue, unless terminated earlier in accordance with this Article 9 (Term), until expiration of the last Royalty Term for the last Licensed Product in the Territory (the "**Term**").

9.2. Termination for Failure to Obtain Antitrust Clearance. If the Effective Date has not occurred within [***] after the Execution Date, this Agreement may be terminated by either Party on written notice to the other Party. In such event, neither Party shall have any further obligations under this Agreement, except for such Party's obligations of non-disclosure pursuant to Article 6 (Covenants).

9.3. Termination for Convenience. At any time after the first anniversary of the Effective Date, Company may terminate this Agreement in its entirety for any reason or no reason upon providing [***] prior written notice to HUTCHMED.

9.4. Termination for Cause.

9.4.1. <u>Termination for Material Breach</u>.

(a) If either Party believes in good faith that the other Party is in material breach of this Agreement, the Manufacturing Technology Transfer Agreement or any Supply Agreement, then the non-breaching Party (the "**Non-Defaulting Party**") may deliver written notice of such breach to the other Party (the "**Defaulting Party**"), which notice shall describe such breach in reasonable detail and state the Non-Defaulting Party's intention to terminate this Agreement. For any such alleged material breach, the allegedly breaching Party will have [***] (or, in the case of payment breach, [***]) from the receipt of the initial notice to cure such breach. If the Party receiving notice of material breach fails to cure the breach within such [***] period, then the Non-Defaulting Party may terminate this Agreement in its entirety effective on written notice of termination to the Defaulting Party. Notwithstanding the foregoing, if such material breach, by its nature cannot be cured within the foregoing cure period or is incurable, but the consequences of such breach can be reasonably alleviated but not within the foregoing cure period (an "**Extended Cure Breach**"), then such cure period shall be extended if, prior to the end of the initial ninety (90) day cure period, the Defaulting Party provides a reasonable written plan for curing or reasonably alleviating the consequences of such material breach and thereafter uses Commercially Reasonable Efforts to cure or alleviate such material breach in accordance with such written plan. Notwithstanding the foregoing, in no event shall such cure period extend for more than [***] after the Defaulting Party provides such written plan to the other Party.

(b) In case the Defaulting Party disputes the existence or materiality of a material breach alleged by the Non-Defaulting Party under Section 9.4.1(a) (Termination for Material Breach), then the issue of whether the Non-Defaulting Party may properly terminate this Agreement on expiration of the applicable cure period will be resolved in accordance with Section 11.1 (Governing Law, Jurisdiction; Dispute Resolution) and the cure periods set forth in Section 9.4.1(a) (Termination for Material Breach) will be tolled for the duration of the dispute resolution proceedings until a final resolution of such dispute. If, as a result of such dispute resolution proceeding, it is determined that the Defaulting Party committed a material breach, the Defaulting Party will have an opportunity to cure such material breach during, as applicable (i) in the case of a payment breach, ten (10) Business Days after such determination, (ii) in the case of an Extended Cure Breach, the period contemplated by (and subject to the terms of) this Section 9.4.1(b), *provided* that the Defaulting Party provides a written plan, as contemplated thereby, within thirty (30) days following such determination, and (iii) in the case of any other material breach, sixty (60) days after such determination. If the Parties dispute whether such material breach was so cured, such dispute will also be determined in accordance with Section 11.1 (Governing Law, Jurisdiction; Dispute Resolution). This Agreement will remain in full force and effect while any such dispute resolution proceeding is pending, such proceeding will not suspend any obligations of either Party hereunder, and each Party will use reasonable efforts to mitigate any damage. Notwithstanding the foregoing and subject to Section 9.9 (Rights Accruing Prior to Expiration or Termination), if any payments become payable during such period as this Agreement remains in effect solely by virtue of the preceding sentence, the Party to whom such payment obligation is attributed shall be entitled to withhold such payment until the date on which it is determined that this Agreement was not terminable by virtue of the asserted material breach giving rise to such dispute. If, as a result of such dispute resolution proceeding, it is determined that (i) the Defaulting Party did not commit such breach, (ii) such breach was not material or (iii) such breach was cured in accordance with this Section 9.4.1 (Termination for Material Breach), then no termination will be effective, and this Agreement will continue in full force and effect.

9.4.2. Termination for Bankruptcy. Each Party will have the right to terminate this Agreement upon delivery of written notice to the other Party in the event that (a) such other Party files in any court or agency pursuant to any statute or regulation of any jurisdiction a petition in bankruptcy or insolvency or for reorganization or similar arrangement for the benefit of creditors or for the appointment of a receiver or trustee of such other Party or its assets, (b) such other Party is served with an involuntary petition against it in any insolvency proceeding and such involuntary petition has not been stayed or dismissed within [***] of its filing, or (c) such other Party makes an assignment of substantially all of its assets for the benefit of its creditors (each of (a) through (c), an "**Insolvency Event**").

9.4.3. Termination for Patent Challenge. HUTCHMED may terminate this Agreement in its entirety by providing written notice of termination to Company if Company, its Affiliates, Sublicensees, or agents or independent contractors acting on behalf of any of the foregoing conducts or assists a Third Party in conducting a Patent Challenge with respect to any Licensed Patent Right or Joint Patent Right. Notwithstanding the foregoing, HUTCHMED will not have a right to terminate this Agreement pursuant to this Section 9.4.3 (Termination for Patent Challenge) where the Patent Challenge is made by Company, its Affiliates or Sublicensees (a) requesting reissue, reexamination, post-grant proceeding or any other administrative proceeding filed or requested to be filed by Company or its Affiliates or Sublicensees, after prior consultation with HUTCHMED, with respect to any Licensed Patent Right, in a good faith effort to (i) reinforce the patentability, validity or enforceability of such Patent Right or (ii) expand the claim scope of such Patent Right with respect to Licensed Products; (b) responding to compulsory discovery, subpoenas or other requests for information in a judicial or arbitration proceeding; (c) complying with any Applicable Law or court order; (d) challenging the validity or the qualification as a Valid Claim of a claim included in the Licensed Patent Rights in defense of claims first brought by HUTCHMED; or (e) in defense of an assertion of the applicable Patent Right by HUTCHMED. Further, this Section 9.4.3 shall not apply if: (x) the applicable Patent Challenge is dismissed or withdrawn within [***] of HUTCHMED's notice to Company under this Section 9.4.3 and not thereafter continued, (y) the applicable Patent Challenge is commenced by a Third Party that after the Effective Date acquires or is acquired by Company or any of its Affiliates or Sublicensees, whether by stock purchase, merger, asset purchase, or otherwise, *provided* that such Patent Challenge commenced prior to the closing of such acquisition, or (z) with respect to any such challenge by any such Sublicensee, Company terminates the sublicense granted to such Sublicensee under Section 2.4 (Right of Reference) within thirty (30) days of HUTCHMED's notice to Company under this Section 9.4.3. Notwithstanding anything to the contrary herein, Company will not use (and will ensure that its Affiliates, Sublicensees or agents or independent contractors acting on behalf of any of the foregoing do not use) any of HUTCHMED's Confidential Information acquired under this Agreement in any proceeding that challenges the validity, enforceability, or scope of any Licensed Patent Rights or Joint Patent Rights. For the avoidance of doubt, a Patent Challenge by Company, its Affiliates, Sublicensees, or agents or independent contractors acting on behalf of any of the foregoing shall not be deemed a material breach by Company under this Agreement.

9.5. Force and Effect during Notice Period. This Agreement will remain in full force and effect until the expiration of any applicable termination notice period; *provided*, *however*, that if Company or any of its Affiliates or Sublicensees achieves any Development Milestone Event or Commercial Sales Milestone Event during the termination notice period, then (a) if such termination notice period relates to a termination by Company pursuant to Section 9.3 (Termination for Convenience) or by HUTCHMED pursuant to Section 9.4 (Termination for Cause), the corresponding Development Milestone Payment or Commercial Sales Milestone Payment is accrued and Company will remain responsible for the payment of such milestone payment even if the due date of such milestone payment may come after the effective date of the termination or (b) if such termination notice period relates to any other termination, no payment shall be owning in respect of the achievement of such Development Milestone Event or Commercial Sales Milestone Event unless this Agreement is not ultimately terminated pursuant to the notice giving rise to such notice period, in which case the applicable payment that would have become due following such notice shall be due and payable at such time as it is determined that such termination shall not occur.

9.6. Effect of Termination. In the event of any termination of this Agreement in accordance with Section 9.3 or 9.4, effective as of the effective date of termination, the following provisions will apply with respect to the then-existing Licensed Compounds and Licensed Products in the Territory:

9.6.1. Termination of Licenses. Subject to Section 9.10 (Survival), except as expressly set forth in this Agreement, all rights and licenses granted from one Party to the other hereunder will immediately terminate and Company will cease any and all use of the Licensed Technology and the Development, Manufacture, Commercialization and exploitation of the then-existing Licensed Compounds and Licensed Products in the Territory, in each case, except as expressly permitted in this Section 9.6 (Effect of Termination).

9.6.2. Continuation of Sublicenses. Any and all Sublicenses granted by Company or its Affiliate pursuant to Section 2.3 (Right to Sublicense) shall, at the Sublicensee's option, survive such termination of this Agreement, except to the extent that any such Sublicensee is in material breach of this Agreement or such Sublicense. In order to effect this provision, at the request of the Sublicensee made within thirty (30) days of the termination of this Agreement, HUTCHMED will enter into a direct license with the Sublicensee on terms that are substantially the same terms as the applicable terms of this Agreement; provided that HUTCHMED will not be required to undertake obligations in addition to those required by this Agreement, and HUTCHMED's rights under such direct license will be consistent with its rights under this Agreement, taking into account the scope of the license granted under such direct license.

9.6.3. Assignment of Regulatory Submissions. With respect to the then-existing Licensed Compounds and Licensed Products in each Terminated Country or the Territory (as applicable), to the extent permitted by Applicable Law, Company will and hereby does, and will cause its Affiliates and Sublicensees (excluding those Sublicensees that enter into a direct license with HUTCHMED pursuant to Section 9.6.2 (Continuation of Sublicenses)) to (a) assign to HUTCHMED all of its rights, title, and interests in and to all Clinical Trial data, Regulatory Submissions and Regulatory Approvals related to such Licensed Compounds and Licensed Products owned or Controlled by Company or any of its Affiliates or its Sublicensees as of the effective date of termination, and (b) take those steps reasonably necessary to transfer ownership of all such assigned Regulatory Submissions and Regulatory Approvals to HUTCHMED, including submitting to each applicable Regulatory Authority a letter or other necessary documentation notifying such Regulatory Authority of the transfer of such ownership of such Regulatory Submissions and Regulatory Approvals.

9.6.4. License Grant to HUTCHMED. With respect to the then-existing Licensed Compounds and Licensed Products in each Terminated Country or the Territory (as applicable), Company will grant, and hereby does grant, to HUTCHMED and its Affiliates an exclusive, royalty-free, worldwide, transferable license or sublicense (as applicable) and right of reference, with the right to sublicense through multiple tiers, under (a) all Clinical Trial data, Regulatory Submissions and Regulatory Approvals related to any then-existing Licensed Compound or Licensed Product then owned or Controlled by Company or its Affiliates or its Sublicensees that are not permitted to be assigned to HUTCHMED or that are permitted to be assigned but the assignment of which has not yet been completed, in each case, pursuant to Section 9.6.3 (Assignment of Regulatory Submissions), (b) Patent Rights and Know-How owned or Controlled by Company as of the effective date of termination that Cover (with respect to Patent Rights) or relate to or are incorporated into (with respect to Know-How) such Licensed Compound or Licensed Product, in each case ((a) and (b)) or that are otherwise owned by Company pursuant to Section 8.1.1, to Develop, subject to Section 9.6.8 (Supply of Product), Manufacture, and Commercialize, such Licensed Compound or Licensed Product, and (c) if, as of the effective date of termination, any Licensed Products have received Regulatory Approval in any country in the Terminated Country(ies) or the Territory (as applicable), use any Licensed Product Trademarks owned or Controlled by Company that identify such Licensed Products for the purpose of Commercializing such Licensed Products (excluding, for clarity, any Trademarks comprising corporate names of Company or its Affiliates or Sublicensees or otherwise used generally to identify any of them or their businesses). If Company is unable to sublicense, or grant a right of reference under, any Patent Rights, Know-How, Clinical Trial data, Regulatory Submissions and Regulatory Approvals owned by Third Parties to HUTCHMED pursuant to this Section 9.6.4 (License Grant to HUTCHMED) without the consent of the Third Party, then, at HUTCHMED's request, Company will endeavor to procure such licenses on behalf of HUTCHMED and, as far as Company is able to procure such licenses, HUTCHMED will pay such fees and be bound by the terms set forth in such licenses.

9.6.5. Ongoing Clinical Trials.

(a) Transfer to HUTCHMED. If, as of the effective date of termination of this Agreement with respect to the Licensed Products in each Terminated Country or the Territory (as applicable), Company or its Affiliates or its Sublicensees are conducting any

Clinical Trials involving any Licensed Products, then, unless prohibited by any Regulatory Authority or Applicable Law, at HUTCHMED's written request on a Clinical Trial-by-Clinical Trial basis, Company will use Commercially Reasonable Efforts to transfer control of all such requested Clinical Trials to HUTCHMED or its designees (including the assignment of all related investigator and other agreements relating to such Clinical Trials). If HUTCHMED so elects, then Company will continue to conduct such Clinical Trials during a transition period in order to minimize interruption of any such Clinical Trials, which transition period HUTCHMED will use reasonable efforts to conclude as quickly as possible.

(b) Company Wind-Down. If HUTCHMED does not elect to assume control of any such Clinical Trials, then Company will, in accordance with accepted pharmaceutical industry norms and ethical practices, wind-down any on-going Clinical Trials of Licensed Products for which it has responsibility in such Terminated Country or the Territory (as applicable) in an orderly manner.

9.6.6. Company Knowledge and Inventory Transfer. With respect to the then-existing Licensed Compounds and Licensed Products in each Terminated Country or the Territory (as applicable), Company will provide to HUTCHMED or its designated Affiliate or Third Party copies of all material data, reports, records, and other material sales and marketing related information in Company's possession and Control to the extent that such data, reports, records, materials, or other information relate to the Development, Manufacture, performance of Medical Affairs, or Commercialization of such Licensed Compounds or Licensed Products. In connection with such transfer, Company will, at HUTCHMED's option, transfer to HUTCHMED or its designated Affiliate or Third Party all inventory of such Licensed Compounds and the Licensed Products and components and works in process held by Company with respect to the Manufacture of such Licensed Products as of the effective date of termination of this Agreement at (i) with respect to any such inventory acquired by the Company or its Affiliate by a Third Party, the cost paid by or on behalf of Company or its Affiliate for such inventory or (ii) with respect to any such inventory Manufactured by the Company or its Affiliate, the Company's or its Affiliate's Supply Price in Manufacturing such inventory. If HUTCHMED does not so elect to have all such inventory transferred to it, the Company or its Sublicensee shall have the right to continue selling such inventory, subject to and in accordance with the terms (including the royalty provisions) hereof for a period of up to one year following the effective date of termination, and shall pay HUTCHMED all royalties and sales milestones for such sale of inventory in accordance with Section 5.2.2 (Commercial Sales Milestones) and 5.3.1 (Royalty Payments), within thirty (30) days of any such sale.

9.6.7. Appointment as Exclusive Distributor. With respect to the Licensed Products in each Terminated Country or the Territory (as applicable), if any such Licensed Products are being Commercialized by Company in any country in the Territory as of the effective date of termination, then, at HUTCHMED's election on a country-by-country basis in the Territory, until such time as all Regulatory Approvals with respect to such Licensed Products in such country have been assigned and transferred to HUTCHMED, either (a) Company will appoint HUTCHMED or its designee as its exclusive distributor of such Licensed Products in such country and grant HUTCHMED or its designee the right to appoint sub-distributors, to the extent not prohibited by Applicable Law or any written agreement between Company or any of its Affiliates and a Third Party, or (b) Company will have the continued right to sell such Licensed Products in such country and the obligation to continue to Commercialize such Licensed Products in such country in accordance with the terms of this Agreement, and Company's obligations under this Agreement with respect to all such Licensed Products that Company sells, including the obligation to remit royalties to HUTCHMED hereunder, will continue in full force and effect during such period.

9.6.8. Supply of Product. Other than in the case of a termination pursuant to Section 9.4.1 (Termination for Material Breach) due to a material breach by HUTCHMED, with respect to the Licensed Products in each Terminated Country or the Territory (as applicable), if Company is Manufacturing any such Licensed Products on the effective date of termination, then, at HUTCHMED's written request, the Parties will negotiate in good faith a supply agreement under which Company will supply to HUTCHMED such quantities of such Licensed Products at the Supply Price until the earlier of (a) such time as HUTCHMED has established an alternate, validated source of supply for such Licensed Products, and (b) two years from the anniversary of the effective date of termination of this Agreement.

9.6.9. Further Assistance. With respect to the then-existing Licensed Compounds and Licensed Products in each Terminated Country or the Territory (as applicable), Company will, and will cause its Affiliates, and use Commercially Reasonable Efforts to cause its Sublicensees, to, provide any other assistance or take any other actions, in each case reasonably requested by HUTCHMED, as necessary to transfer to HUTCHMED the exploitation of such Licensed Compounds and Licensed Products, and will execute all documents as may be reasonably requested by HUTCHMED in order to give effect to this Section 9.6 (Effect of Termination).

9.6.10. Responsibility for Costs. Except as expressly set forth in this Section 9.6 (Effect of Termination), if this Agreement is terminated by Company pursuant to Section 9.4, then within 45 days after receipt of an invoice therefor, along with reasonable documentation of such costs, HUTCHMED will reimburse Company the reasonable and documented costs and expenses incurred by Company in connection with Company's performance of activities under this Section 9.6 (Effect of Termination), and if this Agreement is terminated for any other reason, then Company will bear the costs and expenses incurred by Company in connection with Company's performance of activities under this Section 9.6 (Effect of Termination).

9.7. Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by HUTCHMED and Company are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101 of the United States Bankruptcy Code. The Parties agree that each Party, as licensee of certain rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the United States Bankruptcy Code or any bankruptcy or insolvency law of any other jurisdiction. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against a Party under the United States Bankruptcy Code or any bankruptcy or insolvency law of any other jurisdiction, the other Party shall be entitled to a complete duplicate of (or complete access to, as appropriate) any intellectual property licensed to such other Party and all embodiments of such intellectual property, which, if not already in such other Party's possession, shall be promptly delivered to it (a) upon any such commencement of a bankruptcy proceeding upon such other Party's written request therefor, unless the bankrupt Party elects to continue to perform all of its obligations under this Agreement or (b) if not delivered under clause (a), following the rejection of this Agreement by the bankrupt Party upon written request therefor by the other Party.

9.8. Return of Confidential Information. Upon the termination of this Agreement pursuant to Section 9.2 (Termination for Failure to Obtain Antitrust Clearance), 9.3 (Termination for Convenience) or 9.4 (Termination for Cause) and the completion of the Receiving Party's obligations under Section 9.6 (Effect of Termination), the Receiving Party will return (or, as directed by the Disclosing Party, destroy) all Confidential Information of the Disclosing Party related to the then-existing Licensed Compounds or Licensed Products, as applicable, to the Disclosing Party that is in the Receiving Party's possession or control (other than any Confidential Information required to continue to exercise a Party's rights that survive termination of this Agreement), *provided*, *however*, copies may be retained and stored solely for the purpose of determining its obligations under this Agreement, subject to the non-disclosure and non-use obligation under Article 6 (Covenants). In addition, the Receiving Party will not be required to return or destroy Confidential Information contained in any computer system back-up records made in the ordinary course of business; *provided* that such Confidential Information may not be accessed without the Disclosing Party's prior written consent or as required by Applicable Law.

9.9. Rights Accruing Prior to Expiration or Termination. Expiration or termination of this Agreement will not relieve the Parties of any obligation accruing prior to such expiration or termination. Except as expressly set forth hereunder, any expiration or termination of this Agreement will be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to expiration or termination, including any payment obligation that accrued prior to the effective date of such expiration or termination.

9.10. Survival. The following provisions of this Agreement will survive any termination or expiration of this Agreement: this Section 9.10 (Survival); Sections 2.2 (License to HUTCHMED); 2.4.2 (HUTCHMED Right of Reference); 2.6 (No Other Rights and Retained Rights); 6.1.1 (Confidential Information) through 6.1.6 (Remedies); 8.1.1 (Inventions); 8.1.4 (Joint Technology); 8.2 (Filing, Prosecution and Maintenance of Patent Rights) (solely with respect to Joint Patent Rights); 8.3 (Patent Enforcement) (solely with respect to Joint Patent Rights); 9.9 (Rights Accruing Prior to Expiration or Termination); 11.1 (Governing Law); 11.4 (Waiver and Non-Exclusion of Remedies) through 11.11 (Severability); 11.13 (Publicity); 11.14 (Relationship of the Parties); and 11.16 (Construction) through 11.18 (Guarantees) and Article 10 (Product Liability, Indemnification and Insurance). In addition and without limiting the preceding sentence (a) Sections 9.6 (Effect of Termination) and 9.8 (Return of Confidential Information) will survive any termination of this Agreement in accordance with Section 9.3 (Termination for Convenience) or 9.4 (Termination for Cause) and (b) the following provisions of this Agreement will survive any expiration of this Agreement: Sections 2.1 (License to Company); 2.3 (Right to Sublicense); 2.4.1 (Company Right of Reference); 4.4.2 (Trademarks for Commercialization; Copyrights); 5.3.4 (Fully Paid-Up, Royalty Free License); 8.2 (Filing, Prosecution and Maintenance of Patent Rights); 8.3 (Patent Enforcement); 8.4 (Infringement of Third Party Rights); 9.7 (Rights in Bankruptcy); and 11.15 (Subcontracting).

9.11. [***]

10. PRODUCT LIABILITY, INDEMNIFICATION AND INSURANCE.

10.1. Indemnification by HUTCHMED. Subject to Section 10.5.2 (Claims under the Supply Agreement), HUTCHMED shall indemnify, defend and hold harmless Company, its Affiliates, and each of its and their respective employees, officers, directors, agents and Sublicensees (each, a "**Company Indemnified Party**") from and against any and all losses, damages, liabilities, settlements, penalties, fines and expenses (including reasonable attorneys' fees and expenses) (collectively, "**Liability**") that the Company Indemnified Party may be required to pay to one or more Third Parties to the extent resulting from or arising out of:

(a) any HUTCHMED representation or warranty set forth herein being untrue when made or any breach by HUTCHMED of any of its covenants or obligations hereunder; or

(b) the gross negligence or willful misconduct by or of HUTCHMED, its Affiliates and their respective officers, directors, agents and sublicensees (other than Company, its Affiliates and their respective officers, directors, agents and (sub)licensees) in connection with the activities contemplated by this Agreement;

(c) any claims arising from or related to HUTCHMED's, its Affiliates' or their respective officers', directors', agents' or sublicensees' (other than Company, its Affiliates and their respective officers, directors, agents and (sub)licensees) research, Development or Manufacture of the Licensed Compound; or

(d) any claims arising from or related to the Development, Manufacture, Commercialization or other exploitation of the Licensed Compound or Licensed Products by or on behalf of HUTCHMED, its Affiliates or sublicensees (other than Company, its Affiliates and their respective officers, directors, agents and (sub)licensees) in the Restricted Territory;

except in each case, to the extent caused by the gross negligence or willful misconduct of Company or any Company Indemnified Party, or by breach of this Agreement by Company.

10.2. Indemnification by Company. Company shall indemnify, defend and hold harmless HUTCHMED, its Affiliates, and each of its and their respective employees, officers, directors, agents and sublicensees (each, a "**HUTCHMED Indemnified Party**") from and against any and all Liabilities that the HUTCHMED Indemnified Party may be required to pay to one or more Third Parties to the extent resulting from or arising out of:

(a) any Company representation or warranty set forth herein being untrue when made or a breach by Company of any of its covenants or obligations hereunder; or

(b) the gross negligence or willful misconduct by or of Company, its Affiliates and their respective officers, directors, agents and Sublicensees (other than HUTCHMED, its Affiliates and their respective officers, directors, agents and sublicensees) in connection with the activities contemplated by this Agreement; or

(c) any claims arising from or related to the Development, Manufacture or Commercialization of the Licensed Compound or Licensed Products by or on behalf of the Company, its Affiliates or Sublicensees (other than HUTCHMED, its Affiliates and their respective officers, directors, agents and sublicensees);

except in each case, to the extent caused by the gross negligence or willful misconduct of HUTCHMED or any HUTCHMED Indemnified Party, or by breach of this Agreement by HUTCHMED.

10.3. Procedure. Each Party will notify the other Party in writing if it becomes aware of a claim for which indemnification may be sought hereunder. In case any proceeding (including any governmental investigation) will be instituted involving any Party in respect of which indemnity may be sought pursuant to this Article 10 (Product Liability, Indemnification and Insurance), the Party seeking indemnification (the "**Indemnified Party**") will give prompt written notice of the indemnity claim to the other Party (the "**Indemnifying Party**") and provide the Indemnifying Party with a copy of any complaint, summons or other written or verbal notice that the Indemnified Party receives in connection with any such claim. An Indemnified Party's failure to deliver notice will relieve the Indemnifying Party of liability to the Indemnified Party under this Article 10 (Product Liability, Indemnification and Insurance) only to the extent such delay is materially prejudicial to the Indemnifying Party's ability to defend such claim. If the Indemnifying Party is not contesting the indemnity obligation, the Indemnified Party will permit the Indemnifying Party to control any litigation relating to such claim; *provided*, that any failure by the Indemnifying Party to contest prior to assuming control will be deemed to be an admission of the obligation to indemnify. The Indemnifying Party shall retain counsel reasonably acceptable to the Indemnified Party (such acceptance not to be unreasonably withheld, refused, conditioned or delayed) to represent the Indemnified Party and shall pay the fees and expenses of such counsel related to such proceeding. In any such proceeding, the Indemnified Party shall have the right to participate (but not control) and be represented in any suit or action by advisory counsel of its selection and at its own expense. The Indemnifying Party will act reasonably and in good faith with respect to all matters relating to such claim and will not settle or otherwise resolve such claim without the Indemnified Party's prior written consent which will not be withheld, delayed or conditioned unreasonably; *provided*, that such consent will not be required with respect to any settlement involving only the payment of monetary awards for which the Indemnifying Party will be fully-responsible; *provided*, *further*, that the Indemnifying Party shall keep the Indemnified Party regularly informed of the status of the defense of the claim and shall take into consideration the Indemnified Party's reasonable comments thereon. The Indemnified Party will cooperate with the Indemnifying Party in the Indemnifying Party's defense of any claim for which indemnity is sought under this Agreement, at the Indemnifying Party's cost and expense. The indemnity arrangement in this Article 10 (Product Liability, Indemnification and Insurance) shall not apply to amounts paid in settlement of any action with respect to a claim, if such settlement is effected without the consent of the Indemnifying Party, which consent shall not be withheld or delayed unreasonably. Notwithstanding the foregoing, if the Indemnifying Party notifies the Indemnified Party in writing that it does not intend to assume the defense of any claim subject to indemnification hereunder in accordance with the foregoing or fails to assume the defense of any claim at least [***] before any deadline the passing of which could adversely affect the outcome without responsive action by or on behalf of the Indemnified Party (or, if the Indemnifying Party receives less than [***] notice of such deadline, if it fails to assume such defense as soon as practicable following receipt of notice), the Indemnified Party shall have the right to assume and control such defense and shall have the right to settle or compromise the same without the Indemnifying Party's consent, and the fees and expenses incurred by the Indemnified Party in connection therewith, including its reasonable legal fees and expenses, will be included in the indemnifiable Liability in connection with such claim.

10.4. Insurance. Each Party shall, at its own expense, procure and maintain during the Term and for a period of [***] thereafter, insurance or self-insurance policy/policies adequate to cover its obligations hereunder and which are consistent with normal business practices of prudent companies similarly situated. Such insurance shall not be construed to create a limit of a Party's liability with respect to its indemnification obligations under this Article 10 (Product Liability, Indemnification and Insurance). Each Party shall provide the other Party with written evidence of such insurance or self-insurance upon request. Each Party shall provide the other Party with prompt written notice of cancellation, non-renewal or material change in such insurance or self-insurance that could materially adversely affect the rights of such other Party hereunder, and shall provide such notice within [***] after any such cancellation, non-renewal or material change. The Parties agree that Company may satisfy its obligations under this Section 10.4 (Insurance) through self-insurance.

10.5. Liability Limitations.

10.5.1. No Consequential Damages. EXCEPT WITH RESPECT TO ANY BREACH OF SECTION 2.7 (EXCLUSIVITY) OR SECTION 6.1 (CONFIDENTIALITY), IN NO EVENT WILL EITHER PARTY BE LIABLE TO THE OTHER FOR ANY CONSEQUENTIAL, INCIDENTAL, INDIRECT, SPECIAL, PUNITIVE OR EXEMPLARY DAMAGES (INCLUDING LOST PROFITS, LOSS OF USE, DAMAGE TO GOODWILL, OR LOSS OF BUSINESS) OR DAMAGES BASED UPON A MULTIPLE OF EARNINGS UNDER THIS AGREEMENT, WHETHER BASED ON AN ACTION OR CLAIM IN CONTRACT, TORT (INCLUDING NEGLIGENCE AND STRICT LIABILITY), BREACH OF STATUTORY DUTY OR OTHERWISE, AND EVEN IF FORESEEABLE OR SUFFERED IN CIRCUMSTANCES WHERE A PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH LOSSES, EXCEPT TO THE EXTENT THE DAMAGES RESULT FROM A PARTY'S GROSS NEGLIGENCE, WILLFUL MISCONDUCT OR ARE PAYABLE IN CONNECTION WITH A PARTY'S INDEMNIFICATION OBLIGATIONS UNDER THIS ARTICLE 10 (PRODUCT LIABILITY, INDEMNIFICATION AND INSURANCE) FOR LIABILITY OWED TO THIRD PARTIES.

10.5.2. Claims under the Supply Agreement. Notwithstanding anything to the contrary under this Agreement, but without limiting Company's rights pursuant to Sections 9.4.1 (Termination for Material Breach) and 9.11 (Rights in Lieu of Termination), all claims related to the Supply Agreement, including claims for indemnification, shall be brought under the Supply Agreement and not under this Agreement.

11. MISCELLANEOUS.

11.1. Governing Law, Jurisdiction; Dispute Resolution.

11.1.1. Governing Law. This Agreement, and all claims arising under or in connection therewith, will be governed by and interpreted in accordance with the substantive laws of the state of New York, United States, without regard to conflict of law principles thereof.

11.1.2. Jurisdiction; Venue; Service of Process. Each Party irrevocably submits to the exclusive jurisdiction of (a) the courts of the state of New York located in New York, NY, and (b) the United States District Court for the Southern District of New York, for the purposes of any actions, suits and proceedings (collectively, "**Actions**") arising out of this Agreement. Each Party agrees to commence any such Action either in the United States District Court for the Southern District of New York or if such Action may not be brought in such court for jurisdictional reasons, in the courts of the state of New York located in New York, NY. Each Party irrevocably and unconditionally waives any objection to the laying of venue of any Action arising out of this Agreement in (i) the courts of the state of New York located in New York, NY, and (ii) the United States District Court for the Southern District of New York, and hereby and thereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such Action brought in any such court has been brought in an inconvenient forum.

11.1.3. Dispute Resolution. In the event of a dispute arising out of or relating to this Agreement either Party shall provide written notice of the dispute to the other, in which event the dispute shall be referred to the Executive Officers or their successors, for attempted resolution by good faith negotiations within thirty (30) days after such notice is received. In the event the designated Executive Officers do not resolve such dispute within the allotted thirty (30) days, either Party may, after the expiration of the thirty (30) day period, seek to resolve the dispute in a court of competent jurisdiction. Notwithstanding the preceding, the Parties acknowledge that the failure of the JSC to reach consensus as to any matter, which failure does not involve a breach by a Party of its obligations hereunder, shall not be deemed a dispute which may be referred for resolution by the Parties under this Section 11.1 (Governing Law, Jurisdiction; Dispute Resolution).

11.2. Force Majeure. No liability shall result from, and no right to terminate shall arise, in whole or in part, based upon any delay in performance or non-performance, in whole or in part, by either of the Parties to this Agreement to the extent that such delay or non-performance is caused by an event of Force Majeure. "**Force Majeure**" means an event that is beyond a non-performing Party's reasonable control, including an act of God, strike, lock-out or other industrial/labor dispute not involving the non-performing Party's own employees, war, riot, civil commotion, terrorist act, malicious damage, epidemic, pandemic, quarantine, fire, flood, storm or natural disaster, but excluding any such event arising from or related to the COVID-19 pandemic; *provided* that, the Parties agree that the effects of the COVID-19 pandemic may be a Force Majeure even though the COVID-19 pandemic is known as of the Effective Date to the extent such effects were not reasonably foreseeable by the Parties as of the Effective Date. The Force Majeure Party shall within [***] of the occurrence of the Force Majeure event, give written notice to the other Party stating the nature of the Force Majeure event, its anticipated duration and any action being taken to avoid or minimize its effect. Any suspension of performance shall be of no greater scope and of no longer duration than is reasonably required and the Force Majeure Party shall use reasonable effort to remedy its inability to perform; *provided*, *however*, if the suspension of performance continues or is anticipated to continue for [***] after the date of the occurrence, the unaffected Party shall have the right but not the obligation to perform on behalf of the Force

Majeure Party for a period of such Force Majeure and such additional period as may be reasonably required to assure a smooth and uninterrupted transition of such activities.

11.3. Additional Approvals. Company and HUTCHMED shall cooperate and use respectively all Commercially Reasonable Efforts to make all other registrations, filings and applications, to give all notices and to obtain as soon as practicable all governmental or other consents, transfers, approvals, orders, qualifications authorizations, permits and waivers, if any, and to do all other things necessary or desirable for the consummation of the transactions as contemplated hereby (disregarding, for purposes hereof, the proviso set forth in Section 2.5). Neither Party shall be required, however, to divest or out-license products or assets or materially change its business if doing so is a condition of obtaining any governmental approvals of the transactions contemplated by this Agreement. Without limitation of the foregoing, HUTCHMED will use Commercially Reasonable Efforts to obtain, as promptly as practicable, all approvals, permits, authorizations or clearances from the Human Genetics Resources Administration of China and any other Governmental Authorities as may be necessary, and take such other actions as may be required under Applicable Laws, in order to transfer or disclose to Company and its designees any Licensed Know-How (including all data generated pursuant to all Clinical Trials conducted or being conducted by HUTCHMED, its Affiliates or Third Parties in respect of the Licensed Compound and Licensed Products prior to the date of delivery) as contemplated by this Agreement. HUTCHMED shall notify Company as soon as reasonably practicable if it becomes aware of any Applicable Law that would prohibit or otherwise restrict the transfer to Company of any Licensed Know-How necessary, or believed by HUTCHMED in good faith to be reasonably useful to, exploiting the Licensed Compound and Licensed Products, which notice shall describe such Applicable Law and the scope of the Licensed Know-How that may not be transferred.

11.4. Waiver and Non-Exclusion of Remedies. A Party's failure to enforce, at any time or for any period of time, any provision of this Agreement, or to exercise any right or remedy shall not constitute a waiver of that provision, right or remedy or prevent such Party from enforcing any or all provisions of this Agreement and exercising any rights or remedies. To be effective any waiver must be in writing. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by law or otherwise available except as expressly set forth herein.

11.5. Notices.

11.5.1. Notice Requirements. Any notice, request, demand, waiver, consent, approval or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be deemed given only if delivered by hand or sent by facsimile transmission (with transmission confirmed) or by internationally recognized overnight delivery service that maintains records of delivery, addressed to the Parties at their respective addresses specified in Section 11.5.2 (Address for Notice) or to such other address as the Party to whom notice is to be given may have provided to the other Party in accordance with this Section 11.5.1 (Notice Requirements). Such notice shall be deemed to have been given as of the date delivered by hand or transmitted by facsimile (with transmission confirmed) or on the second Business Day (at the place of delivery) after deposit with an internationally recognized overnight delivery service. This Section is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

11.5.2. Address for Notice.

HUTCHMED:

Building 4, 720 Cailun Road,
China (Shanghai) Pilot Free Trade Zone, Shanghai 201203,
P. R. China.
For the attention of Chief Executive Officer

With a copy to:

Level 18 Metropolis Tower, 10 Metropolis Drive, Hung Hom
Kowloon, Hong Kong
For the attention of Group General Counsel

With a copy to (which shall not constitute notice):

Ropes & Gray LLP
800 Boylston Street
Boston, MA 02199
Attention: Marc Rubenstein
Email: marc.rubenstein@ropesgray.com

With a copy to (which shall not constitute notice):

Ropes & Gray LLP
800 Boylston Street
Boston, MA 02199
Attention: Amanda Austin
Email: amanda.austin@ropesgray.com

Company:

Takeda Pharmaceutical Company Limited
1-1 Doshomachi 4-chome, Chuo-ku, Osaka 540-8645
Attention: General Counsel, Legal Department
Facsimile: (+81) 6-6204-2055 75

with a copy to (which shall not constitute notice):

Takeda Pharmaceuticals U.S.A., Inc.
95 Hayden Ave Lexington, MA 02421
Attention: Regional General Counsel

Facsimile: 224-554-7831

with a copy to (which shall not constitute notice):

Mayer Brown LLP
1221 Avenue of the Americas
New York, NY 10020
Attention: Reb D. Wheeler
Email: rwheeler@mayerbrown.com

11.6. Entire Agreement. This Agreement, along with the Manufacturing Technology Transfer Agreement, the Supply Agreement, Quality Agreement, Pharmacovigilance Agreement any other agreement contemplated hereunder, constitutes the entire agreement between the Parties with respect to the subject matter of the Agreement. This Agreement supersedes all prior agreements, including that certain Confidentiality and Non-Disclosure Agreement entered into by the Parties dated August 17, 2022, whether written or oral, with respect to the subject matter hereof. Each Party confirms that it is not relying on any representations, warranties or covenants of the other Party except as specifically set out in this Agreement. Nothing in this Agreement is intended to limit or exclude any liability for fraud. All Schedules or Exhibits referred to in this Agreement are intended to be and are hereby specifically incorporated into and made a part of this Agreement. In the event of any inconsistency between any such Schedules or Exhibits and this Agreement, the terms of this Agreement shall govern.

11.7. Amendment. Any amendment or modification of this Agreement must be in writing and signed by authorized representatives of both Parties.

11.8. Assignment. Neither Party may assign its rights or delegate its obligations under this Agreement, in whole or in part without the prior written consent of the other Party, except that each Party shall always have the right, without such consent, (a) to perform any or all of its obligations and exercise any or all of its rights under this Agreement through any of its Affiliates, and (b) on written notice to the other Party, assign any or all of its rights and delegate or subcontract any or all of its obligations hereunder to (i) any of its Affiliates, (ii) a successor of all or substantially all of the business of such Party, whether by way of merger, sale of stock, sale of assets or other transaction (or series of transactions) or (iii) a successor of that portion of Company’s business to which this Agreement pertains. Any permitted successor or assignee of rights or obligations hereunder shall, in a writing to the other Party, expressly assume performance of such rights or obligations. Notwithstanding the foregoing, each Party shall remain responsible for any failure to perform on the part of any such Affiliates. Any attempted assignment or delegation in violation of this Section shall be void.

11.9. No Benefit to Others. The provisions of this Agreement are for the sole benefit of the Parties and their successors and permitted assigns, and they shall not be construed as conferring any rights in any other persons except as otherwise expressly provided in this Agreement.

11.10. Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of which taken together shall be deemed to constitute one and the same instrument. An executed signature page of this Agreement delivered by facsimile transmission shall be as effective as an original executed signature page.

11.11. Severability. To the fullest extent permitted by Applicable Law, the Parties waive any provision of law that would render any provision in this Agreement invalid, illegal or unenforceable in any respect. If any provision of this Agreement is held to be invalid, illegal or unenforceable, in any respect, then such provision will be given no effect by the Parties and shall not form part of this Agreement. To the fullest extent permitted by Applicable Law and if the rights or obligations of any Party will not be materially and adversely affected, all other provisions of this Agreement shall remain in full force and effect and the Parties will use their best efforts to negotiate a provision in replacement of the provision held invalid, illegal or unenforceable that is consistent with Applicable Law and achieves, as nearly as possible, the original intention of the Parties.

11.12. Further Assurance. Each Party shall perform all further acts and things and execute and deliver such further documents as may be reasonably necessary or as the other Party may reasonably require to implement or give effect to this Agreement.

11.13. Publicity. Notwithstanding Section 6.1.5 (Use of Name and Disclosure of Terms), it is understood that each Party will issue a press release announcing the execution of this Agreement, (a) for Company, as set out in Schedule 11.13(a) (Company Press Release), and (b) for HUTCHMED, as set out in Schedule 11.13(b) (HUTCHMED Press Release). Any subsequent press releases relating to the Agreement or the activities hereunder shall be subject to Section 6.1.5 (Use of Name and Disclosure of Terms), *provided* that contents of any press release or similar publicity disclosed in prior releases properly made hereunder can be re-released or re-published by either Party without a requirement for re-approval or review by the other Party.

11.14. Relationship of the Parties. The status of a Party under this Agreement shall be that of an independent contractor. Nothing contained in this Agreement shall be construed as creating a partnership, joint venture, or agency relationship between the Parties or, except as otherwise expressly provided in this Agreement, as granting either Party the authority to bind or contract any obligation in the name of or on the account of the other Party or to make any statements, representations, warranties, or commitments on behalf of the other Party. All Persons employed by a Party or any of its Affiliates shall be employees of such Party or its Affiliates and not of the other Party or such other Party's Affiliates and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such Party or its Affiliates, as applicable.

11.15. Subcontracting. Either Party may, in its sole discretion, use one or more Affiliates or Third Party contractors to perform any or all of its obligations or permitted licensed activities under this Agreement, *provided* that the subcontracting Party shall remain responsible for its obligations under the Agreement and shall be responsible for the performance of each such Affiliate and Third Party subcontractor; *provided*, *further*, that the prior written consent or approval of Company shall be required prior to HUTCHMED subcontracting any of its obligations with respect Interim Manufacturing Services.

11.16. Construction. Except where the context requires otherwise, whenever used the singular includes the plural, the plural includes the singular, the use of any gender is applicable to all genders and the word "or" has the inclusive meaning represented by the phrase "and/or". Whenever this Agreement refers to a number of days, unless otherwise specified, such number refers to calendar days. The headings of this Agreement and any descriptions of Schedules and Exhibits or descriptions of cross references are for convenience of reference only and do not define, describe, extend or limit the scope or intent of this Agreement or the scope or intent of any provision contained in this Agreement. The terms "including," "include(s)," "such as," and "for example" as used in this Agreement mean including the generality of any description preceding such term and shall be deemed to be followed by "without limitation." Reference to any statute means such statute as amended from time to time and includes any successor legislation thereto and any regulations promulgated thereunder.

11.17. English Language. This Agreement will be written and executed in, and all other communications under or in connection with this Agreement, will be in the English language. Any translation into any other language will not be an official version thereof, and in the event of any conflict or discrepancy in interpretation between the English version and such translation, the English version will prevail and control.

11.18. Guarantees.

11.18.1. <u>Payment Guarantee</u>. In consideration for Company entering into this Agreement, the HUTCHMED Guarantor irrevocably and unconditionally guarantees to Company the punctual performance of all obligations of HUTCHMED related to the payment of monies under this Agreement and undertakes to Company that whenever HUTCHMED does not pay any amount when due under or in connection with this Agreement, the HUTCHMED Guarantor shall immediately on demand pay that amount as if it was the principal obligor, so that the same benefits are conferred on Company as it would have received if such obligation had been performed and satisfied by HUTCHMED.

11.18.2. <u>Performance Guarantee</u>. The HUTCHMED Guarantor, as principal obligor and as a separate and independent obligation and liability from its obligations and liabilities in Section 11.18.1 (Payment Guarantee) undertakes to indemnify and hold each of the Company Indemnified Parties harmless from and against any loss or costs suffered or incurred by it as a result of the non-performance by HUTCHMED of any of its obligations under this Agreement. This guarantee is a continuing guarantee and will extend to the ultimate balance of sums payable by HUTCHMED under this Agreement, regardless of any intermediate payment or discharge in whole or in part.

11.18.3. <u>Waivers</u>. The obligations of the HUTCHMED Guarantor will not be affected by any act, omission, matter or thing which, but for this Section 11.18.3 (Waivers), would reduce, release or prejudice any of its obligations under this Agreement including (a) any time, waiver or consent granted to a Party or any other person, (b) the taking, variation, compromise, exchange, renewal or release of, or refusal or neglect to perfect, take up or enforce, any rights against a Party under this Agreement, (c) the insolvency (or similar proceedings) of a Party, any incapacity or lack of power, authority or legal personality of a Party or change in control, ownership or status of a Party, (d) any amendment to this Agreement (subject to such amendment not increasing the extent of the HUTCHMED Guarantor's liability under this Section 11.18 (Guarantees) without the HUTCHMED Guarantor's consent), (e) any illegality, invalidity or unenforceability of any obligation of any person under this Agreement, or (f) any other act, event or omission which might operate to discharge, impair or otherwise affect any of the obligations of the HUTCHMED Guarantor or any of the rights, powers and remedies conferred on a Party under this Agreement. The HUTCHMED Guarantor waives any right which it may have to first require the a Party to proceed against the other Party before claiming from the HUTCHMED Guarantor under this Section 11.18 (Guarantees).

[*Signature page follows*].

IN WITNESS WHEREOF, duly authorized representatives of the Parties have duly executed this Agreement to be effective as of the Effective Date.

Takeda Pharmaceuticals International AG

By /s/ Naomi De Roo
Name: Naomi De Roo
Title: Authorized Signatory

HUTCHMED Limited (和记黄埔医药（上海）有限公司)

By /s/ Weiguo Su
Name: Weiguo Su
Title: CEO & CSO

Takeda Pharmaceuticals International AG

By /s/ Nils Kjaergaard
Name: Nils Kjaergaard
Title: Regional General Counsel EUCAN

Solely for the purposes of Section 11.18 (Guarantees):

HUTCHMED (China) Limited (和黄医药（中国）有限公司)

By /s/ Weiguo Su
Name: Weiguo Su
Title: CEO & CSO

Schedule 1.38

Deemed Non-Competing Products

Schedule 1.86

HUTCHMED Trademarks

Schedule 1.110(a)

Fruquintinib

Schedule 1.112

Licensed Patent Rights

Schedule 4.1.2

HUTCHMED Development Plan

Schedule 4.1.3

Initial Development Plan

Schedule 4.2.1

Key Terms of Regulatory Transition Plan

Schedule 4.3.2

Terms of Clinical and Commercial Supply Agreement

Schedule 4.3.3

Terms of Manufacturing Technology Transfer

Schedule 6.2.1

Patient Information

Schedule 11.13(a)

Company Press Release

Schedule 11.13(b)

HUTCHMED Press Release

Exhibit 12.1

Certification by the Principal Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Weiguo Su, certify that:

1. I have reviewed this annual report on Form 20-F of HUTCHMED (China) Limited (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: February 28, 2023
By: /s/ Weiguo Su
Name: Weiguo Su
Title: Chief Executive Officer

Exhibit 12.2

Certification by the Principal Executive Officer Pursuant to
Section 302 of the Sarbanes-Oxley Act of 2002

I, Cheng Chig Fung, Johnny, certify that:

1. I have reviewed this annual report on Form 20-F of HUTCHMED (China) Limited (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: February 28, 2023
By: /s/Cheng Chig Fung, Johnny
Name: Cheng Chig Fung, Johnny
Title: Chief Financial Officer

Exhibit 13.1

Certification by the Principal Executive Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Securities and Exchange Commission
100 F Street, N.E.
Washington, D.C. 20549

Ladies and Gentlemen:

In connection with the annual report of HUTCHMED (China) Limited (the “Company”) on Form 20-F for the year ended December 31, 2022 as filed with the Securities and Exchange Commission (the “Report”), I, Weiguo Su, the Chief Executive Officer of the Company, hereby certify as of the date hereof, solely for purposes of Title 18, Chapter 63, Section 1350 of the United States Code, that to the best of my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated.

This Certificate has not been, and shall not be deemed, “filed” with the Securities and Exchange Commission.

Date: February 28, 2023
By: /s/ Weiguo Su
Name: Weiguo Su
Title: Chief Executive Officer

Exhibit 13.2

Certification by the Principal Executive Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Securities and Exchange Commission
100 F Street, N.E.
Washington, D.C. 20549

Ladies and Gentlemen:

In connection with the annual report of HUTCHMED (China) Limited (the “Company”) on Form 20-F for the year ended December 31, 2022 as filed with the Securities and Exchange Commission (the “Report”), I, Cheng Chig Fung, Johnny, the Chief Financial Officer of the Company, hereby certify as of the date hereof, solely for purposes of Title 18, Chapter 63, Section 1350 of the United States Code, that to the best of my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated.

This Certificate has not been, and shall not be deemed, “filed” with the Securities and Exchange Commission.

Date: February 28, 2023
By: /s/Cheng Chig Fung, Johnny
Name: Cheng Chig Fung, Johnny
Title: Chief Financial Officer

Exhibit15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-240180, No. 333-224391 and No.333-212406) and Form F-3 (No. 333-237574) of HUTCHMED (China) Limited of our report dated February 28, 2023 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Shenzhen, the People’s Republic of China
February 28, 2023

Exhibit 15.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-240180, No. 333-224391 and No.333-212406) and Form F-3 (No. 333-237574) of HUTCHMED (China) Limited of our report dated March 4, 2021 relating to the financial statements, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers
Hong Kong
February 28, 2023

Exhibit 15.3

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-240180, No. 333-224391 and No.333-212406) and Form F-3 (No. 333-237574) of HUTCHMED (China) Limited of our report dated February 28, 2023 relating to the financial statements of Shanghai Hutchison Pharmaceuticals Limited, which appears in this Annual Report on Form 20-F.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Shanghai, the People’s Republic of China
February 28, 2023

Exhibit 15.4

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-240180, No. 333-224391 and No.333-212406) and Form F-3 (No. 333-237574) of HUTCHMED (China) Limited of our report dated December 7, 2021 relating to the financial statements of Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited, which appears in this Annual Report on Form 20-F.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Guangzhou, the People's Republic of China
February 28, 2023

Exhibit 15.5

February 28, 2023

Matter No.: 837029
Doc Ref: 108779456
(852) 2842 9595
Felicity.Lee@conyers.com

HUTCHMED (China) Limited
48th Floor, Cheung Kong Center
2 Queen's Road Central
Hong Kong

Dear Sirs,

Re: HUTCHMED (China) Limited (the "Company")
Annual Report on Form 20-F

We hereby consent to the filing of this letter as an exhibit to the Company's annual report on Form 20-F for the year ended December 31, 2022 (the "**Annual Report**") with the U.S. Securities and Exchange Commission and to the inclusion therein of the reference to our name on page 206 of the annual report under the heading "Taxation – Overview of Tax Implications of Various Other Jurisdictions – Cayman Islands Taxation" in the form and context in which they appear, and further consent to the incorporation by reference into the Company's registration statement on Form S-8 (File No. 333-240180) that was filed on July 30, 2020 and the Company's registration statement on Form F-3 (File No. 333-237574) that was filed on April 6, 2020 of the summary of our opinion under the heading "Taxation - Overview of Tax Implications of Various Other Jurisdictions - Cayman Islands Taxation" in the Annual Report. In giving such consent, we do not thereby admit that we come within the category of persons whose consent is required under Section 7 of the Securities Act, or the Rules and Regulations of the U.S. Securities and Exchange Commission thereunder.

Yours faithfully,

/s/Conyers Dill & Pearman
Conyers Dill & Pearman

Exhibit 15.6

HUTCHMED

February 28, 2023

VIA EDGAR

Division of Corporation Finance
U.S. Securities & Exchange Commission
100 F Street, NE
Washington, D.C. 20549

Re: HUTCHMED (China) Limited
Submission under the Item 16I(a) of Form 20-F

Attn: Division of Corporation Finance
Office of Life Sciences

Dear Sir/Madam,

In compliance with the Holding Foreign Companies Accountable Act, HUTCHMED (China) Limited (the "Company") is submitting via EDGAR the following information as required under Item 16I(a) of Form 20-F.

For the immediately preceding annual financial statement period, the Company's auditor, PricewaterhouseCoopers Zhong Tian LLP (a registered public accounting firm that The United States Public Company Accounting Oversight Board was unable to inspect or investigate completely) issued an audit report for the Company.

To the Company's best knowledge and based on an examination of our register of members and public filings made by our shareholders, including among others, the Schedule 13G/A filed by Capital International Investors on February 13, 2023, the Company respectfully submits that it is not owned or controlled by a governmental entity in the foreign jurisdiction as of the date of this submission.

As of February 15, 2023, Hutchison Healthcare Holdings Limited owns approximately 38.5% of the Company's total outstanding shares. Based on an examination of the Company's register of members and public filings made by the Company's shareholders, no other shareholder owns more than 5% of the Company's outstanding shares as of February 15, 2023. Hutchison Healthcare Holdings Limited is an indirect wholly owned subsidiary of CK Hutchison Holdings Limited, which is a private company incorporated in the Cayman Islands and listed on The Stock Exchange of Hong Kong Limited.

In addition, the Company is not aware of any governmental entity that is in possession of, direct or indirect, of the power to direct or cause the direction of the management and policies of the Company, whether through the ownership of voting securities, by contract, or otherwise.

Should any member of the Staff have any questions or comments regarding the Company's submission set forth above, please do not hesitate to contact me by phone at (852) 2121-3809 or by facsimile at (852) 2128-8281, or you may contact our outside legal counsel, James C. Lin, Davis Polk & Wardwell, at (852) 2533-3386.

Very truly yours,

/s/ Johnny Cheng

Name: Johnny Cheng
Title: Chief Financial Officer

cc: Weiguo Su, Chief Executive Officer
Charles Nixon, General Counsel
James C. Lin, Davis Polk & Wardwell