Bellevue Healthcare Trust

JUNE 2022

Factsheet

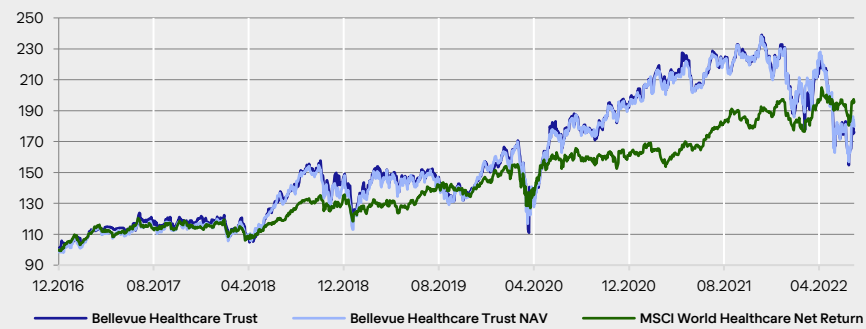
London Stock Exchange (LSE)

Marketing document

Investment focus

Bellevue Healthcare Trust intends to invest in a concentrated portfolio of listed or quoted equities in the global healthcare industry. The investable universe for the fund is the global healthcare industry including companies within industries such as pharmaceuticals, bio-technology, medical devices and equipment, healthcare insurers and facility operators, information technology (where the product or service supports, supplies or services the delivery of healthcare), drug retail, consumer healthcare and distribution. There is no restrictions on the constituents of the fund's portfolio by index benchmark, geography, market capitalisation or healthcare industry sub-sector. Bellevue Healthcare will not seek to replicate the benchmark index in constructing its portfolio. The Fund takes ESG factors into consideration while implementing the afore-mentioned investment objectives.

Indexed performance since launch



Cummulated & annualized performance

Cummulated

	1 M	1 Y	2 Y	3 Y	4 Y	5 Y	ITD
Share	-2.0%	-21.6%	-1.1%	20.6%	32.3%	46.7%	76.1%
NAV	2.1%	-19.8%	-0.5%	22.2%	38.9%	57.3%	79.8%
BM	0.4%	10.8%	22.3%	42.8%	64.5%	70.1%	95.5%

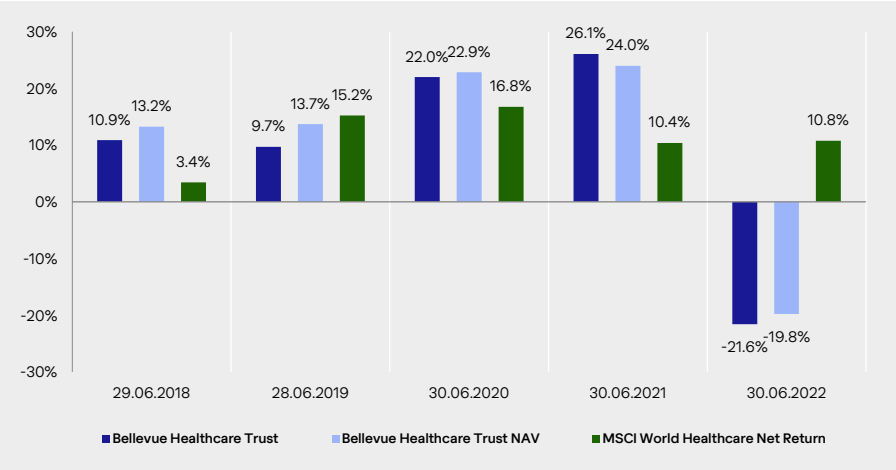
Annualized

1 Y	3 Y	5 Y	ITD
-21.6%	6.4%	8.0%	10.7%
-19.8%	6.9%	9.5%	11.1%
10.8%	12.6%	11.2%	12.8%

Annual performance

	2017	2018	2019	2020	2021	YTD
Share	14.8%	4.9%	22.7%	29.1%	16.6%	-23.8%
NAV	12.7%	8.6%	25.9%	25.7%	15.2%	-20.3%
BM	9.4%	8.8%	18.4%	10.3%	20.8%	-0.3%

Rolling 12-month-performance



Fund facts

Share price	GBp 150.60
Net Asset Value (NAV)	GBp 153.53
Market Capitalisation	GBp 900.7 mn
Investment manager	Bellevue Asset Management (UK) Ltd.
Administrator	Sanne Funds Services (UK) Ltd.
Launch date	01.12.2016
Fiscal year end	Nov 30
Benchmark	MSCI World Healthcare Net Return
ISIN code	GB00BZCNLL95
Bloomberg	BBH LN Equity
Number of ordinary shares	586'624'189
Management fee	0.95%
Performance fee	none
Min. investment	n.a.
Legal entity	UK Investment Trust (plc)
EU SFDR 2019/2088	Article 8

Key figures

Beta	1.29
Correlation	0.32
Volatility	29.6%
Tracking Error	19.5
Active Share	95.26
Sharpe Ratio	0.46
Information Ratio	-0.04
Jensen's Alpha	-5.29

Source: Bellevue Asset Management, 30.06.2022;
Calculation over 3 years.

Source: Bellevue Asset Management, 30.06.2022; all figures in GBp %, total return / BVI-methodology
Past performance is not a reliable indicator of future results and can be misleading. Changes in the rate of exchange may have an adverse effect on prices and incomes. All performance figures reflect the reinvestment of dividends and do not take into account the commissions and costs incurred on the issue and redemption of shares, if any. The reference benchmark is used for performance comparison purposes only (dividend reinvested). No benchmark is directly identical to the fund, thus the performance of a benchmark is not a reliable indicator of future performance of the Bellevue Healthcare Trust to which it is compared. There can be no assurance that a return will be achieved or that a substantial loss of capital will not be incurred.

Top 10 positions

Jazz Pharmaceuticals	8.1%
Sarepta Therapeutics	6.8%
Option Care Health	6.4%
Insmed	5.7%
United Health Group	5.6%
Axonics	5.3%
CareDx	4.4%
Amedisys	4.3%
Apellis Pharmaceuticals	4.3%
Charles River	4.0%
Total top 10 positions	54.9%

Sector breakdown

Focused Therapeutics	26.4%
Med-Tech	16.2%
Services	14.7%
Diagnostics	10.7%
Managed Care	9.5%
Diversified Therapeutics	8.1%
Tools	5.2%
Healthcare IT	4.7%
Health Tech	3.6%
Dental	1.0%

Geographic breakdown

United States	93.8%
China	3.1%
Canada	2.1%
Switzerland	1.0%

Market cap breakdown

Mega-Cap	15.1%
Large-Cap	8.5%
Mid-Cap	51.7%
Small-Cap	24.7%

Source: Bellevue Asset Management, 30.06.2022;
For illustrative purposes only. Holdings and allocations are subject to change. Any reference to a specific company or security does not constitute a recommendation to buy, sell, hold or directly invest in the company or securities. Where the subfund is denominated in a currency other than an investor's base currency, changes in the rate of exchange may have an adverse effect on price and income.

Welcome to our June jocundity. If nothing else, these whipsawing markets offer an opportunity to dissect historical performance and decision-making, to see what has or has not worked and why. Sometimes (all too frequently at the moment), the market makes little sense. We have been reflecting though and this forms the basis of this month's musings.

Macro remains king and fear of capital loss predominates over greed for opportunistic bottom fishing. As the quarterly reporting season gets underway, prepare for a slew of negative earnings revisions across the wider market. Typically, sell-side analysts are only marginally less behind the curve than central bankers and our own prime minister.

For those with a time horizon longer than a tik-tok video, the key question at this point should relate to where to find above inflation, visible and 'quality' (i.e. dependable) growth. Ladies and gentlemen, look no further...

Monthly review

The wider market

During June, the MSCI World Index second-worst month since March 2020's COVID-related rout, with the Index declining 8.8% in dollars (5.5% in sterling). As a reminder, the worst month post-COVID was April 2022, when the Index fell 8.4% in dollars. For UK investors, the market fall feels a little less awful because sterling continues to grind lower. Until of course they try to buy something here; prices are going to be rising for some time.

Amongst their many 'achievements', superlative-chasing team Boris cannot yet claim to have driven sterling to new all-time lows: there is a little way to go to reach the trough of 1984 (which, to be fair, was much more about Reaganomics super-charging the US out of the late 70s doldrums than the UK under-performing). We wouldn't bet against Boris just yet; $1:10 here we come!

Once again, it was the twin spectres of geo-political escalation and recession that concerned investors. On the latter, we have moved on somewhat from the nebulous fear that an economic slowdown was inevitable due to inflationary pressures to a growing realisation that central bank policies may induce a recession by raising rates too far, too fast.

Having fallen >23% from its January all-time high to make a new 24-month lows in mid-June, the Index staged something of a mini-rally in the latter part of the month. However, this is the same pattern that we saw in May and in March. A 'sell the rally' mindset remains quite prevalent, even if there are more and more indications that the outlook is now discounting recession.

A pessimist may counter that the 'peak to trough' fall in the last two bear markets (2000-2003 & 2007-2009) was >50%, so there is some way further to go, but the forward earnings multiples in 2000 were more elevated and 2008 was arguably a bigger existential crisis than today when one looks at employment, which remains strong: the economy really tanks when lots of people lose their jobs and cannot find another one, whereas today's tight labour market is characterised by a skills shortage such that there are more vacancies than people able (or willing) to fill them. The stock market dynamic is also very different in terms of the weighting of earnings to less cyclical service-driven businesses.

The Index's make-up of the best and worst performers has evolved slightly compared to April's rout, reflecting the extent to which recession is already discounted in some consumer discretionary sectors and the fact that energy prices are no longer rising at the same pace as before. We enclose the full sector performance breakdown (in dollars) in Figure 1 overleaf:

Sector	Monthly perf (USD)
Pharmaceuticals, Biotechnology	-2.0%
Household & Personal Products	-2.4%
Media & Entertainment	-2.9%
Telecommunication Services	-3.9%
Food, Beverage & Tobacco	-3.9%
Food & Staples Retailing	-4.4%
Healthcare Equipment & Services	-4.8%
Insurance	-5.4%
Transportation	-5.6%
Commercial & Professional Services	-6.5%
Utilities	-7.2%
Software & Services	-7.7%
Real Estate	-8.0%
Technology Hardware & Equipment	-8.6%
Consumer Durables & Apparel	-9.3%
Retailing	-9.5%
Capital Goods	-10.0%
Diversified Financials	-11.1%
Consumer Services	-11.2%
Automobiles & Components	-11.3%
Banks	-12.3%
Energy	-14.9%
Materials	-15.4%
Semiconductors & Semiconductor	-17.8%

Source: Bellevue Asset Management, 30.06.2022

As the Q2 reporting season unfolds over the next few weeks, we expect healthcare to shine in terms of relative estimates momentum, seeing a lesser degree of negative revisions to current and future year earnings than the market as a whole.

Our expectation is grounded in the high gross margin dynamics of healthcare businesses (less raw material, energy and labour input costs), allied with a lack of correlation on the demand side to a slowing economic backdrop and positive pricing power. All being well, this should be a supportive backdrop in terms of continued relative performance for the sector versus the wider marketplace.

Healthcare

The broader 'risk off' mindset was again a positive dynamic for the relative performance of healthcare, albeit not one supportive of absolute positive returns. The MSCI World Healthcare Index finished the month up 0.25% in sterling terms (-3.3% in dollars), although this belies a meaningful degree of inter-month volatility, as illustrated in Fig 3 in the next section of the factsheet. The performance dispersion by sub-sector is illustrated in Figure 2:

	Weighting	Perf (USD)	Perf (GBP)
Generics	1.0%	5.2%	7.6%
Distributors	11.1%	1.3%	5.0%
Tools	0.6%	0.7%	4.4%
Focused Therapeutics	7.2%	-0.1%	3.4%
Conglomerate	37.2%	-0.9%	2.7%
Diversified Therapeutics	1.5%	-0.9%	2.1%
Services	12.7%	-4.6%	-1.1%
Managed Care	1.4%	-4.6%	-1.1%
Med-Tech	8.2%	-5.2%	-1.7%
Dental	2.5%	-6.9%	-3.6%
Facilities	13.1%	-10.2%	-6.9%
Other HC	0.5%	-11.2%	-7.9%
Healthcare IT	1.6%	-11.5%	-8.6%
Diagnostics	0.4%	-14.8%	-11.7%
Healthcare Technology	1.0%	-18.3%	-15.3%
Index perf		**-3.3%**	**0.3%**

Source: Bloomberg/MSCI and Bellevue Asset Management (UK) Ltd. Weightings as of 31.05.2022. Performance to 30.06.2022.

It was an unusual dynamic, with the best performers including Healthcare IT and Healthcare Technology; sectors more typically associated with a 'risk on' dynamic. Managed Care and the Therapeutics names continued to do well, the former being the beneficiary of the same factors that drove a negative result for Facilities (as described below).

As the most consumer discretionary area, it is little surprise to see Dental toward the bottom of the pile. Sentiment to Facilities (hospitals) was adversely impacted by some trading updates at a major investment conference where commentary referred to ongoing labour pressures and sluggish procedure volume recovery, latterly confirmed with a profit warning from US hospitals operator UHS. This in turn impacted sentiment toward Medical Technology and Diagnostics companies, whose product demand is linked to procedure volumes and positively impacted Managed Care: less procedure bills to pay equals more profits.

The observation that procedure volumes are stubbornly sticking at around 95% of 2019 levels when in fact they should see low single-digit annual volume growth (making the 2022 baseline expectation more like 109%) is an interesting and almost existential question to ponder. Where is the missing 15%? One cannot blame COVID mortality for all of this and it is not because mass unemployment has driven down the insured population; quite the opposite in fact. The answer is not satisfactorily clear as yet from available data sources, but it is one that we hope to revisit in a future factsheet over the summer.

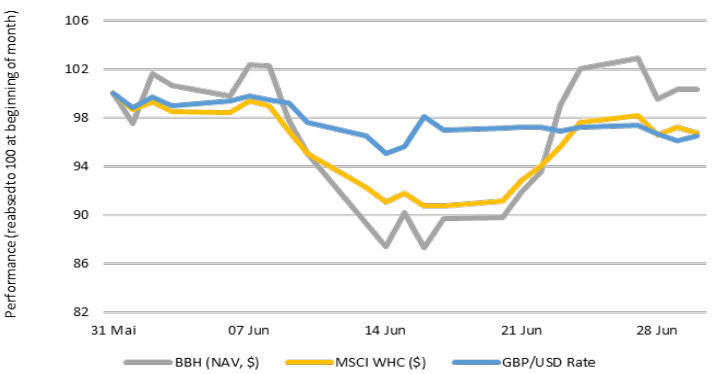
Fund flow data continues to suggest that broad interest in the sector remains muted. People are not rushing in to increase gross exposure and bottom-fish for bargains in the quality growth bucket yet. They seem quite happy riding out the macro maelstrom in the most boring things they can find (i.e. Large-Cap Pharma, Managed Care, Distributors).

The Trust

On a relative basis, it was a better month for the Trust where we finished the month modestly ahead of the benchmark, with the Trust's net asset value rising 2.1% to 153.53p. FX was again a material tailwind for the (+350bp, in line with that seen for the MSCI World Healthcare Index).

Importantly for us, the more constructive dynamic in the second half of the month saw a very strong performance from several of our holdings, confirming what should be obvious: if people start looking for more exposure to quality growth from within healthcare, then they are going to want to buy the things that we own. Whilst it still feels too early in the interest rate cycle to call the top of the fear-induced, 'risk-off' mindset, and the beginnings of a shift in the debate from purely macro to stock specifics would be a most welcome development.

Five of our ten sub-sectors delivered positive returns this month. Focused Therapeutics was the primary driver of the positive overall outcome, with Diagnostics and Services the key detractors. In both those latter cases, the weakness was broad-based. We only had one company (in the Medical Technology sub-sector that saw negative stock-specific newsflow). The evolution of the NAV during the period is illustrated in Figure 3:



Source: Bellevue Asset Management, 30.06.2022

The investment portfolio remains unchanged, with the same 29 stocks. We saw modest inflows from the issuance of 0.2m shares via the tapping programme and our gross borrowings remain unchanged. Despite the positive portfolio performance, the leverage ratio actually increased from 11.5% at the end of May to 12.1% as we deployed some cash on hand from the month end as we continue to take advantage of attractive valuations in a number of sub-sectors.

The evolution of the portfolio is summarised in Figure 4 below. We added to five positions in the portfolio and reduced six. The increased weighting in Dental was driven by active allocation as we continue to build our position. Diagnostics was entirely driven by negative share price development and the vast majority of the change in Focused Therapeutics is also share price driven. We added to our Healthcare Technology holding and reduced exposure to Healthcare IT on the back of strong performance. We reduced Managed Care and added to Medical Technology and Services on weakness. Our Tools holdings were unchanged.

	Subsectors end Apr 22	Subsectors end May 22	Change
Dental	0.0%	0.7%	Increased
Diagnostics	11.7%	11.9%	Increased
Diversified Therapeutics	10.9%	8.1%	Decreased
Focused Therapeutics	25.3%	24.5%	Decreased
Healthcare IT	4.9%	4.9%	Unchanged
Healthcare Technology	4.0%	3.5%	Decreased
Managed Care	9.6%	9.8%	Increased
Med-Tech	13.5%	15.2%	Increased
Services	15.1%	15.8%	Increased
Tools	4.9%	5.6%	Increased
	100.0%	**100.0%**	

Manager's Musings

Oncological obtrusion

There is a lot of depressing stuff going on in the world right now and we are hardly bringing levity to proceedings with the cold fact that 40% of the people reading this missive will be diagnosed with cancer during their lifetimes. Of those whose death is attributed to this awful affliction, half of them will at least be over 70, but a good innings already lived will be scant consolation to their loved ones.

Cancer is cruel, but for many the treatment is equally as bad; therapy courses are often limited not by what is optimal from an efficacy perspective, but by what the patient can endure. For all the medical progress, we still ply people with poison in the hope that their fast-metabolising cancer cells will die in disproportionate numbers. The nerves, immune system, gut and hair follicles are similarly bestowed with high metabolic rates, leading to all the horrendous side effects this approach entails.

Whilst we have made some progress in prolonging life over recent decades, for many, their treatment will bring only a few months of additional survival, the quality of which is always the most important question. There are two key drivers of improved cancer survival rates (that means living longer, not being 'cured'): earlier diagnosis and improved treatment. Let us put diagnostics to one side for now briefly summarise the progress made in non-radiation treatment over the past century or so.

Chemotherapy treatment for cancer began in the late 1930s, initially using the chemical warfare agent known as HN-2 nitrogen mustard that was created during the First World War (and banned by the Geneva Convention in the 1920s). Various less toxic derivatives were subsequently developed specifically for treating cancer. This was followed shortly by the first anti-metabolites in the 1940s, which blocked metabolic activity. The 1950s and 1960s saw a raft of novel poisons that interrupted cell division and proliferation come to market, and increasingly these were used in combination to enhance their cytotoxic effects.

The 1970s arguably mark the emergence of the first targeted chemical agent, Nolvadex (tamoxifen). Rather than seeking to poison fast growing cells in general, this specifically blocked oestrogen receptors and thus was useful for treating and preventing the recurrence of hormone-positive breast tumours but still there were long-term side effects given the wide-ranging role oestrogen plays in female health (the surgical removal of the ovaries that produce oestrogen to reduce breast cancer risk or recurrence is a long-standing surgical approach).

More advanced targeted treatments slowly began to emerge, whereby antibodies targeted receptors that were over-expressed on certain tumours. Roche/Genentech's Herceptin (approved 1998) and Rituxan (approved 1997) were the first such therapies but were still reliant on the co-administration of cytotoxic agents for the primary treatment of the relevant cancers.

The next major step forward arguably came with oral tyrosine kinase inhibitors such as Gleevec (approved 2001) and Iressa (approved 2002, albeit later withdrawn and then re-authorised). As pills, these offered a more convenient, potentially longer-term therapy for certain tumours that would, like Nolvadex, help to reduce recurrence.

Aside from expense, the problem with these highly targeted approaches is that cancers routinely mutate and, over time, it is likely that some cells will evade this particular signal and then begin to proliferate anew. Small molecule tyrosine kinase inhibitors are now a widely used group of therapies across a range of cancers but have seldom displaced concomitant use of other therapies with broader toxicity profiles in first line treatment. In short, treatment tolerability has improved less than outcomes.

Another great hope was the development of Avastin (approved 2004), the first drug to target the growth of new blood vessels. It has been well understood since the 1970s that a tumour mass cannot grow beyond a certain size without a dedicated blood supply and by inhibiting this, tumour growth should be suppressed. While Avastin has demonstrated utility across a range of tumour types, it tends to be effective only when combined with cytotoxic therapies and is not without burdensome side effects in and of itself, limiting its usage to only a sub-set of patients.

A Brave New World

A decade or so ago, many of us believed that a new era of oncology was just around the corner (we could have said "hoped" instead of "believed" but in truth we, like many others, really felt this); one where the cytotoxic therapies might be consigned to history, replaced by the emergence of a new generation of therapies seeking to harness the immune system as the cornerstone of chemo. The ASCO oncology meeting was the banner event of every investor's year, and there were probably as many investment professionals as medics, pouring over data to find the next 'big thing', generating literally thousands of pages of sell-side research.

The most interesting question about cancer is surely not "why does it kill one in six of us?" but rather "why we do not all get it?". The answer lies with our immune system. Cancer begins when cells malfunction and proliferate in an uncontrolled manner. These malfunctions occur because of random mutations during regular cellular turnover and this stuff goes wrong A LOT.

By way of an example, consider the beautiful, flawless skin of a newborn baby, free from moles, papules and blemishes and then look at your own skin. Each of those discolourations is an aberration of cellular proliferation and many contain B-RAF or FGFR-3 mutations that are associated with skin cancer. For most of us, these marks are of no concern. They are not, nor will they become, cancerous lesions.

Why is this the case? That is an incredibly complex question, but the simple answer is that the body produces signals that turn these cells quiescent (i.e. they become dormant and no longer divide). There is an old saying "Never scratch a mole".

Whilst it is highly unlikely one could transform a quiescent cell body into a malignancy, experiments with zebra fish (a model animal for melanomas) have shown that repeated injury of a benign skin growth, inducing cell division as part of the repair and healing process, can indeed turn them cancerous by over-riding the quiescence process.

The immune system plays a key role in this process of cellular quiescence, and some cancerous cells continue to grow and spread because they produce chemical signals that neutralise these immune responses, evading shutdown. Some have likened these signals to a cloaking device.

In a healthy individual, the natural role of these 'checkpoint' signals is to modulate the intensity of the immune response. As is all too evident from debilitating auto-immune diseases such as arthritis or Crohn's, the immune system has a powerful arsenal of weapons that are capable of wanton destruction in a scorched earth defence against invading pathogens.

These auto-immune diseases arise when the immune response goes haywire and attacks healthy uninfected tissue, and blocking of various checkpoint signals has been shown to play a role in the development of diseases such as rheumatoid arthritis. Whilst you do not want to let the immune system run amok, you do not want to overly suppress it either: organ transplant recipients taking immuno-suppressive medicines to prevent organ rejection are at a two-fold increased lifetime risk of cancer.

Many people will cite the early 2000s as the dawn of immune therapy for cancer, but the observation that the immune response could target tumours pre-dates this period by more than 100 years: in 1891, a physician called William Coley at Memorial Sloan Kettering used an early form of immunotherapy (called 'Coley's toxin': fluid isolated from skin infections and containing a bacterium called Streptococcus Pyogenes) into soft tissues sarcomas to induce an immune response. He published a paper citing positive results in 10 patients that was largely ignored, probably in part because x-ray therapy had just become possible and was being widely promoted.

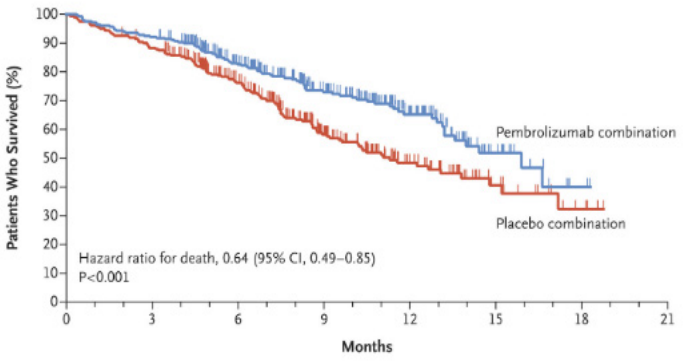
With greater understanding comes greater sophistication and the modern era has been about 'checkpoint inhibitors' that are supposed to prevent tumours from evading the immune response by shutting down these modulating signals, and 'immune primers' that are akin to hitting the accelerator pedal on the immune response, encouraging it to unleash the big guns.

The Floors of Perception

Checkpoint inhibitors have proven to be very effective in melanoma, but that is a cancer which has a propensity to self-resolve in some fortunate people and so is perhaps not a good model for assessing wider anti-tumour efficacy. We have so far seen approvals (initially in melanoma) for three checkpoint signals: CTLA-4 (first approval 2011), PD-1/PD-L1 (first approval 2014) and, more recently LAG-3 (approved 2021). These have also latterly found their way into first line treatment for a broad range of ~20 solid tumours.

However, they are no panacea. Hippocrates 'rule of thirds' has been painfully evident, with around a third of patients not responding to these drugs, a third responding incredibly well and a third not doing as well as expected. Predicting who will fall into which bucket has been more difficult than initially hoped, and at $10,000 a month or more, that is potentially a lot of wasted resources.

That having been said, the third who do very well often show durable responses. For the first time, we can imagine overall survival ('Kaplan-Meier') curves (see opposite) that not only separate between treatment and placebo, but where the treatment arm does not inevitably reach 0% still alive after long-term follow-up. A small minority can dare to dream of a functional cure. In aggregate though, the incremental benefit of adding checkpoint therapy in first-line lung cancer is measured in terms of a few months of additional life.



Source: Bellevue Asset Management, 30.06.2022

Moreover we have, by and large, failed to ditch the cytotoxics. As the chart above illustrates, chemotherapy is still widely co-administered with checkpoint inhibitors, even though they harm the immune system. The overall doses given and sequencing of the therapies has been nuanced, but cancer therapy is still arduous for many patients, impacting quality of life. If one were certain that a curative outcome were on the table, then a year of suffering side effects might seem a compelling risk/reward. However, this is not the reality for most.

And what about the 'Immune primers'? These have proven even less fruitful. The receptors for OX-40, IDO, IL-2 and IL-12 have not proven to be viable druggable targets, leading to products either lacking meaningful efficacy or having unacceptable side effect issues, even in melanoma. As one can imagine, turning the immune system up to 11 is going to unleash some side effect risks. It is also important to remember that the awful feelings of fatigue and muscle pain associated with 'flu come not from the virus but from these immune stimulating chemicals being produced in response to it. Administering them to anyone is going to be unpleasant.

Ends and Means

Checkpoint inhibitors and immune stimulators have not been the only avenues of innovation. Cell therapies, bi-specific antibodies, antibody-drug-conjugates and expansions of the oral tyrosine kinase inhibitor armamentarium have, at the margin, helped to push those Kaplan-Meier plots rightwards. Indubitably, a well-insured American receiving a cancer diagnosis today is in a far better place than they were a decade ago.

However, we are not talking about a paradigm shift. Despite all manner of accelerated approval pathways and compassionate use programmes, this incremental and often halting progress is hard fought, in terms of the years of clinical development and in terms of dollars. Working out just how much gets spent globally on cancer clinical trials is difficult, but there are a range of estimates out there spanning a range of $30-70 billion dollars per annum.

Let's take the midpoint of $50bn and reflect on how much progress we have gotten since the launch of the first checkpoint inhibitor for a collective spend of $550 billion. That's a lot of cash and recoupling this 'investment' drives prices higher: spending on cancer medicines in the US and EU has more than tripled in the past 15 years and is now a double-digit percentage of total drug spend. The average annual cost of therapy for a novel oncology drug is ~$150,000. This cannot continue.

Notwithstanding this wall of money, picking winners is getting harder as well. The US Government website clinicaltrials.gov currently lists 1,820 phase 3 or phase 4 cancer trials that are actively recruiting patients and there are some 800 molecules in clinical development programmes. Keeping track of all of this is becoming a full-time job in itself.

The Art of Seeing

The keen-eyed will be wondering what happened to the diagnostics comment in the third paragraph; wait no more. Whilst a Kaplan-Meier plot offers a definitive hard endpoint when comparing one intervention to another in a given situation, a positive outcome does not necessarily contribute to a meaningful shift in the number that society tracks more broadly – overall cancer survival. A drug intervention may be robust, but it may apply only to a sub-set of patients with rare conditions and maybe add only weeks or months to life expectancy.

Despite all of the scientific progress, the key determinant of survival remains the stage of disease at the time of diagnosis. For the four most common cancers (lung and colorectal for all, followed by breast and prostate for women and men; these four account for more than half of total new cases), there is a lot of space for tissue to grow and then shed metastases into the body before it's physical size manifests as disruption of function and becomes obvious, unlike a melanoma for example, where tumours are often easily visible.

As a consequence, symptomatic diagnoses is often in stage III (locally advanced) and stage IV (spread to other sites of the body) of the disease. This makes a huge difference to the likely outcome. For example, the current SEER 5-year survival rate for non-small cell lung cancer is 26% overall, but 64% for a localised, resectable tumour and only 8% for metastatic disease spread beyond the lung. That is an eight-fold difference in your survival odds for the same disease.

Keener minds than ours have tried to estimate the contributions of improved diagnostic tools and surveillance (mammograms and smears, routine PSA testing etc.) versus better medical interventions (drugs and surgical tools) in the overall progress in improved cancer survival. There is a range, but it looks to us to be around 2/3 improved diagnosis and 1/3 improved treatment.

We think this trend is likely to continue. Firstly, it is cheaper and easier to develop a robust diagnostic than it is to develop a novel therapeutic. Secondly, in terms of molecular sophistication, there is a huge amount of opportunity for improving the power and accuracy of such diagnostics and also opportunities to improve workflow efficiency in the collecting and analysing of various sample types.

Finally, we cannot forget that cancer treatment is an arms race; destroy the tumour before it randomly mutates such that the proposed treatment will no longer be viable. We are understanding more and more about these processes and the direction of likely escape mutations. As such, we expect continued diagnostic surveillance to become a larger feature of treatment (and thus share of the treatment wallet).

Point counter point

To the science geek, oncology has been the most exciting area of healthcare investment to follow over the past 10 years and our readers will not struggle to find voluminous and largely impenetrable sell-side tomes on various markets and the key protagonists within them. What most of these reports have failed to do well is to distil all of this down into an investable conclusion beyond "everything's a buy" and rarely do people try an pick a winner (why bother when the future looks so awesome; just have some skin in the game).

Some 10 years on from all the excitement and more than five years since the launch of BBH, we are prepared to offer an opinion. In aggregate, oncology R&D is not a winning investment opportunity. This may seem a bold statement, so let us elucidate rather than elide:

The clever eggs over at Goldman Sachs have constructed a series of basket indices that track the investment performance of key themes within healthcare. We can compare a concurrent series for GS HC Oncology (innovative cancer medicines) with GS HC Genomics (novel diagnostics companies producing many of the tests referred to previously) and also to the wider Biotechnology sector and to the US S&P500 Healthcare Index.

We will illustrate total returns from the beginning of 2015 (the earliest common date for these two series) to the end of Q3 2021 (when the market started its weird factor bashing of small healthcare companies, which will distort these indices). The total return from the Nasdaq Biotech Index would be +57% and the S&P HC +116%. Genomics would have yielded an impressive +140%. Oncology? A measly +18%, For the cynics who think the choice of Q3 21 an end point is misleading, the underperformance of oncology widens further versus the rest of the market if we follow it through to now, but the smaller Genomics companies get hit hard so the relative performance gap between the two baskets narrows considerably, but is still >30%.

We are not immune to the above and have previously succumbed to oncological obsequity; you'll find one of our names on some bullish bloviations on the oncology investment opportunities of yore. Over its lifetime, the Trust has made two specific and focused bets on oncology innovation. They both failed, in terms of making acceptable returns, and in achieving the aims that underpinned the investment thesis. We made a third, broader oncology play and this worked in the commercial sense but did not ultimately meet our investment return hurdle rate.

In contrast, we have made a number of investments in diagnostics companies, including some focused on oncology. One of these has failed, but diagnostics overall remains our most lucrative area in terms of returns since inception. There is clearly a lesson in here...

The 2022 ASCO meeting took place in June as usual. It looked pretty dull to us; bereft of meaningful breakthroughs. However, we weren't really paying that much attention this time, since we aren't doing oncology R&D plays anymore. There are more transparent, less crowded opportunities out there and that is where we are spending our time.

For the sake of humanity, we hope the progress continues, but our job is not to dish out grant money for noble research endeavours, it is to try and make money for our investors.

We always appreciate the opportunity to interact with our investors directly and you can submit questions regarding the Trust at any time via:

shareholder_questions@bellevuehealthcaretrust.com

As ever, we will endeavour to respond in a timely fashion and we thank you for your continued support during these volatile months.

Paul Major and Brett Darke

Objective

The fund's investment objective is to achieve capital growth of at least 10% p.a., net of fees, over a rolling three-year period. Capital is at risk and there is no guarantee that the positive return will be achieved over that specific, or any, time period.

Risk Return Profile

This product should form part of an investor's overall portfolio. It will be managed with a view to the holding period being not less than three years given the volatility and investment returns that are not correlated to the wider healthcare sector and so may not be suitable for investors unwilling to tolerate higher levels of volatility or uncorrelated returns.

The risk indicator assumes you keep the product for 5 years. The actual risk can vary significantly if you cash in at an early stage and you may get back less.

The summary risk indicator is a guide to the level of risk of this product compared to other products. It shows how likely it is that the product will lose money because of movements in the markets or because the fund is not able to pay you.

This fund is classified as 6 out of 7, which is a medium-high risk class. This rates the potential losses from future performance at a medium-high level, and poor market conditions will likely impact the capacity to pay you.

The portfolio is likely to have exposure to stocks with their primary listing in the US, with significant exposure to the US dollar. The value of such assets may be affected favourably or unfavourably by fluctuations in currency rates.

This fund does not include any protection from future market performance so you could lose some or all of your investment.

If the fund is not able to pay you what is owed, you could lose your entire investment.

Target market

The fund is available for retail and professional investors in the UK who understand and accept its Risk Return Profile.

Chances

- Healthcare has a strong, fundamental demographic-driven growth outlook.
- The fund has a global and unconstrained investment remit.
- It is a concentrated high conviction portfolio.
- The fund offers a combination of high quality healthcare exposure and a 3.5% dividend yield.
- Bellevue Healthcare Trust has an experienced management team and strong board of directors.

Inherent risks

- The fund invests in equities. Equities are subject to strong price fluctuations and so are also exposed to the risk of price losses.
- Healthcare equities can be subject to sudden substantial price movements owning to market, sector or company factors.
- The fund invests in foreign currencies, which means a corresponding degree of currency risk against the reference currency.
- The price investors pay or receive, like other listed shares, is determined by supply and demand and may be at a discount or premium to the underlying net asset value of the Company.
- The fund may take a leverage, which may lead to even higher price movements compared to the underlying market.

Management Team

Paul Major
Portfolio Manager
since inception of the fund

Brett Darke
Portfolio Manager
since inception of the fund

Awards

Sustainability Profile – ESG

Exclusions:	[X] Compliance UNGC, HR, ILO	[X] Controversial weapons
	[X] Norms-based exclusions	
ESG Risk Analysis:	[X] ESG Integration	
Stewardship:	[X] Engagement	[X] Proxy Voting

CO2 intensity (t CO2/mn USD sales):	26.5 (low)	MSCI ESG coverage: 100%
MSCI ESG Rating (AAA - CCC):	A	MSCI ESG coverage: 100%

Based on portfolio data as per 30.06.2022 (quarterly updates) – ESG data base on MSCI ESG Research and are for information purposes only; compliance with global norms according to the principles of UN Global Compact (UNGC), UN Guiding Principles for Business and Human Rights (HR) and standards of International Labor Organisation (ILO); no involvement in controversial weapons; norms-based exclusions based on annual revenue thresholds; ESG Integration: Sustainability risks are considered while performing stock research and portfolio construction; Best-in-class: systematic exclusion of "ESG laggards"; MSCI ESG Rating ranges from "leaders" (AAA-AA), "average" (A, BBB, BB) to "laggards" (B, CCC). Note: in certain cases the ESG rating methodology may lead to a systematic discrimination of companies or industries, the manager may have good reasons to invest in supposed "laggards". The CO2 intensity expresses MSCI ESG Research's estimate of GHG emissions measured in tons of CO2 per USD 1 million sales; for further information c.f. www.bellevue.ch/sustainability-at-portfolio-level

Important information

This document is only made available to professional clients and eligible counterparties as defined by the Financial Conduct Authority. The rules made under the Financial Services and Markets Act 2000 for the protection of retail clients may not apply and they are advised to speak with their independent financial advisers. The Financial Services Compensation Scheme is unlikely to be available.

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