EDISON

Abzena

Initiation of coverage

Biological (r)evolution

Pharma & biotech

Abzena offers a range of key services and technologies that enable its customers to develop safer and more effective biological products. This provides stable but growing revenues today, with the potential to generate substantial future revenues from small royalties on successful commercialisation of products created with Abzena's technologies. Six candidates are now in clinical development; most notable is Gilead's simtuzumab with Phase II trials ongoing for NASH, PSC and IPF. We value Abzena at £95m (97.5p/share) on its services/royalty mix.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
03/13	3.9	(0.4)	N/A	0.0	N/A	N/A
03/14	3.8	(3.7)	N/A	0.0	N/A	N/A
03/15e	5.9	(4.9)	(6.42)	0.0	N/A	N/A
03/16e	6.6	(4.7)	(4.15)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items.

A profitable services business…

The purchase of Antitope in July 2013 brought in a profitable research services business (FY14 pro forma: £5.8m sales/54% GM/22% PM), primarily from major pharma customers accessing its immunogenicity technology platform. A biological product's immunogenicity has implications for safety and efficacy, so accurate, rapid and early assessment (key skills offered by Antitope) is vital to improving clinical success and is increasingly sought after by the regulators.

…offers significant upside potential…

Also through Antitope, Abzena offers protein engineering techniques to 'humanise' antibodies and reduce immunogenicity. A number of antibodies that utilised this technology are now in clinical development, fully funded by the licencee. Abzena has disclosed six such candidates, with Gilead's simtuzumab the most high profile so far, given its potential across a range of indications. A small royalty on these antibodies would offer potentially significant free cash flow to the group.

…and supports next-generation ADC development

Abzena's antibody drug conjugate (ADC) technology is another key offering, via its PolyTherics business. First-generation ADCs (Adcetris/Kadcyla) are now marketed cancer treatments, but there is scope to significantly improve safety and efficacy, particularly by developing better 'linkers'. PolyTherics' ThioBridge linker offers the prospect of a much more stable, homogeneous and flexible ADC product. Abzena would receive greater economics (up to 5% royalty) on these ADCs and a number of companies are in the early stages of developing ADCs using ThioBridge.

Valuation: £95m (97.5p/share) on services/royalty mix

Our fair value for Abzena is £95m (97.5p/share), based on a three-phase DCF of the services business (£35.5m) and risk-adjusted royalties from existing and future licensed antibody/ADC products (£43m). Cash of £18.7m (at 30 Sep 2014), after a £20m IPO on AIM, provides financial stability and flexibility to seek new assets.

2 March 2015

Price	**82.0p**
Market cap	**£80m**

Net cash (£m) at 30 September 2014	18.7
Shares in issue	97.4m
Free float	39%
Code	ABZA
Primary exchange	AIM
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	2.0	(3.1)	N/A
Rel (local)	N/A	N/A	N/A
52-week high/low	85.0p		77.0p

Business description

Abzena is a UK group offering a range of services and technologies for the development of better biopharmaceuticals. Antitope (immunogenicity testing, protein engineering, cell line development) and PolyTherics (bioconjugation, polymer/synthetic chemistry) are the operating business units.

Next events

FY15 results	June 2015
New services business announcements	2015
Start of Phase II studies with GS-5745 (Gilead)	H215
Fresh ADC licence deals and/or options exercised	2015

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Edison profile page

Investment summary

Company description: Building better biologicals

Abzena is a provider of biological research services aimed at creating more effective and safer biological products. The group has evolved through the combination of three key businesses: PolyTherics, Antitope and Warwick Effect Polymers. PolyTherics, founded in 2001 by Imperial College and the School of Pharmacy, University of London, provides bioconjugation technologies. Antitope, founded in 2004 by Dr Matthew Baker (now Abzena's CSO) and Dr Frank Carr, offers immunogenicity assessment, protein engineering and cell line development services and was acquired by PolyTherics in 2013 for £11.5m (cash+equity). Warwick Effect Polymers, founded in 2001 as a spin-out from the University of Warwick to develop speciality biopolymers (eg PolyPEG), was acquired by PolyTherics in 2012 for £1m (equity). Abzena listed on AIM in July 2014, raising £20m (£18.6m net) from the sale of 25m new shares at 80p. Invesco (26.6%), Imperial Innovations (23.6%) and Woodford (10.4%) are cornerstone investors. The group is primarily based on the Babraham Research Campus in Cambridge (UK) and employs nearly 100 staff.

Valuation: £95m (97.5p/share) on services/royalty mix

Our fair value for Abzena is £95m or 97.5p per share, based on a three-phase DCF of the services business (£35.5m) and risk-adjusted royalties from existing and future licensed products (£43m). We include estimated end-FY15e cash of £16.5m. For future royalty revenues we estimate peak sales, launch dates, probabilities of success and small royalties (up to 1%) for the programmes in clinical development. Approximately one-third of the value of future royalties is currently assigned to simtuzumab. We also include seven further projects (of which three would be ADCs, earning up to a 5% royalty) that should emerge, with one new drug launch per year from 2021-26.

We do not include a terminal value or any estimates for potential milestones that Abzena could receive on successful development of these products (more likely from the ADCs), providing upside to our current estimates. We note that our inclusion of just seven future products could be conservative given that Abzena currently has 30 licence or option agreements in place.

Sensitivities: Low-risk business model

With stable and growing revenues from its services business and a licensed portfolio of drugs that does not require investment to develop, Abzena operates a relatively low-risk business model. However, the biological services industry is highly competitive and will require Abzena to continually invest in enhancing its technologies and offering to the sector. This may require the purchase of new assets to strengthen its position. While potential future royalty revenues on sales of products developed using Abzena's technologies appear to offer pure upside, the development of these candidates is not within Abzena's control. Advancing these candidates into late-stage clinical studies will require significant investment and/or a larger partner, so success will depend on the ability of Abzena's licensees (except Gilead) to secure the finance and/or partner.

Financials: IPO provides a solid financial platform

Consolidated FY14 revenues of £3.78m included eight months of Antitope services sales (August 2013 to March 2014), with pro forma revenues in FY14 of £5.8m. Abzena reported H115 revenues of £2.44m, and has guided for a stronger H215, resulting in FY15 revenues in line with the FY14 pro forma of £5.8m. Abzena's listing on AIM raised net proceeds of £18.6m and the group held cash of £18.7m at 30 September 2014. This provides a solid base from which to seek out new assets/technologies to expand the service offering and potential customer base. M&A activity can reasonably be expected, resulting in a more stepwise change to growth (not in our base model).

Significant long-term upside from technology licences

Abzena generates revenues from the provision of services and licences to its technologies, particularly protein/antibody engineering and bioconjugation. Services accounts for 90% of group revenues today (£3.6m reported in FY14; £5.8m pro forma) and annual growth of approximately 5-10% is expected. Longer term, significant revenues could be secured from small royalties on the sales of its customers' products created using Abzena's technologies. To date, six antibody candidates, developed using Abzena's humanising technology (Composite Human Antibody), have been disclosed as in active clinical development with customers currently conducting Phase I and II studies. Most notable is Gilead Sciences' simtuzumab, currently undergoing Phase II studies for NASH, PSC and IPF. In Exhibit 1 we summarise Abzena's service and technology platforms.

Exhibit 1: Abzena's service and technology offerings

Technology	Subsidiary	Products	Revenue type	Details
Immunogenicity assessment	Antitope	EpiScreen/iTope & TCED	Service only	Accurate, sensitive and rapid ex vivo and in silico (computer) testing for the potential generation of anti-drug antibodies (ADAs) to therapeutic antibodies/proteins; and identification of immunogenic sequences (T-cell epitopes) that cause immune response (which can then be 'fixed' by Abzena's Composite Human Antibody or Composite Protein).
Cell line development	Antitope	Composite CHO (Chinese hamster ovary)	Service only	Development of stable and highly expressing mammalian cell lines, suitable for commercial production (for clinical trials) of antibodies by the licencee (or CMO). Suitable for Abzena engineered products or biosimilars.
Protein engineering	Antitope	Composite Human Antibodies/ Composite Proteins	Service & Licence	Creation of fully humanised antibodies and deimmunised proteins to reduce the risk of immune responses (immunogenic sequences removed/critical sequences retained). Fully integrated offering with manufacturing cell line development and bioconjugation.
Bioconjugation – PK optimisation	PolyTherics (+ Warwick Effect Polymers)	TheraPEG/ HiPEG/CyPEG/ PolyPEG	Service & Licence	Optimisation of the pharmacokinetics (PK) and pharmacodynamics (PD) of therapeutic peptides and proteins, using site-specific conjugation (PEGylation) technologies, involving linkers or polymers (eg low viscosity polymer PolyPEG enables administration of conjugated proteins at high concentrations). Extends half-life (ie reduces rate of elimination from body) to reduce the frequency of dosing.
Bioconjugation – ADCs	PolyTherics	ThioBridge	Service & Licence	Site-specific conjugation of chemotherapy drugs to antibodies and antibody fragments, creating more stable and homogeneous antibody drug conjugates (ADCs) using the ThioBridge linker. Range of cytotoxic payloads available.

Source: Abzena presentation, Edison Investment Research. Note: Green shading indicates longer-term licensing potential.

For context in terms of the current value and priority of its technology platforms, we summarise the revenue streams that Abzena now generates from all its service offerings in Exhibit 2. Revenues are presented on a consolidated basis for PolyTherics (with just eight months of the Antitope business in FY14), with pro forma numbers (assuming full consolidation of Antitope from 1 April 2013) and Antitope standalone numbers as well. Antitope, and specifically its immunogenicity services, makes up the bulk of current revenues (~12% CAGR over last three years). We note that Antitope is a profitable business unit, with a 54% gross margin and 22% net profit margin in FY14.

Exhibit 2: Abzena's revenue structure (£000s)

Consolidated revenues*	FY14	FY14 (pro forma)	FY13	FY12	Antitope (standalone)	FY14	FY13	FY12
Immunology (Antitope)	2,447	3,500			**Revenue**	**5,585**	**4,947**	**4,247**
Protein Engineering (Antitope)	724	1,200			Gross profit	3,036	2,656	2,049
Cell Line Development (Antitope)	419	900			**Gross margin**	**54%**	**54%**	**48%**
Conjugation (PolyTherics)	55		353	390	EBIT	1,178	1,709	1,035
Total services revenue	**3,645**		**353**	**390**	**Profit / (loss) for the year**	**1,256**	**1,917**	**(413)**
Licences/milestones/royalties (PolyTherics)	135		3,548	1,126	Net profit margin	22%	39%	N/A
Total revenue (consolidated)	**3,780**		**3,901**	**1,516**	**Total pro forma revenue**	**5,775**	**8,848**	**5,763**

Source: Abzena Admission Document (June 2014). Note: *Consolidated revenues refers to PolyTherics; in FY14 this includes 12 months of Warwick Effect Polymers and eight months of Antitope, following the acquisition in July 2013.

Approximately 70% of the services (Antitope) revenue in FY14 was derived from repeat customers, yet the customer base is relatively broad, with the top 10 customers accounting for ~50% of total revenues. Geographically, these revenues in FY14 were broadly split between North America (57%) and Europe (40%, of which 18% in the UK).

Reducing immunogenicity

Immune responses to therapeutic protein products can be an issue for both patient safety and product efficacy. In terms of safety, immunologically based adverse events such as anaphylaxis, cytokine release syndrome, and neutralisation of endogenous proteins required for critical biological functions have caused drug developers to terminate the development of what otherwise may have been efficacious therapeutic proteins. Similarly for efficacy, unwanted immune responses to therapeutic proteins, primarily through the production of anti-drug antibodies (ADAs), can reduce effectiveness by preventing binding to the target or hastening clearance from the body.

It is therefore important to try and reduce and/or remove the potential for a therapeutic protein or antibody product to elicit an undesirable ADA immune response (immunogenicity) in patients. Assessing the potential for a therapeutic protein or antibody to be immunogenic, before it is given to patients, provides the opportunity to select or create a non-immunogenic variant, thereby reducing the risk of failure (for safety and/or efficacy) in clinical development.

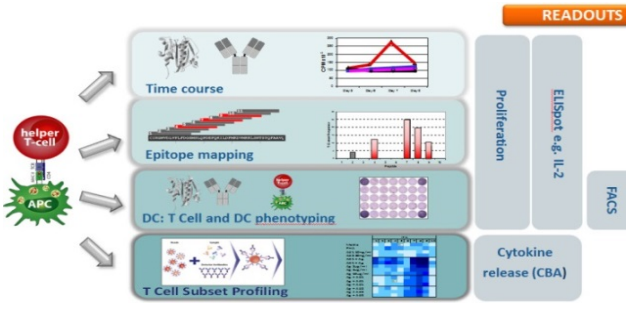
With this in mind, in August 2014 the FDA published guidelines entitled *Immunogenicity Assessment for Therapeutic Protein Products* covering the need for comprehensive immunogenicity assessment during the early development of biological products. While Abzena has already established a track record in this area, these regulatory initiatives (the EMA has also published similar guidelines) reinforce the growing need for the rapid, sensitive and accurate immunogenicity tools that Abzena offers.

Retain the good, identify/reject the bad

The risk that a therapeutic protein is immunogenic (ie generates an ADA response) increases when certain amino acid sequences, referred to as T-cell epitopes, are present. T-cell epitopes activate CD4+ T-cells, which in turn instruct B-cells to produce ADAs. Abzena's technology assesses the potential immunogenicity of the whole protein and precisely identifies any T-cell epitopes. These can then be removed and replaced with non-immunogenic sequences, a process referred to as protein engineering. However, during this process it is important to ensure that the sequences and structure of the therapeutic protein or antibody that are necessary for its function are retained, so that the resulting product is both non-immunogenic and effective.

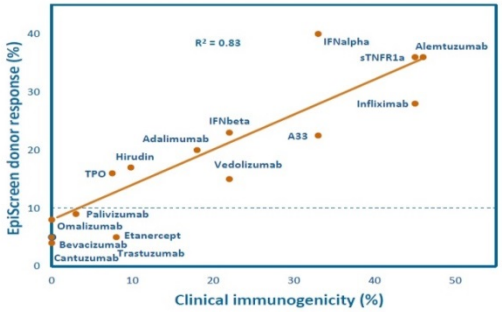
Antitope's EpiScreen is a highly accurate and sensitive ex vivo T-cell assay, to identify and map T-cell epitopes within proteins and antibodies (Exhibit 3). iTope and TCED are in silico (computer modelling) methods used to cross-reference the assay results. To validate the approach, Abzena's researchers have published data which show a strong correlation between T-cell activation identified by EpiScreen and the clinically reported ADA responses in patients to a number of approved biological agents[1] (Exhibit 4).

Exhibit 3: EpiScreen ex vivo T-cell assay formats



Source: Abzena (October 2014)

Exhibit 4: Correlation of clinical with EpiScreen data



Source: Baker and Jones (2007).

1 Baker, MP and Jones, TD. Identification and removal of immunogenicity in therapeutic proteins. Curr Opin Drug Discov Devel. 2007 Mar; 10 (2) : 219-27.

EpiScreen has been used by a wide range of pharmaceutical companies for the preclinical immunogenicity analysis of their therapeutic proteins and antibodies. Some of Abzena's major pharmaceutical customers include Amgen, GlaxoSmithKline, AstraZeneca (MedImmune), Novartis, Novo Nordisk and Pfizer. In FY14, 51 EpiScreen immunogenicity assessment studies were completed, and Abzena generated £3.5m of immunology service revenue (on a pro forma basis, Exhibit 2). There is also a significant level of repeat business, with some customers having commissioned more than 10 separate studies.

Complementary humanising antibody and cell line services

As described above, protein engineering is the process of replacing one or more of the amino acids that make up a protein or antibody, normally with the aim of removing potentially immunogenic sequences. As such, Abzena's protein engineering and manufacturing cell line services are complementary to its immunogenicity assessment service.

Multiple techniques exist for the humanisation of antibodies (modifying antibodies produced from animal cell lines to increase their similarity to antibodies produced in humans), although these do not always lead to complete removal of the T-cell epitopes. The design of Abzena's Composite Human Antibody begins with the identification of the key amino acid sequences in the original antibody that are critical for high affinity and specificity to bind to the intended molecular target. Database screening of more than 100,000 unrelated human antibodies that do not contain potentially immunogenic T-cell epitopes is then used to filter and select multiple sequence segments ('composites') to create the antibody candidate. The EpiScreen tool is used to confirm that the immunogenic T-cell epitopes have been removed from the antibody, while assays are also run to confirm that the desirable binding characteristics of the original antibody have been retained. A similar process can be adapted to deimmunise proteins (Composite Protein), such as naturally occurring toxins being developed to kill tumour cells.

The final part of Antitope's core services offering is its mammalian cell line, primarily using Chinese hamster ovary (CHO) for the production of antibodies, including those developed using the Composite Human Antibody technology. These cells lines, optimised to produce large amounts of protein product, can then be transferred to the customer or their CMO partner, for large-scale and cGMP standard production of the final antibody.

Validation points to future revenue streams

Abzena's Antitope business currently generates service revenues from its antibody engineering and cell line manufacturing technologies, with £1.2m and £0.9m respectively in FY14 (pro forma basis). Yet it is the successful clinical development and subsequent commercialisation of products that have been created using Abzena's technologiesthat offer significant long-term revenue potential. Currently, this primarily relates to six antibody candidates (developed using the Composite Human Antibody technology) now in Phase I or II clinical studies, with further products including ThioBridge-based antibody drug conjugates (ADCs) expected to follow in due course (see ADC review below). The six antibody candidates disclosed by Abzena are summarised in Exhibit 5.

Most notable is Gilead's simtuzumab, originally developed by Arresto Biosciences before its $225m acquisition by Gilead in 2010, which at the time was undergoing Phase I studies. There are now four Phase II studies underway with simtuzumab, for non-alcoholic steatohepatitis (NASH), primary sclerosing cholangitis (PSC) and idiopathic pulmonary fibrosis (IPF); all significant opportunities given the unmet medical need in these indications.

Exhibit 5: Composite Human Antibodies in clinical development

Product	Antibody target	Company	Potential indications	Status	Notes
Simtuzumab (GS-6624)	LOXL2	Gilead Sciences	Non-alcoholic steatohepatitis (NASH)	Phase IIb	2x Phase II studies initiated in 2012, with IV (n=259) and SC (n=222) formulations; enrolment complete; treatment for up to 240 weeks; primary endpoints = event free survival (EFS); mean change in hepatic venous pressure gradient (HVPG) + morphometric collagen on liver biopsy.
			Primary sclerosing cholangitis (PSC)	Phase IIb	225-pt study initiated in 2013, with SC formulation; enrolment complete; 96-week treatment; primary endpoint = collagen reduction in liver biopsy.
			Idiopathic pulmonary fibrosis (IPF)	Phase II	500-pt study (RAINIER) initiated in 2013 with SC formulation; 80% enrolled; treatment for up to 254 weeks; primary endpoint = progression free survival (PFS).
OPN-305	TLR2	Opsona Therapeutics	Delayed renal graft function (DGF)	Phase II	278-pt study initiated in 2012; primary endpoint = incidence of DGF/need for dialysis within first 7 days following renal transplantation; data mid-2016.
			Myelodysplastic syndrome (MDS)	Phase I/II	40-pt Phase I/II study initiated in Jan 2015, in 2nd-line lower risk MDS; primary endpoint = dose and frequency based on DLT toxicity; data mid-2016.
VPI-2690B	αVβ3 receptor	Vascular Pharma	Diabetic nephropathy	Phase II	300-pt study initiated in 2014 for diabetic nephropathy in type I and II diabetic patients; 48-wk treatment period; primary endpoint = change from baseline in albuminuria; data H217.
GS-5745	MMP-9	Gilead Sciences	Ulcerative colitis (UC); gastric cancer; Crohn's disease (CD)	Phase II-ready	Feb 2015: Gilead announces plans to advance clinical development in ulcerative colitis and gastric cancer in 2015; Phase II also planned in Crohn's disease; 74-pt Phase I in mod-to-severe UC complete.
NKTT120	iNKT cells	NKT Therapeutics	Sickle cell disease	Phase Ib	21-pt Phase I dosing/safety study ongoing; encouraging data from first 18 patients at ASH 2014; awaiting final data (H115); possible Phase II start in H215.
SDP 051	Cadherin 11	Adheron Therapeutics	Rheumatoid arthritis, fibrotic conditions (NASH), cancer	Phase I	Jan 2014: Phase I complete; safe and well-tolerated up to 10 mg/kg per day. Preclinical studies demonstrate activity across cancer, rheumatoid arthritis and fibrotic conditions including NASH.

Source: Abzena presentation (Dec 2014), Edison Investment Research, clinicaltrials.gov

It should be noted that simtuzumab was also developed for a number of cancer indications, but Phase II studies in myelofibrosis, colorectal cancer and pancreatic cancer all recently failed to meet their primary efficacy endpoints. However, we note that Gilead commented on its FY14 analyst call (3 Feb 2015) that "myelofibrosis is biologically different from liver and pulmonary fibrosis", therefore these negative cancer results should not necessarily have read-across to the ongoing studies.

Gilead also announced on its FY14 call that it intends to advance the development of its anti-MMP9 antibody GS-5745 specifically for ulcerative colitis and gastric cancer, with Phase II studies also planned in Crohn's disease.

Beyond this disclosed clinical-stage pipeline, we note that over the last five years Abzena has announced at least 27 collaborations with biotech companies and research organisations over its licensable antibody/protein humanisation and bioconjugation (ADC/PK optimisation) technologies. Also, these are just the ones where the partner has agreed to Abzena's disclosure, as some companies would prefer such licences to remain confidential for competitive reasons. Abzena has stated publicly that it currently has 30 licence and licence option agreements, including some that cover multiple potential products (eg de-immunised toxins for cancer and ADC products).

ADCs – seeking a perfect union of MAb, linker and drug

Antibody drug conjugates (ADCs) are a still emerging class of cancer therapeutics, harnessing the tumour-targeting properties of antibodies with highly potent cytotoxic drugs. The ADC binds to the target antigen on the tumour cell surface and enters the cell, whereupon the payload is released by cleavage of the linker (by acid conditions or enzymes) or when the antibody is degraded in the cell if a non-cleavable linker is used. The released drug then kills the cell (and sometimes adjacent tumour cells) according to the mechanism of action. The payloads now being used in ADCs (tubulin polymerisation inhibitors or DNA-damaging agents) are so potent that they would cause too much damage to healthy cells if used as a standalone chemotherapeutic agent.

With both antibodies and cytotoxic drugs often used independently to treat cancer, attaching a toxic payload to a tumour cell selective antibody appears an elegant and highly effective solution. However, in reality the development of ADCs has proved challenging, but this is typical of novel

drug development, as demonstrated by the long and arduous route to successful development of antibodies, which now accounts for five of the top 10 biggest selling drugs globally.

The first ADC to reach the market was Mylotarg (gemutzumab ozogamicin) in 2000, for the treatment of acute myeloid leukaemia (AML), but the product was withdrawn in 2010 following safety concerns and lack of efficacy. However, two more recent ADC product launches have been far more successful, Seattle Genetics' Adcetris (brentuximab vedotin) approved in 2011 to treat Hodgkin's lymphoma and anaplastic large cell lymphoma ($325m sales in FY14) and Roche's Kadcyla (trastuzumab emtansine) approved in 2013 for HER2+ve breast cancer ($590m sales in FY14). Kadcyla was developed using ImmunoGen's ADC technology. Seattle Genetics and ImmunoGen remain the dominant players in the field, in terms of these approved products and the mid- to late-stage pipeline of ADC candidates (Exhibit 6).

Exhibit 6: ADC portfolio – marketed and late-stage pipeline (at least Phase II)

Product	Company	ADC licensor	Antibody target	Payload	Status	Indications
Adcetris (brentuximab vedotin)	Seattle Genetics		CD30	Auristatin (MMAE)	Marketed	2011: FDA accelerated approval for Hodgkin's lymphoma and anaplastic large cell lymphoma; $325m sales in FY14; Multiple Phase III studies ongoing for CTCL/PTCL/NHL.
Kadcyla (trastuzumab emtansine, T-DM1)	Roche	ImmunoGen	HER2	Maytansine (DM1)	Marketed	Feb 2013: FDA approval for HER2+ve metastatic breast cancer; $590m sales in FY14; Phase II/III studies ongoing for gastric cancer + NSCLC.
Pinatuzumab vedotin (RG7593)	Roche	Seattle	CD22	Auristatin (MMAE)	Phase II	NHL; diffuse large B-cell lymphoma.
Polatuzumab vedotin (RG7596)	Roche	Seattle	CD79b	Auristatin (MMAE)	Phase II	NHL; diffuse large B-cell lymphoma.
Lifastuzumab vedotin (RG7599)	Roche	Seattle	NaPi2b	Auristatin (MMAE)	Phase II	Ovarian cancer (platinum-resistant).
SAR3419	Sanofi	ImmunoGen	CD19	Maytansine (DM4)	Phase II	NHL (DLBCL); B-cell ALL.
ABT-414	AbbVie	Seattle	EGFR	Auristatin (MMAF)	Phase II	Glioblastoma multiforme; squamous cell tumours.
MLN0264	Takeda	Seattle	GCC	Auristatin (MMAE)	Phase II	Advanced GI malignancies.
Glembatumumab vedotin (CDX-011)	Celldex Therapeutics	Seattle	GPNMB	Auristatin (MMAE)	Phase II	Breast cancer; advanced melanoma.
PSMA ADC	Progenics	Seattle	PSMA	Auristatin (MMAE)	Phase II	Prostate cancer (metastatic castration-resistant, CRPC).
Indatuximab ravtasine (BT-062)	Biotest	ImmunoGen	CD138	Maytansine (DM4)	Phase II	Multiple myeloma; other solid tumours.
Labetuzumab-SN-38 (IMMU-130)	Immunomedics		CEACAM5	SN-38 (irinotecan metabolite)	Phase II	Metastatic colorectal cancer.
Sacituzumab govitecan (IMMU-132)	Immunomedics		TROP2	SN-38 (irinotecan metabolite)	Phase II	Triple-negative breast cancer (TNBC); SCLC; pancreatic cancer; colorectal cancer.

Source: Edison Investment Research, BioCentury, clinicaltrials.gov

Linker is at the heart of the matter

Yet Adcetris and Kadcyla are regarded as first-generation ADC products, with stability and heterogeneity issues that may limit their effectiveness and increase unwanted side effects. At the heart of the technology is the linker used to attach the payload to the antibody, which is where Abzena's ThioBridge may offer a number of advantages over the competition. Also, when coupled with Abzena's immunogenicity tools, antibody engineering and manufacturing cell line development, the company has an increasingly strong ADC offering.

The linkers developed by ImmunoGen and Seattle are reactive towards either the amino side chains of lysine residues (in Kadcyla), or to the thiol side chains in cysteine residues, created from reducing inter-chain disulfide bonds (Adcetris). However, both approaches have limitations. Conjugation to lysines, of which there can be more than 80 on a given antibody, cannot be precisely controlled, which leads to a heterogeneous mixture of ADCs with different drug-to-antibody (DAR) ratios. Having a consistent DAR of four is suggested as ideal for an ADC. Too low and naked antibodies compete with ADCs to bind the target, too high and the ADC becomes less stable with a greater chance that the payload is released before reaching the tumour, causing tolerability issues. Attachment via cysteine residues is an alternative to conjugation to lysines, as there are far fewer

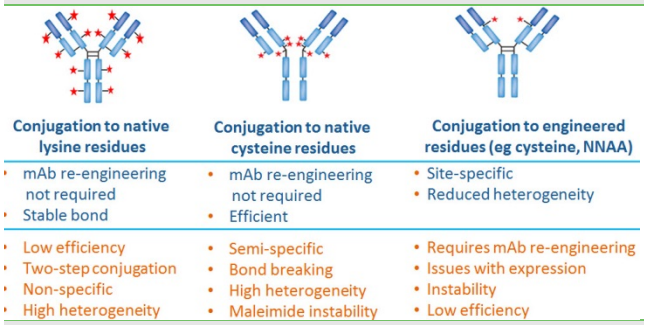
cysteine residues in an antibody. An intact IgG1 antibody has four inter-chain disulfide bonds that can be reduced to release eight free cysteine thiols, which can then serve as sites for conjugation. This therefore produces a mixture of ADCs with a still variable DAR ranging from 0-8, while the disulfide bond remains broken after conjugation, which affects the integrity of the antibody, potentially impairing its ability to bind to its tumour cell target.

Another method developed to overcome a heterogeneous mixture of ADCs with variable DARs is to use antibodies with engineered cysteine residues, ensuring site-specific conjugation of the payload. This produces a more homogeneous ADC with a DAR of two, although the stability of the linker (maleimide) is still sub-optimal. A further re-engineering approach is to incorporate non-natural amino acids into the antibody as sites for conjugation, which also improves homogeneity while offering flexibility in the number of sites and therefore DAR ranges. However, re-engineering antibodies is complex and therefore may be costly, could introduce stability issues and the final product could be more immunogenic and may therefore attract greater scrutiny from the regulators. Some of the issues with current ADC technologies are summarised and presented in Exhibit 7.

Using native disulfides guarantees 4:1 homogeneity

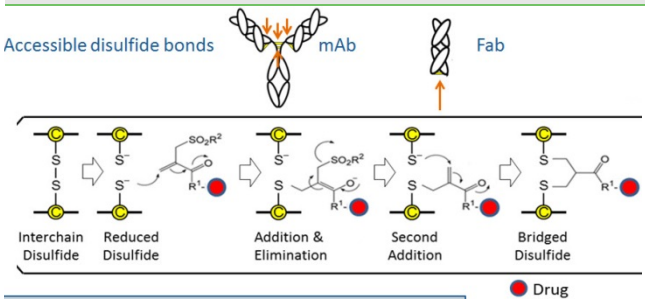
Abzena's ThioBridge has the potential to addresses or avoid these issues of instability, heterogeneity and tolerability by targeting native disulfide bonds in an antibody. Using chemistry similar to PolyTherics' TheraPEG technology used in the attachment of polyethylene glycol to therapeutic proteins (PEGylation), the disulfide bond is reduced and then effectively re-bridged with a reagent including the cytotoxic drug (Exhibit 8). This leaves the antibody structurally intact and does not require any engineering. Also, with four accessible, naturally occurring inter-chain disulfides per antibody, a ThioBridge ADC should have a high percentage of DAR 4.

Exhibit 7: Issues with current ADC technologies



Source: Abzena (October 2014). NNNA = non-natural amino acid

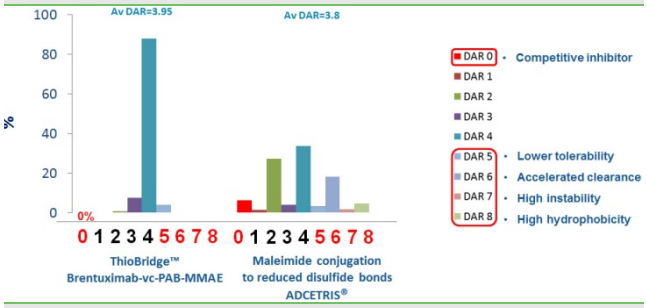
Exhibit 8: ThioBridge conjugation



Source: Abzena (October 2014)

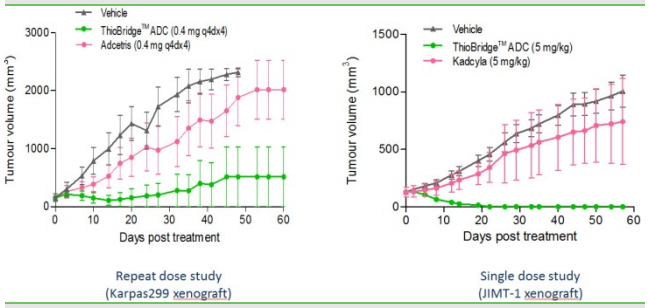
Abzena has conducted a number of assessments using its ThioBridge linker instead of, or compared to, the linker technologies used in Kadcyla and Adcetris. Exhibit 9 demonstrates how ThioBridge improves homogeneity with 80-90% DAR 4 vs Adcetris. Similarly, in vivo cancer models have shown ThioBridge ADCs to be more efficacious than Adcetris and Kadcyla (Exhibit 10).

Exhibit 9: ThioBridge improves homogeneity



Source: Abzena (October 2014)

Exhibit 10: ThioBridge vs existing ADCs (in vivo)



Source: Abzena (February 2015)

In Exhibit 11 we review the competitive landscape for companies developing ADC technologies. We suggest that the overall profile of ThioBridge (coupled with Abzena's complementary immunogenicity/antibody engineering/cell line manufacturing) offers a compelling case for partners to seek out Abzena for the development of a new generation of ADC products.

Exhibit 11: ADC linker technologies

Company	Linker	Payload release mechanism	DAR average	Mixture	Candidate status
Seattle Genetics	Dipeptide: valine-citrulline	Cleavable (cathepsin B)	4:1	Heterogenous	Marketed: Adcetris
	Maleimidocaproyl (mc) moiety	Non-cleavable (Ab degradation in lysosome)	Unknown	Heterogenous	Phase II: ABT-414
ImmunoGen	SPDB (disulfide bond)	Cleavable (by thiol-disulfide exchange reactions)	3.5:1	Heterogenous	Phase II: indatuximab ravtasine (BT-062), SAR3419
	SMCC (thioether linker)	Non-cleavable (Ab degradation in lysosome)	3.5:1	Heterogenous	Marketed: Kadcyla
Immunomedics	Carbonate (CLA2A)	Cleavable (pH-sensitive)	7.6:1	Heterogenous	Phase II: IMMU-130, IMMU-132
	Hydrazone	Cleavable (pH-sensitive)	Unknown	Heterogenous	Phase I: milatuzumab-doxorubicin
Abzena (PolyTherics)	ThioBridge (site-specific conjugation via disulfide bridging)	Cleavable or non-cleavable options	4:1	Homogenous	Preclinical
Ambrx	Not specified (Ab involves engineering with non-native amino acids)	Cleavable	2:1	Homogenous	Preclinical
Antikor	OptiLink (lysine residue-based)	Cleavable	10-12:1	Homogenous	Preclinical
Igenica	SNAP bifunctional linkers (site-specific conjugation via disulfide bridging)	Cleavable or non-cleavable options	4:1	Homogenous	Preclinical
Meditope Biosciences	Meditope (Fab region binding)	Cleavable	2:1	Homogenous	Preclinical
Mersana Therapeutics	Customisable linker chemistries (Fleximer payload platform)	Cleavable or non-cleavable options	20-30:1	Homogenous	Preclinical
Sutro BioPharma	Not specified (Ab involves engineering with non-native amino acids)	Cleavable	Multiple	Homogenous	Preclinical
ThioLogics	Thiomaleamate–PABC	Cleavable	Unknown	Homogenous	Preclinical

Source: Edison Investment Research

Valuation

Our fair value for Abzena is £95m or 97.5p per share, based on a three-phase DCF of the services business (£35.5m) and risk-adjusted royalties from existing and future licensed products (£43m). We include estimated end-FY15 cash (at 31 March 2015) of £16.5m. Our valuation model and key inputs are summarised in Exhibit 12.

Exhibit 12: Abzena valuation model and key assumptions

	rNPV (£m)	rNPV/share (p)	Key assumptions
Services business	35.5	36.44	3-phase DCF: 2015-2020 (6-10% growth), 2021-2025 (2-5% growth), 2% TV on 2025 FCF (steady-state); 10% WACC; 12% effective tax rate; 45% COGS; 25% of Group admin expense
Licensed biological product royalties	43.0	44.14	Risked-adjusted royalties (1-5%) on partner's product sales; 12.5% WACC; 12% effective tax rate; 50% of Group R&D expense (risk-adjusted); no milestones included
Portfolio sub-total	**78.5**	**80.58**	
Cash (FY15e)	16.5	16.95	Estimated at 31 March 2015
Overall valuation	**95.0**	**97.53**	97.4m shares outstanding (basic)

Source: Edison Investment Research

For future royalty revenues we summarise our estimates for the key potential drivers (peak sales, launch dates, probabilities of success, royalty rates) in Exhibit 13. Our peak sale estimates are driven by the indications currently being pursued by Abzena's partners (see Exhibit 5). Based on our understanding of Abzena's business model, we assume royalty rates of up to 1% (Edison estimate) on antibody candidates, with up to a 5% royalty for ADC products given the greater technological and IP contribution from Abzena (the company has guided up to mid-single digit royalties on its ADCs). Abzena invests significantly in its IP across its technologies (20 patent families), and its ThioBridge ADC linker is core to this. The potential royalty portfolio includes the six disclosed clinical programmes, with approximately one-third of the value of future royalties assigned to simtuzumab. We also add another product we have identified through partner announcements:

Therapix (previously NasVax) plans to initiate a Phase I study in early 2016 with its potential orally administrated anti-CD3 antibody for NASH and diabetes (Antitope and NasVax signed a humanisation deal in 2011; Therapix lists a 0.5% royalty to Antitope in its 2013 annual report).

We also include seven further projects (of which three would be ADCs) that should emerge over the next few years, with effectively one new drug launch per year from 2021-26. We do not include a terminal value or any estimates for potential milestones that Abzena could receive on successful development of these products (more likely from the ADCs), providing upside to our current estimates. We note that our inclusion of just seven future products could be conservative given that Abzena currently has 30 licence or option agreements in place. Abzena has stated that a "West Coast biotech company" has a ThioBridge option agreement to develop up to 10 ADC products.

Exhibit 13: Valuation assumptions by product

Product - Partner	Status	Peak sales ($m)	Probability of success	Launch date
Simtuzumab - Gilead Sciences	Phase II	3,000	35%	2019
OPN-305 - Opsona Therapeutics	Phase II	750	35%	2020
VPI-2690B - Vascular Pharmaceuticals	Phase II	1,000	35%	2021
GS5745 - Gilead Sciences	Phase II-ready	2,500	35%	2022
NKT120 - NKT Therapeutics	Phase Ib	250	25%	2021
SDP 051 - Adheron Therapeutics	Phase I	1,000	15%	2023
TRX-318 - Therapix Biosciences	Pre-clinical	1,000	10%	2023
New Product 1	*Phase I*	*1,000*	*15%*	*2021*
New Product 2	*Preclinical*	*1,000*	*5%*	*2022*
New Product 3	*Preclinical*	*750*	*5%*	*2023*
New Product 4	*Preclinical*	*750*	*5%*	*2024*
New Product 5 (ADC)	*Preclinical*	*1,000*	*7.5%*	*2024*
New Product 6 (ADC)	*Preclinical*	*1,000*	*7.5%*	*2025*
New Product 7 (ADC)	*Preclinical*	*1,500*	*7.5%*	*2026*

Source: Edison Investment Research

Sensitivities

With stable and growing revenues from its services business and a licensed portfolio of drugs that does not require investment to develop, Abzena operates a relatively low-risk business model. However, the biological services industry is highly competitive and will require Abzena to continually invest in enhancing its technologies and offering to the sector. This may include the need to acquire new assets/companies, which adds an element of execution risk, but with shrewd selection of targets this should only help to strengthen Abzena's position and therefore the investment case.

Although the potential future revenue streams from royalties on sales of products developed using Abzena's technologies appear to offer pure upside, the development of these candidates is not within Abzena's control. With the notable exception of Gilead, a number of candidates are being developed by relatively small private companies that may struggle to secure the finance required to develop their products in a timely and effective manner. Advancing these candidates into late-stage clinical studies will require significant investment and/or a larger partner, so success will depend on the ability of Abzena's smaller licensees to secure the finance/partner.

Financials

Abzena's reported group accounts reflect consolidation of revenues/expenses for PolyTherics, as the acquiring company of Antitope (in July 2013), and Warwick Effect Polymers (2012). FY14 revenues of £3.78m therefore include eight months of Antitope business sales (Aug 2013 to Mar 2014), whereas pro forma revenues in FY14 were £5.8m (as if Antitope were fully consolidated from 1 April 2013). Abzena reported H115 revenues of £2.44m and has guided for a stronger H215,

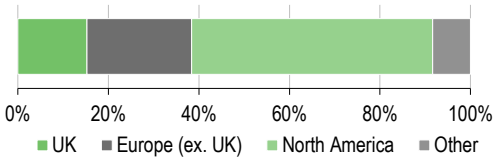
meaning that FY15 revenues are expected to be in line with FY14 pro forma of £5.8m. Immunology revenues account for approximately 50% of group revenues. Abzena listed on AIM in July 2014, raising £20m (£18.6m net) from the sale of 25m new shares at 80p. As a result, the group held cash of £18.7m at 30 September 2014. This provides a solid base from which to seek out new assets/technologies to expand the service offering and potential customer base. M&A activity can reasonably be expected, resulting in a more stepwise change to growth (not in our base model).

Exhibit 14: Financial summary

£'000s	2012	2013	2014	2015e	2016e	2017e	2018e
Year end 31 March	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS							
Revenue	**1,516**	**3,901**	**3,780**	**5,859**	**6,641**	**7,357**	**8,156**
of which: Immunology	*0*	*0*	*2,447*	*3,118*	*3,492*	*3,806*	*4,110*
Protein engineering	*0*	*0*	*724*	*1,466*	*1,591*	*1,734*	*1,873*
Cell line development	*0*	*0*	*419*	*405*	*463*	*505*	*545*
Conjugation (ADC/PEG)	*390*	*353*	*55*	*664*	*745*	*812*	*877*
Total Service revenues	***390***	***353***	***3,645***	***5,653***	***6,291***	***6,857***	***7,406***
Licenses/milestones/royalties	*1,126*	*3,548*	*135*	*206*	*350*	*500*	*750*
Cost of Sales	(301)	(103)	(1,735)	(3,031)	(3,145)	(3,086)	(3,333)
Gross Profit	**1,215**	**3,798**	**2,045**	**2,828**	**3,495**	**4,271**	**4,823**
R&D expenses	(628)	(1,729)	(2,028)	(3,010)	(3,161)	(3,319)	(3,485)
SG&A expenses	(1,945)	(2,571)	(4,196)	(5,531)	(5,669)	(5,811)	(5,927)
EBITDA	**(1,127)**	**(259)**	**(3,472)**	**(4,795)**	**(4,274)**	**(3,760)**	**(3,523)**
Operating Profit (before GW and except)	**(1,234)**	**(387)**	**(3,746)**	**(5,027)**	**(4,728)**	**(4,280)**	**(4,046)**
Intangible Amortisation	(17)	(71)	(292)	(529)	(507)	(478)	(442)
Depreciation	(107)	(128)	(274)	(233)	(454)	(520)	(523)
Exceptionals	(40)	0	(413)	0	0	0	0
Operating Profit	**(1,291)**	**(458)**	**(4,451)**	**(5,556)**	**(5,234)**	**(4,758)**	**(4,489)**
Other	0	0	0	0	0	0	0
Net Interest	7	10	15	83	67	53	35
Profit Before Tax (norm)	**(1,227)**	**(377)**	**(3,731)**	**(4,945)**	**(4,660)**	**(4,227)**	**(4,011)**
Profit Before Tax (FRS 3)	**(1,284)**	**(448)**	**(4,436)**	**(5,473)**	**(5,167)**	**(4,705)**	**(4,454)**
Tax	216	291	534	611	620	565	534
Profit After Tax (norm)	**(1,011)**	**(86)**	**(3,197)**	**(4,333)**	**(4,040)**	**(3,662)**	**(3,477)**
Profit After Tax (FRS 3)	**(1,068)**	**(157)**	**(3,902)**	**(4,862)**	**(4,547)**	**(4,141)**	**(3,919)**
Average Number of Shares Outstanding (m)	1.1	1.3	1.4	67.6	97.4	97.4	97.4
EPS - normalised (p)	**N/A**	**N/A**	**N/A**	**(6.42)**	**(4.15)**	**(3.76)**	**(3.57)**
EPS - FRS 3 (p)	**N/A**	**N/A**	**N/A**	**(7.20)**	**(4.67)**	**(4.25)**	**(4.02)**
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET							
Fixed Assets	**1,507**	**1,581**	**10,139**	**10,347**	**10,144**	**9,676**	**9,134**
Intangible Assets	1,167	1,108	9,446	8,916	8,410	7,931	7,489
Tangible Assets	340	473	693	1,431	1,734	1,744	1,645
Other	0	0	0	0	0	0	0
Current Assets	**3,383**	**3,395**	**5,856**	**19,708**	**15,364**	**11,692**	**8,314**
Stocks	0	0	295	431	431	431	431
Debtors	660	289	2,263	2,150	2,150	2,150	2,150
Cash	2,410	2,754	2,757	16,516	12,163	8,546	5,199
Other	313	352	541	611	620	565	534
Current Liabilities	**(546)**	**(570)**	**(1,278)**	**(1,224)**	**(1,224)**	**(1,224)**	**(1,224)**
Creditors	(546)	(570)	(1,160)	(1,218)	(1,218)	(1,218)	(1,218)
Short term borrowings	0	0	0	0	0	0	0
Other	0	0	(118)	(6)	(6)	(6)	(6)
Long Term Liabilities	**(147)**	**(140)**	**(1,183)**	**(1,122)**	**(1,122)**	**(1,122)**	**(1,122)**
Long term borrowings	0	0	0	0	0	0	0
Other long term liabilities	(147)	(140)	(1,183)	(1,122)	(1,122)	(1,122)	(1,122)
Net Assets	**4,197**	**4,266**	**13,534**	**27,709**	**23,162**	**19,022**	**15,102**
CASH FLOW							
Operating Cash Flow	**(1,697)**	**362**	**(4,654)**	**(4,981)**	**(4,237)**	**(3,788)**	**(3,551)**
Net Interest	0	0	0	0	0	0	0
Tax	277	245	251	612	526	620	565
Capex	(231)	(273)	(146)	(969)	(758)	(530)	(424)
Acquisitions/disposals	25	0	(6,133)	0	0	0	0
Financing	2,646	0	10,670	19,037	0	0	0
Dividends	0	0	0	0	0	0	0
Other	7	10	(6)	60	115	81	63
Net Cash Flow	1,027	344	(18)	13,759	(4,353)	(3,617)	(3,348)
Opening net debt/(cash)	**(1,383)**	**(2,410)**	**(2,754)**	**(2,757)**	**(16,516)**	**(12,163)**	**(8,546)**
Other	0	0	21	(0)	0	(0)	(0)
Closing net debt/(cash)	**(2,410)**	**(2,754)**	**(2,757)**	**(16,516)**	**(12,163)**	**(8,546)**	**(5,199)**

Source: Abzena accounts (AIM Admission Document), Edison Investment Research. Note: Historical financial information relates to PolyTherics (with consolidation of Antitope only as of 1 August 2013).

EDISON

Contact details	Revenue by geography (FY14)
Babraham Research Campus Babraham Cambridge CB22 3AT UK +44 (0)1223 903 498 www.abzena.com	

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS 2012-16e	N/A	ROCE 15e	N/A	Gearing 15e	N/A	Litigation/regulatory	◖
EPS 2014-16e	N/A	Avg ROCE 2012-16e	N/A	Interest cover 15e	N/A	Pensions	○
EBITDA 2012-16e	N/A	ROE 15e	N/A	CA/CL 15e	16.1	Currency	◖
EBITDA 2014-16e	N/A	Gross margin 15e	48.3%	Stock days 15e	26.9	Stock overhang	○
Sales 2012-16e	44.7%	Operating margin 15e	N/A	Debtor days 15e	133.9	Interest rates	○
Sales 2014-16e	32.5%	Gr mgn / Op mgn 15e	N/A	Creditor days 15e	75.9	Oil/commodity prices	◖

Management team

Chief Executive Officer: John Burt, DPhil

Joined PolyTherics in November 2010, initially as Chief Business Officer, then becoming CEO in May 2011. Following the acquisition of Antitope and creation of Abzena, John is CEO of the group. Co-founder and CEO of Thiakis (2004-08, when Thiakis was acquired by Wyeth). Previous roles include finance, technology licensing and business and corporate development responsibilities at Vanguard Medica, GlaxoSmithKline and Imperial Innovations.

Chief Financial Officer: Julian Smith

Joined PolyTherics as CFO in September 2013, now CFO for the group. Julian was Chief Financial and Operations Officer at Imperial Innovations (2006-13). Before Imperial Innovations, Julian was CFO of RadioScape and group financial controller of Mobile Systems International.

Chief Scientific Officer: Matthew Baker, PhD

Co-founder of Antitope in 2004, and CSO of the group since the merger with PolyTherics in July 2013. Before Antitope Matthew was VP for biologics discovery at Biovation (subsidiary of Merck KGaA). Matthew has a background in B- and T-cell immunology and completed post-doc roles in Cambridge (UK), after obtaining a PhD in cellular immunology at the University of Birmingham (UK).

Senior VP Corporate Development: Sally Waterman, PhD

Joined PolyTherics in October 2009 as Chief Operating Officer and became Senior VP of corporate development in December 2013. Sally's previous roles include director of R&D at Protherics, VP of R&D at KS Biomedix, VP of non-clinical development at Vernalis and director of scientific operations at Pharmakopius.

Principal shareholders	(%)
Invesco Asset Management	26.6
Imperial Innovations	23.6
Woodford Investment Management	10.4
Proven Growth and Income VCT	4.0
The Advantage Enterprise & Innovation Fund	3.4

Companies named in this report

Gilead Sciences (GILD); Seattle Genetics (SGEN); ImmunoGen (IMGN); Immunomedics (IMMU); Celldex Therapeutics (CLDX); Roche (ROG); Opsona Therapeutics; Vascular Pharmaceuticals; NKT Therapeutics; Adheron Therapeutics

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