EDISON

Avacta Group

Initiation of coverage

Affimer - potential best-in-class antibody mimetic

Pharma & biotech

Avacta is developing its Affimer technology for use in therapeutic and diagnostic/reagent applications. The potential of the Affimer technology lies in its formatting capabilities, particularly in the creation of bispecific and TMAC Affimer drug conjugates. Its lead therapeutic asset (AVA004) is a programmed death-ligand 1 (PD-L1)-targeting Affimer for which the company expects to submit an investigational new drug (IND) application in Q420. AVA004 will serve as the first clinical validation of the Affimer technology and will form the base of the clinical development of a PD-L1/LAG-3 bispecific (AVA021) and the first TMAC Affimer drug conjugate (AVA004/100). We value Avacta at £51m or 44p/share.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/17	2.7	(7.9)	(9.8)	0.0	N/A	N/A
12/18	2.8	(10.4)	(13.5)	0.0	N/A	N/A
12/19e	3.2	(12.3)	(9.0)	0.0	N/A	N/A
12/20e	5.2	(12.4)	(9.0)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Formatting capabilities point to future potential

Avacta is progressing its therapeutic Affimers towards the clinic with its PD-L1 (AVA004) and PD-L1/lymphocyte-activation gene 3 (LAG-3) (AVA021) product candidates expected to start oncology clinical trials in 2021 and 2022 respectively. Post the clinical validation of AVA004, we expect Avacta will focus on the development of the AVA021 bispecific (a component of which is AVA004) and its TMAC Affimer drug conjugate (AfDC) (in collaboration with Tufts University) that targets PD-L1 and uses an I-DASH toxin together with a novel fibroblast activation protein (FAP)α cleavable linker (AVA004/100).

TMAC drug conjugate into the clinic in 2020

Avacta has accelerated its tumour microenvironment activated drug conjugates (TMAC) programme and will now test the novel FAPα cleavable linker in a Phase I trial in 2020. The FAPα cleavable linker will be conjugated to a well-known chemotherapeutic agent (doxorubicin) rendering it inactive until the linker is cleaved in the tumour microenvironment. The FAPα cleavable linker forms a key component of AVA004/100, for which Avacta expects to submit an IND application in late 2021.

Partnerships continue to validate technology

Avacta's partnerships continue to show the potential of Affimers for multiple applications; most recently it announced a deal with LG Chem worth over $300m (+ royalties) to develop a range of therapeutic Affimers. In February 2019, Moderna exercised its option on an Affimer developed in its partnership with Avacta.

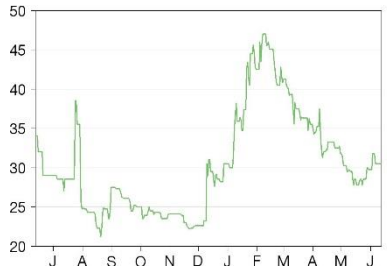
Valuation: £51m or 44p/share

We value Avacta at £51m or 44p/share based on a sum-of-the-parts valuation built on an rNPV for AVA021, the LG Chem partnership and the peer valuation of the reagents/diagnostic and animal health divisions, in addition to adding in net cash. AVA021 (PD-L1/LAG-3) contributes approximately 50% to our valuation.

13 June 2019

Price	**30.5p**
Market cap	**£35m**
£:$ 1.30, £:€ 1.17, $:€ 0.89	
Net cash (£m) at end January 2019	11.79
Shares in issue	116.2m
Free float	78.9%
Code	AVCT
Primary exchange	AIM
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	3.4	(14.1)	(10.3)
Rel (local)	1.6	(16.3)	(5.3)
52-week high/low		47.0p	21.2p

Business description

Avacta is focused on the development of its Affimer technology for use in therapeutic and diagnostic/reagent applications. Assets include AVA004 (PD-L1), AVA021 (PD-L1/LAG-3) and AVA004/100 (PD-L1/I-DASH).

Next events

AVA017 LAG-3 candidate selection	H219
AVA004/100 TMAC animal model POC	H219
FY19 results	October 2019

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Edison profile page

Investment summary

Company description: Antibody mimetics

Avacta is a UK biopharmaceutical company specialising in the development of its proprietary Affimer platform. Its lead assets are its PD-L1 Affimer (AVA004), its PD-L1/LAG-3 bispecific Affimer (AVA021) and its PD-L1 TMAC drug conjugate (AVA004/100) for use in cancers, both in preclinical development. In addition to Avacta's therapeutic platform, it has a diagnostic reagents division and an animal health division. Avacta has multiple partnerships, notably with LG Chem, Moderna and Tufts University. Avacta raised net £10.9m in August 2018 (c 46,000 shares at 25p/share) and had net cash as of 31 January of £11.8m. In 2018, Avacta's average employee count grew to 114 compared with 103 in 2017.

Valuation: £51m or 44p/share

We value Avacta at £51m or 44p/share. This is based on a sum-of-the-parts model including a risk-adjusted NPV of AVA021 (PD-L1/LAG-3 bispecific) (rNPV: £23.9m) and LG Chem research partnership (rNPV: £7.7m) and a peer valuation of both its reagents and animal health divisions (c £7.2m), in addition to adding in net cash (£11.8m). The main driver of our valuation is AVA021, which contributes approximately 50% of the total valuation. We assume AVA021 is out-licensed before the Phase I start in 2022 and model c £300m of milestones split across an upfront payment, clinical and commercial milestones. Due to the early nature of its development, we model its market potential in a basket of relapsed refractory cancers that are PD-L1/LAG-3 positive and for which patients have already received PD-L1 treatment. This is benchmarked against the total PD-L1 global market, resulting in approximate market penetration of 5%, generating peak sales of c £800m. The next most advanced asset, the AVA004/100 (PD-L1/I-DASH) product candidate (first product from the TMAC platform), is of significant scientific interest; however, due to the very early nature of development and the complexities involved in the asset, we await for its advancement into the clinic before considering its inclusion into our valuation. Potential significant upside exists if Avacta is successfully able to develop the TMAC platform. For the LG Chem partnership, we model the $180m milestone payments for the deal with payments spread to 2030 on assumed classical drug development timelines (eg Phase I start).

Sensitivities: Clinical validation needed

Avacta is subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable outcomes in clinical trials, trial shortfalls or failures, cash-flow limitations, success of competitors and negative commercial decisions by partners or potential partners. Cancer immunotherapy has become a highly competitive landscape and Avacta's technology platforms are still in relatively early stages of development. The key short-term sensitivities for Avacta relate to crystallising value from the early-stage pipeline, particularly the PD-L1/LAG-3 bispecific (AVA021). Additionally, the entry of the first Affimer into the clinic (PD-L1 Affimer) will be critical inflection point for the company as the technology is tested in humans for the first time. If Affimers are found to be immunogenic or generate severe side effects, it would affect any potential applications. We note AVA021 represents 50% of our valuation and any failure of the asset or changes to timings would materially affect our valuation.

Financials: Cost base expected to rise as the clinic approaches

The net loss for H119 was £5.2m (vs £3.95 in H118) driven by the decrease in revenues and increase in R&D investment. Net cash at 31 January 2019 was £11.79m and we forecast a current cash reach into 2020. We forecast illustrative debt of £10m in 2020 to fund operations into 2021.

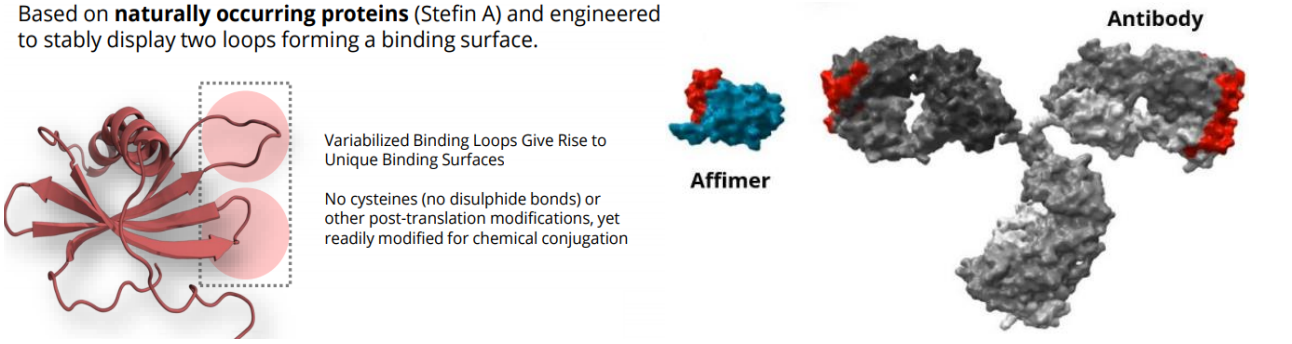
Affimers: First human data will be a key inflection point

Avacta is built around its proprietary Affimer platform of engineered proteins (acquired IP in 2012; current patents), which are engineered to possess binding capabilities similar to antibodies (antibody mimetics). Since the FDA approved the first antibody in 1985 (muromonab), antibodies have become the dominant therapeutic options for countless diseases with total sales of antibodies recently reaching $120bn globally in 2018 (source: EvaluatePharma). Although antibodies are, and will continue to be, the dominant therapeutic option in many diseases, there are numerous disadvantages including their relatively bulky size, complexity in creation and manufacturing, difficulties in formatting (making drug conjugates, bispecifics etc) and a high cost of production.

Avacta has developed Affimers to address many of these problems and offer an array of potential advantages including high expression levels (in eukaryotic and prokaryotic cells), customisable kinetics (K_{off}, K_{on} etc), stability (AVA04 demonstrated stability up to seven months in phosphate-buffered saline at 4°C) and solubility (400mg/ml dimeric Affimers, 200mg Affimer Fc). One of the key capabilities of Affimers is their formatting flexibility which allows the relatively simple construction of complex molecules such as TMAC drug conjugates (AVA004/100) and bispecifics (AVA021). This could be an important differentiator for the platform. While technically promising, the platform remains in its infancy (not yet tested in humans) and significant risk remains in their ability to perform in a therapeutic clinical context. Questions including whether Affimers will generate an unwanted immune reaction and subsequently be neutralised in the body (preclinical data to date have determined a non-immunogenic nature), whether they are therapeutically safe and if there inherently short half-life will limit efficacy are all still to be answered (formatting with other component as a bispecific or AfDC will increase half-life). Key to Avacta's future prospects will be it rapidly achieving Affimer data in human patients (IND forecast to be submitted for AVA004 in Q420).

All therapeutic Affimers are based on stefin A (Exhibit 1), a human protease inhibitor. They are typically 12–14kDa in size (approximately 10-fold smaller than antibodies), which brings the advantage of typically better tissue penetration and increased packing density (for diagnostics/reagent applications). However, their small size means Affimers have a relatively short half-life (hours). This can sometimes be advantageous in limiting systemic toxicity (the Affimer acts at site of interest and is cleared from the body before it has a chance to act elsewhere), there are often multiple scenarios where a longer half-life is need. Avacta has developed half-life extending technologies in the form of serum albumin binding (Affimer XT platform) to address this. Preclinical data to date have demonstrated minimal disruption of Affimer binding to its target when using the XT format. Additionally, the ease of formatting of Affimers means novel drug conjugates and multi-specific Affimers can be created, which offer unique ways to increase the half-life.

Exhibit 1: Affimer structures



Source: Avacta

Affimers are selected by phage display (-10^{10} library size) and produced in *E. Coli* protein expression systems. The time between the initial screen of the Affimer to animal models is typically

six months, putting it on par with therapeutic antibody development. Lot-to-lot variability is a common problem for antibodies (mainly for polyclonal and less so for monoclonal and synthetic); however, as Affimers are manufactured by a non-eukaryotic process there is more lot-to-lot consistency. Due to Affimers' simple, stable, known structure, they can be easily functionalised, which aids in the ability to produce drug conjugates of bispecific molecules without the loss of binding or stability.

While the aforementioned capabilities are key for Affimers to differentiate themselves from antibodies, one key strength is the unencumbered patent protection Avacta holds on the technology. This is a result of Affimers not being based on antibodies and gives Avacta freedom to operate in areas where antibody patents exist and, for example, allows it to go after many well-known targets (eg PD-L1) without infringing on other antibody patents and is a significant attraction for potential partners.

Therapeutic pipeline

Avacta has multiple Affimer assets in early-stage development (Exhibit 2) across three key technology areas: checkpoint antagonists (AVA004 and AVA017), costimulatory agonists (AVA026 and AVA023) and drug conjugates (AVA004/100). Although AVA004, AVA017 and AVA023 are similar to other assets in development in the sector, its Affimer TMAC drug conjugates, of which AVA004/100 is the most advanced, could prove be a key driver of value in the long term. The Affimer TMAC drug conjugates are based around a FAPα cleavable linker that connects a deadly toxin with a tumour-targeting Affimer. The FAPα cleavable linker is cleaved in the tumour microenvironment (demonstrated to date by data in animal and in-vitro models) and it could enable the localised release of tumour killing toxins in humans. Combined with the multiple formatting options of Affimers, a range of possible combinations and product candidates could emerge. The proprietary (FAPα) cleavable linker to be used in AVA004/100 will be tested separately next year, while an IND application testing the full Affimer drug conjugate is expected to be submitted for AVA004/100 in late 2021.

Its most advanced asset in the pipeline is AVA004, a PD-L1 targeting Affimer for which Avacta expects to submit an IND application by the end of 2020. Most recently it was announced that a clinical development candidate has been selected for AVA004 and that the Phase I study is expected to test AVA004 in 20 to 30 patients with PD-L1 positive solid tumours. The trial will test both intravenous and subcutaneous routes of administration. This clinical trial will provide the first proof of concept for Affimers in humans and would de-risk the entire platform if successful. While the data produced by AVA004 will be informative, we do not expect Avacta to progress the asset past Phase I trials and will instead utilise it to inform the design of its bispecific PD-L1/LAG3 AVA021 and drug conjugate AVA004/100 trials. We believe this decision will be driven by the significantly increased potential value of developing (if successful) a unique therapy instead of a similar version of an already available commercial product (eg another PD-L1 monotherapy in the case of AVA004). We believe long-term value for Avacta is developing the AVA021 bispecific (component of which is AVA004), which is expected to enter the clinic in 2022 and its TMAC AfDC (in collaboration with Tufts University) that targets PD-L1 and uses an I-DASH toxin (AVA004/100) coupled together with a FAPα cleavable linker (IND filling expected in H221).

Exhibit 2: Therapeutic pipeline (key assets)

Asset/target	Status	Notes
AVA004/ PD-L1	Preclinical	Plan to submit an IND by end 2020
AVA017/ LAG-3	Lead optimisation	Unlikely to be developed into the clinic
AVA021/ PD-L1 and LAG-3	Pre-clinical	Plan to initiate a Phase I trial in 2022.
AVA004/100/ PD-L1/I-DASH	Discovery	IND filing planned for late 2021
AVA003 Affimer XT (serum albumin)	Pre-clinical	N/A
AVA026/4-1BB	Discovery	N/A
AVA023/CD40	Discovery	N/A

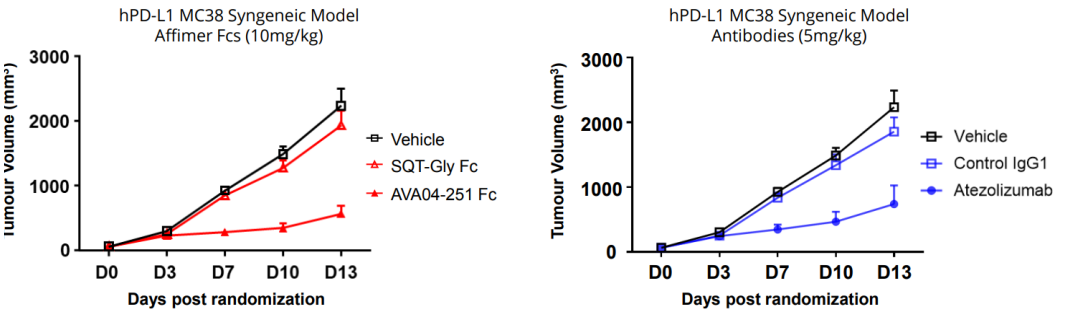
Source: Avacta

Checkpoint antagonists: PD-L1 and LAG-3

Avacta's lead assets are based on targeting PD-L1 and LAG-3. The most advanced is AVA004, in development as a PD-L1 inhibitor. Avacta expects to submit an IND by end 2020 with data potentially in 2021. This will be a major inflection point for Avacta as it will represent the first human dataset for an Affimer. As usual, the initial Phase I trial will focus on safety but evidence of efficacy could prove an important early indicator of how the Affimer technology compares to antibodies, particularly PD-L1 inhibitors. Preclinical mouse model data have demonstrated that AVA004 produced comparable changes in tumour volume to that of atezolizumab (Tecentriq) (Exhibit 3) and avelumab (Bavencio) and durvalumab (imfinzi). We forecast that AVA04 will not be developed past Phase I (as it will have enabled the proof of concept of Affimer technology in humans) and Avacta will focus on AVA021 (LAG-3/PD-L1 bispecific) and AVA004/100 (PD-L1/I-DASH AfDC).

AVA017 is designed to be an Affimer LAG-3 inhibitor. It is in lead optimisation and Avacta expects to select a lead candidate in H219. Avacta has no plans to develop AVA017 as a monotherapy into the clinic and will utilise it as part of AVA021, which will combine AVA017 and AVA004 into an LAG-3/PD-L1 bispecific. Avacta predicts the first patient is likely to be treated with AVA021 in 2022.

Exhibit 3: Comparison of AVA04 to atezolizumab in a mouse tumour model



Source: Avacta

Since the commercial launch of Keytruda (Merck) and Opdivo (Bristol Myers Squib) in melanoma in 2014, PD-L1 immune checkpoint inhibitors (ICIs) have become the standard of care in many cancers (FY18 sales of Opdivo and Keytruda were $7.6bn and $7.2bn respectively). PD-L1 is a transmembrane protein that plays a key role in immune regulation. The binding of receptor PD-1 to its ligand PD-L1 activates suppressive signals that limit immune activation, an effect that cancerous cells exploit to limit the response against them. PD-L1 inhibitors have been developed to try and prevent this immune suppression and have proven successful across a range of cancers. PD-L1 ICIs, alone or in combination, have quickly become the standard of care for many patients; however, the best responses generally remain confined to high PD-L1-expressing patients. For example, Keytruda's approved label (Keynote-042) in stage three non-small cell lung cancer (NSCLC) demonstrated it had a 39% overall response rate (ORR) as a monotherapy in first-line patients whose tumour proportion score (TPS) for PD-L1 expression was above 50%; however, in a broader patient population (TPS score of 1% and above), the ORR fell to 27%. Across indications, companies are now looking to test ICIs in combination with other treatments to broaden their

therapeutic window. Avacta is aiming to address this with assets including its AVA021 bispecific and its first TMAC Affimer drug conjugate AVA004/100.

LAG-3 demonstrating potential in the clinic

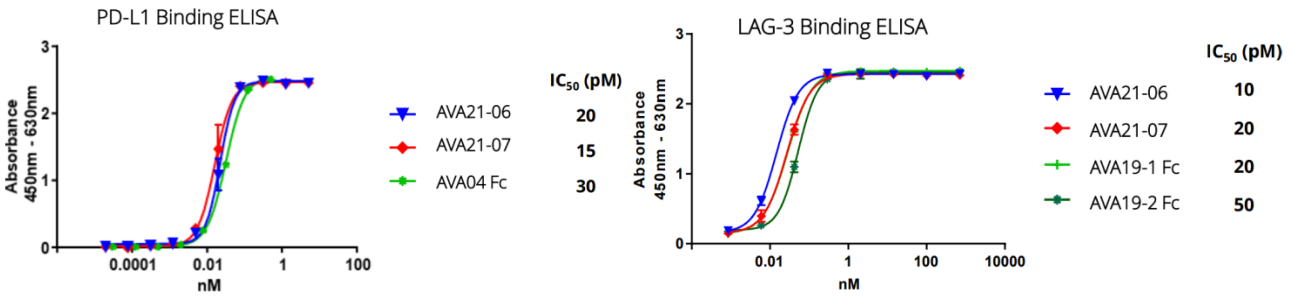
Like PD-L1, LAG-3, also known as CD233, is a transmembrane protein immune checkpoint receptor found on T-cells. LAG-3 is typically upregulated to control T-cell activation and prevent over activation of T-cells (and subsequent autoimmunity). In cancer models it has been demonstrated that persistent expression of antigens to T-cells enables continuous LAG3 expression and subsequently T-cell exhaustion (limited killing, proliferation and cytokine production). It is thought that inhibition of LAG-3 could prevent T-cell exhaustion and lead to tumour killing activity. The target has received significant interest and there are currently 45 LAG-3 trials ongoing (according to clinicaltrials.gov) either alone or in combination with other therapies. One of the most advanced is relatlimab (Bristol Myers Squib) and is in 19 active studies across multiple cancer types, the most advanced of which is a Phase III study testing relatlimab in combination with nivolumab (Opdivo) in first-line advanced melanoma.

Data were presented at ESMO 2017 on the combination of relatlimab and nivolumab in melanoma patients who have previously progressed on anti-PD-L1 therapy. Overall (n=68) ORR (one complete response, six partial responses) and disease control rate (DCR) were 11.5% and 49% respectively. In patients with LAG-3 expression ≥1%, the ORR was 18% (n=33) compared with 5% in patients with LAG-3 expression <1% (n=22). The combination demonstrated a similar AE profile to that of nivolumab alone.

Multiple other LAG-3 antibodies are in development (GSK:GSK2831781, MacroGenics: MGD013, Merck: MK-4280), notably FS118 from F-star, a bispecific (targets LAG-3 and PD-L1) that is in a Phase I trial across a range of advanced/metastatic cancers (expected enrolment of 51 patients). F-star originally partnered FS118 with Merck in 2017; however, it has recently had the rights returned and will now develop and commercialise it.

Whether a LAG-3/PD-L1 bispecific will be more potent than separate mAbs in combination has yet to be clinically determined; however, early pre-clinical data hint at the potential. Data on AVA021 (LAG-3/PD-L1 bispecific) remain early but recently presented data (at the Avacta R&D day, February 2019) demonstrated that in ELISA-binding assays, AVA021 bound PD-L1 and LAG-3 as well as single-target Affimers (Exhibit 4), demonstrating the conjugation of the two Affimers did not affect binding. More advanced pre-clinical data demonstrating the potential of a LAG-3/PD-L1 bispecific come from F-star, which demonstrated in a colon carcinoma mouse model that FS118 more potently inhibited tumour growth than a combination of an LAG-3 mAb and PD-L1 mAb. Recently F-star presented data at ASCO 2019 from its enrolling Phase I trial that demonstrated no dose-limiting toxicities were observed to date in the first 29 patients recruited.

Exhibit 4: Comparison of bispecific binding of LAG-3/PD-L1 Affimer (AVA21) vs monospecific Affimers



Source: Avacta

Partners: Affimers attractive across applications

Avacta's range of partnerships continues to demonstrate the potential of Affimers for multiple applications (Exhibit 5). These include classical discovery partnerships with LG Chem and Moderna, deals focused on specific applications such as the development of AfDCs with Tufts University and partnerships focused on testing the potential of Affimers in cell and gene therapies with Oncosec and Memorial Sloan Kettering.

Exhibit 5: Current active partners

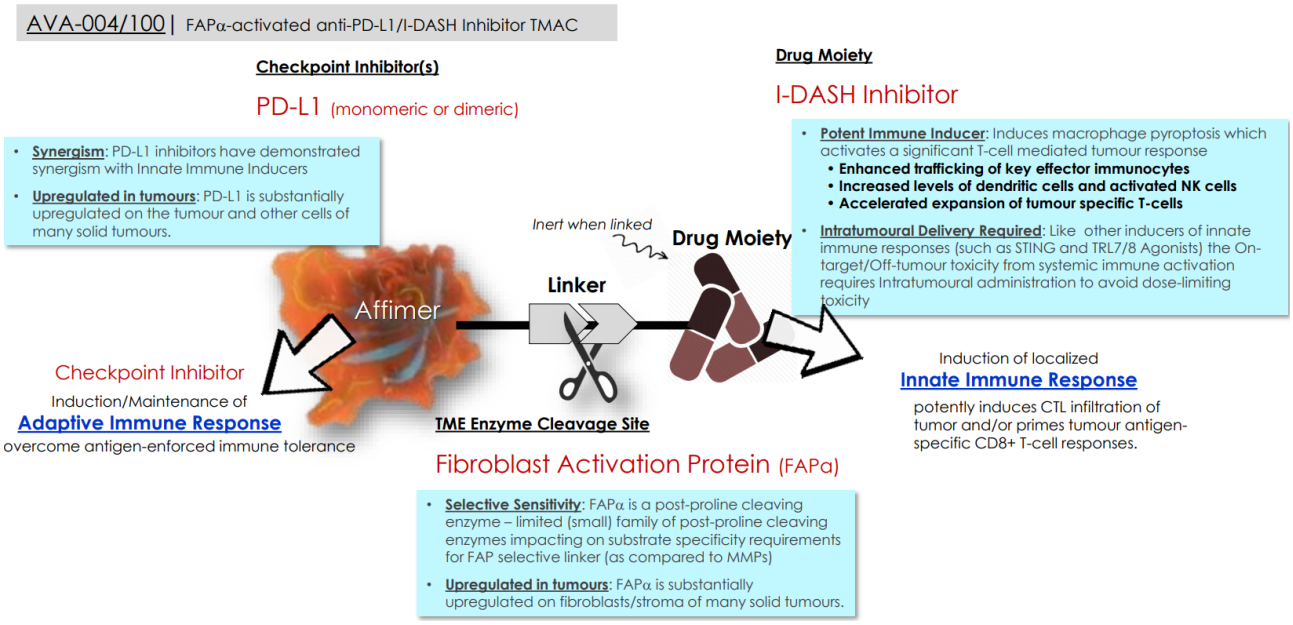
Partner	Notes
LG Chem Life Sciences	In December 2018, Avacta announced a partnership with LG Chem Life Sciences to develop therapeutic Affimers for multiple targets. Avacta is responsible for generating Affimers to the undisclosed targets and for early optimisation work. Both parties will then collaborate to progress the candidates through to drug candidate selection, after which LG Chem will be responsible for all pre-clinical and clinical development in addition to worldwide marketing. LG Chem aims to have the first clinical trial regulatory submission in 2021. At H119 results, further financial information on the deal was disclosed. The deal included an upfront payment of $2.5m, near-term milestone payments of $5.5m and long-term clinical milestones of $180m. LG Chem will reimburse Avacta for any incurred R&D costs associated with the collaboration and pay Avacta royalties on any potential future product sales. In addition, if LG Chem exercises its option for additional targets, Avacta will be eligible to receive up to $130m in option fees and milestones.
Moderna	In May 2015, Avacta entered into a licensing partnership ($500,000 upfront) with Moderna Therapeutics to develop Affimers for undisclosed targets. Under the terms of the agreement, Moderna has exclusive access to the Affimer technology for certain targets and Moderna is able to extend the partnership to other targets. Moderna was also liable to pay Avacta for R&D relating to pre-clinical work. In February 2019, Moderna opted in on an undisclosed target that granted the company an exclusive product licence. Under the terms of the agreement, Avacta can now potentially receive clinical development milestones and royalties (on potential future sales) on the asset. The scope and size of any milestones are undisclosed and we have no information regarding when clinical development will initiate or if it will at all.
Oncosec	In January 2018, Avacta and OncoSec entered into a collaboration to develop gene therapy delivery of therapeutic Affimers. OncoSec's gene delivery technology, ImmunoPulse, has clinically demonstrated safe and efficient delivery into a patient's tumour in previous clinical trials. The collaboration will test whether ImmunoPulse can deliver clinically relevant concentrations of Affimers including AVA04 (PD-L1) in in-vivo tumour models.
Memorial Sloan Kettering Cancer Center (MSK)	In November 2016, Avacta entered into a research collaboration with MSK to use Affimers for CAR-T therapies. The collaboration is led by Renier J. Brentjens, MD, PhD, director of cellular oncology and was originally focused on developing Affimer CAR-T cells that target CD19. Generating Affimers to CD19 proved problematic, research has now shifted to finding binders to CD22.
New England Biolabs	In October 2018, Avacta agreed an Affimer reagent licensing deal with NEB to commercialise a product incorporating the Affimer technology. The product is for use in both life science research and diagnostic assays and is in final stages of product testing. Under the terms of the agreement Avacta will receive royalties on sales (may occur as soon as 2019). NEB and Avacta will continue its collaboration with the aim to generate further products.
Tufts/Bach Biosciences	In July 2018, Avacta announced a collaboration with Bach Biosciences, a company founded on the research of William Bachovchin at Tufts University School of Medicine, Boston. The collaboration aims to develop novel AfDC using Tufts' novel linker chemistry that is designed to release attached drugs in only a tumour. The first proof-of-concept AfDC will involve the use of a PD-L1 Affimer and an I-DASH small molecule inhibitor. AVA004/100 (PD-L1/I-DASH) is now in discovery.

Source: Avacta

Tufts/Bach Biosciences: Novel conjugate potential

The collaboration with Tufts/Bach Biosciences aims to develop novel AfDC using Tufts novel linker chemistry that is designed to release attached drugs in the tumour microenvironment. This TMAC platform coupled with the Affimer technology could generate a unique pipeline of assets. The first proof of concept AfDC will involve the use of a PD-L1 Affimer (AVA004/100/ PD-L1/I-DASH), an FAPα cleavable linker and an I-DASH small molecule inhibitor (Exhibit 6). Avacta recently accelerated its TMAC programme and will now test the novel FAPα cleavable linker in a Phase I trial in 2020. The FAPα cleavable linker will be conjugated to a well-known chemotherapeutic agent (doxorubicin), rendering it inactive until the linker is cleaved in the tumour microenvironment. The FAPα cleavable linker is key to Avacta's drug conjugate ambitions and these clinical data will be an important inflection point for the technology. The first Affimer drug conjugate to use the FAPα cleavable linker is AVA004/100, for which Avacta expects to submit an IND application in late 2021.

Exhibit 6: AVA004/100



Source: Avacta

The third component of AVA004/100 is the I-DASH inhibitor. The inhibition of DASH enzymes has been demonstrated both in preclinical and clinical populations to promote tumour regression (Positive Phase II study in NSCLC). However, one of the key problems with DASH inhibitors to date has been the dose-limiting toxicities commonly associated with chemotherapies (Phase III trial testing talabostat receives a clinical hold and is later terminated). Avacta and Tufts believe AfDC can address the toxic problems seen with DASH inhibitors as administration of I-DASH is theorised to be limited to the tumour microenvironment. Additionally, the inherently short half-life of Affimers could be beneficial in reducing toxicity; however, it could limit efficacy. As AVA004/100 remains in the early stages of development, clinical data will be needed to confirm or disprove these hypotheses.

Reagents and diagnostics: Stable base

Avacta's reagent and diagnostic division, a separate team based in Wetherby (therapeutics team based in Cambridge) continues to be a key component of the business and Avacta continues to develop in house technologies with the aim of providing a stable revenue base for the company. The ability of Affimers to retain their chemical and thermal stability in a wide array of environments means the technology is suited to a variety of applications; combine this with the ability to easily functionalise Affimers with an array of compounds (enzymes, dyes etc) and Affimers quickly present themselves as ideal research tools.

Avacta has ongoing paid technology evaluations with numerous undisclosed partnerships, including global in vitro diagnostic, pharma, biotech and bioprocessing companies. Avacta is pursuing three commercialisation strategies:

- Paid-for evaluations of Affimer technology with the aim to generate licence deals where the technology is incorporated into partner products (multiple evaluations ongoing).
- Custom Affimer services to support partner in-house R&D (eg anti-idiotypics).
- Development of diagnostic assays to be partnered out. Aim to generate two diagnostic assets with supporting data packages during 2019, with the aim of out-licensing them once the work is complete.

Paid-for evaluations and the development of diagnostic assays remain important for the long-term growth of the division. In the short term, custom reagents, particularly anti-idiotypics, remain important income generators and continue to demonstrate revenue growth. Anti-idiotypics are antibodies or, in Avacta's case, Affimers that bind to the idiotope (variable part of an antibody that includes the unique antigen-binding site) of another antibody. These are needed in setting up pharmacokinetic assays that measure total or free-drug levels in pre-clinical/clinical samples, an important step in the drug-creation process.

Anti-idiotypics are a significant growth area for Avacta. It recently launched a marketing campaign and set up multiple new contracts (£40k revenue per anti-idiotypics). As the majority of antibodies in development will typically need an anti-idiotypic, Avacta believes there is significant market potential and estimates an ongoing revenue stream of several million pounds at peak. We note that while Affimers potentially offer advantages in the creation of anti-idiotypics, market leaders such as Bio-Rad will be difficult to displace.

In October 2018, Avacta agreed an Affimer-reagent licensing deal with NEB to commercialise a product incorporating Affimer technology. The product is for use in both life science research and diagnostic assays and is in final stages of testing. Under the terms of the agreement, Avacta will receive royalties on sales (may occur as soon as this year). NEB and Avacta will continue their collaboration with the aim to generate further products.

Animal health: Pre-Affimer legacy business

Avacta Animal Health remains a legacy of the original Avacta business before the acquisition of the Affimer IP in 2012. Employing approximately 20 people, Avacta Animal Health is focused on four main categories: allergy diagnostic tests, immunotherapy vaccine sales, export sales and contract research organisation services. Trading in H119 was broadly in line (£0.69m vs £0.77m in H118) with H118 and Avacta expect a pick-up in H219 numbers as the seasonal effects of the allergy business boost sales. The division continues to market its capabilities with the pet allergy awareness campaign in its fifth year. In the long term we expect Avacta to spin-off or sell the animal health division as it continues to focus on its therapeutic ambitions.

Antibody mimetics continue to generate interest

As the limits of antibody technology become ever clearer, more investment is being made into the sector to develop antibody mimetic technology. Here we highlight a few key competitors.

Molecular Partners (MOLN) is a Switzerland-listed biotechnology company (market cap: CHF340m) focused on developing its DARPin platform. The platform is based on a large library (10^{12}) of small proteins with single domains (15kDa) that are used as building blocks for its therapeutic molecules (currently up to six DARPin proteins can be linked together). Multiple assets are in clinical trials with lead assets MP0250 (inhibit VEGF and HGF) in multiple myeloma and Abicipar (inhibit VEGF) in wet age-related macular degeneration. Abicipar is in development with its partner Allergan, which expects to file a BLA in H119. Recently a clinical trial testing MP0250 in combination with Tagrisso in EGFR mutated NSCLC was placed on clinical hold due to adverse events.

Pieris Pharmaceuticals (PIRS) is a Nasdaq-listed biotechnology company (market cap: $184m) focused on developing its Anticalin technology. The technology is built on engineered lipocalins (a family of proteins that transport small hydrophobic molecules, 18–40KDa), which, in a similar vein to Affimers, have a ridged backbone and a (four-loop) variable region. Its most advanced assets are in Phase I clinical trials, including a PRS-343, a 4-1BB/HER2 bispecific being tested in a range of

HER2 positive solid cancers and PRS-060 a IL4Ra inhibitor for use in asthma (partnered with AstraZeneca).

Bicycle Therapeutics (BCYC) is a recently Nasdaq-listed biotechnology company (23 May, market cap: $278m) focused on developing its bicycle technology. Bicycles are short synthetic peptides constrained to form two loops to stabilise their structure and form regions for binding. The company has one asset in the clinic, BT1718, which targets membrane Type 1 Matrix Metalloproteinase (MT1-MMP) and is believed to be indicated in cancer metastasis. A Phase I trial (carried out by Cancer Research UK) in an array of solid tumours is ongoing.

As evidenced by MOLN, PIRS and BCYC, there is significant investor interest in antibody mimetic platforms, particularly those with clinical assets.

Valuation: £51m or 44p/share

We value Avacta at £51m or 44p/share. Our sum-of-the-parts valuation allows the assessment of a diverse set of technologies that have different applications albeit all based on the same Affimer technology. This is outlined below:

- The Affimer therapeutic platform based on rNPV of its PD-L1/LAG-3 bispecific and LG Chem research partnership examined against comparative transactions and recent IPOs.
- The Affimer reagents (research and diagnostics) business, based on a sales multiple.
- The Affimer animal health business based on a sales multiple.

Exhibit 7: Avacta sum-of-the-parts valuation

	Therapeutics	Reagents/diagnostics	Animal health	Net cash	Total
Total (£m)	31.63	3.12	4.12	11.79	50.66
Per share (p)	27.23	2.69	3.55	10.15	43.61

Source: Edison Investment Research

Affimer therapeutic platform

We base our rNPV of the Affimer therapeutic platform on AVA021 (PD-L1/LAG-3) and the LG Chem research partnership. We do not value the rest of the early-stage pipeline or any other partnership.

Exhibit 8: rNPV of therapeutic division

Product/partner	Estimated launch	Probability	Peak sales (£m)	Milestones (£m)	NPV (£m)	rNPV (£m)	Per share (p)
AVA021 (PD-L1/LAG-3)	2030 in EU/US	2.5%	776	c 300m	151	24	20.59
LG Chem	N/A	5%	N/A	c 180m	51	8	6.64

Source: Edison Investment Research

For AVA021, we model its market potential in a basket of relapsed refractory cancers, which are PD-L1/LAG-3 positive and for which patients have already received PD-L1 treatment. The early nature of its development means the exact cancer population that AVA021 will be tested in has not yet been defined. Based on comparative trial with F-star's PD-L1/LAG-3 bispecific FS118, which is being tested in a Phase I trial in an array of advanced/metastatic cancers following progression on PD-L1 treatment. We believe a similar trial design is reasonable for Avacta. In the long term, the competitive positioning of AVA021 (if clinically successful), particularly the cancer in which it is used, will be key to any success. We assume AVA021 is out-licensed pre-Phase I start (but after initial Phase I data from the PD-L1 Affimer AV004) in 2022 and model in c £300m of milestones split across an upfront payment, clinical and commercial milestones. We have additionally assumed a tiered royalty rate of between 5% to 10% and a launch probability of 2.5%. Our model is benchmarked against the total PD-L1 global market resulting in approximate market penetration of 5%, generating peak sales of c £800m in the US and EU. We will update our AVA021 model

accordingly as the clinical programme progresses. We forecast a launch in both the EU and US in 2030 at a starting price of c $100,000 in the US and at a 30% discount in the EU.

For the LG Chem partnership we model the $180m milestone payments for the deal with payments spread to 2030 on assumed classical drug development timelines (eg Phase I start); however, as we have no information on the therapeutic indication or target, significant sensitivity relates to these timelines, and milestones could be spread over longer or shorter periods or could not be received at all. We also do not model royalties due to a lack of information on potential patient populations. We forecast that the first Affimer will enter a Phase I clinical trial in 2022 and will update our model once more information is available.

While the other assets in the pipeline are important for Avacta's long-term ambitions, we have limited visibility over their development. While AVA004 (PD-L1) is more advanced then AVA021 we note that there are no plans to develop it past Phase I trials as Avacta plans to focus its late-stage development on AVA021 once AVA004 has provided proof of concept of Affimers in humans. Additionally, due to the crowded PD-L1 market we believe AVA004 has little commercial potential on its own although its unique IP position (as an Affimer) could be attractive to partners.

The next most advanced asset, the AVA004/100 (PD-L1/I-DASH) product candidate, is of significant scientific interest; however, due to the very early nature of development and the complexities involved in the asset, we await for its advancement into the clinic before considering its inclusion into our valuation. We additionally note that Avacta has multiple partnerships outside of the LG Chem deal; however, due to limited financial visibility on these partnerships we do not include them in our valuation.

Reagents/diagnostics and animal health

We value the reagents and diagnostics divisions on a sales multiple of a relevant comparable. In 2012 German monoclonal antibody company Morphosys divested its research antibody business Antibodies by Design (AbD Serotec) to research tools company Bio-Rad to focus on its human therapeutic antibody business. AbD, which had FY12 sales of €18.3m, was divested for €53m, which included cash in the business of €5m. This implies an enterprise value (EV) of €48m and a sales multiple of 2.62x.

We have estimated the FY18 sales of Avacta Animal Health and Avacta Reagents to have been £1.57m and £1.19m (not including assumed milestone payments) respectively. Combining the sales of the Avacta services businesses and the implied AbD sales multiple, we derive a component valuation for the Avacta services businesses of £7.24m. While the AbD services business was much more mature than Avacta's services businesses with c 6x the sales of Avacta's reagents and animal health businesses, we have not included any growth in Avacta's services businesses, despite Avacta's FY19 sales targets for the services business growing by 25% to £1.5m.

Benchmarks: Upside potential on entering the clinic

Due to the early nature of Avacta's therapeutic assets and the range of variables in a potential valuation, we have benchmarked our sum-of-the-parts valuation for Avacta to recent relevant deals and IPOs.

On the deal front, the transaction signed between F-star, a private Cambridge, UK-based preclinical-stage developer of bispecific antibody fragments and Merck for an anti-LAG-3/PD-L1 bispecific (FS118) provides a useful comparison. The deal was signed in June 2017 on the basis of preclinical data and included payments of €115m in the first two years for a total transaction value of €1bn. While we note that the ownership of F-stars PD-L1/LAG3 bispecific FS118 has been recently transferred back to F-star, we believe the comparison still valid. Utilising a risk-adjusted VC (venture capital) based methodology, a 15-year timespan of milestone payments, a 12.5% discount

rate and a 50% risk adjustment for whether a similar deal would be signed we obtain a £201m valuation including Avacta's cash and services business.

Alternatively, substituting the exit valuation of the F-star transaction with the average IPO valuations (less cash, or enterprise valuations) of two recent relevant NASDAQ IPOs (Harpoon Therapeutics and Bicycle Therapeutics, both in Phase I for their lead assets) results in a VC valuation of Avacta plus its cash and the services businesses of £82m.

Based on these benchmarks we believe Avacta's sum-of-the-parts valuation of £54m or 47p/share is valid considering the pre-clinical status of its lead asset.

Financials: Funded into 2020

H119 revenue was £0.97m, a 44% decrease from H118 (£1.47m) driven by a significant reduction in life sciences revenue to £0.29m (vs £0.69m in 1H18). This was a result of the planned reduction in Moderna R&D income as development at Avacta completed and assets were transitioned to Moderna. In H219, Avacta expects revenue to pick up as the LG Chem partnership comes online and we forecast FY19 revenues of £3.2m (vs FY18: £2.8m) driven by income from LG Chem and Moderna in addition to the reagents/diagnostics and animal health divisions. We note a substantial increase in FY20 revenue compared with previous years due to the assumption of additional milestone payments from LG Chem.

Admin expenses remained one of the biggest contributors to the cost base and increased slightly to £4.12m (vs H118: £4.0m). COGS fell in the period from £0.46m in H118 to £0.31m in H119 and R&D costs increased substantially to £2.41m (vs H118: £1.47m) as a result of increased investment in the Affimer therapeutics programmes. We forecast FY19 administrative costs of £8.6m (vs FY18: £8.5m), COGS of £0.83m (vs FY18: £0.9m) and R&D of £6.1m (vs FY18: £3.8m). The substantial y-o-y increase in R&D costs is a result of the expected ramp in AVA004 related expenses as the asset moves towards the clinic.

Net loss for H119 was £5.2m (vs £3.95 in H118) driven by the aforementioned decrease in revenues and increase in R&D costs. We forecast FY19 net loss of £10.5m.

Net cash as of 31 January 2019 was £11.79m, mainly as result of the net £10.9m capital raise in August 2018. We forecast a cash reach into 2020; however, we forecast a cash raise (by illustrative debt) in 2020 of £10m to fund operations into 2021. This is for illustrative purposes only and the funding gap could be provided by additional partnerships, an equity raise or debt. Further funding needs beyond 2021 will predominately depend on the income received from new and existing business and the ramp of R&D costs in relation to the clinical programmes.

Exhibit 9: Financial summary

Accounts: IFRS, year-end: December, £000s	2017	2018	2019e	2020e
INCOME STATEMENT				
Total revenues	2,735	2,763	3,190	5,161
Cost of sales	(941)	(893)	(829)	(1,032)
Gross profit	1,794	1,870	2,361	4,129
SG&A (expenses)	(7,178)	(8,518)	(8,603)	(8,689)
R&D costs	(2,597)	(3,783)	(6,106)	(7,821)
Other income/(expense)	0	0	0	0
Exceptionals and adjustments	0	0	0	0
Depreciation and amortisation	0	0	0	0
Reported EBIT	(7,981)	(10,431)	(12,348)	(12,382)
Finance income/(expense)	88	41	39	28
Other income/(expense)	0	0	0	0
Exceptionals and adjustments	0	0	0	0
Reported PBT	(7,893)	(10,390)	(12,309)	(12,354)
Income tax expense (includes exceptionals)	1,526	1,561	1,849	1,856
Reported net income	(6,367)	(8,829)	(10,460)	(10,498)
Basic average number of shares, m	65.2	65.4	116.2	116.2
Basic EPS (p)	(9.8)	(13.5)	(9.0)	(9.0)
BALANCE SHEET				
Property, plant and equipment	3,453	3,054	2,760	2,542
Goodwill	0	0	0	0
Intangible assets	12,299	12,204	12,256	12,301
Other non-current assets	0	0	0	0
Total non-current assets	15,752	15,258	15,016	14,843
Cash and equivalents	9,166	5,220	4,976	3,558
Inventories	158	187	174	216
Trade and other receivables	1,277	1,288	1,487	2,406
Other current assets	5,200	1,500	2,088	2,683
Total current assets	15,801	8,195	8,725	8,864
Non-current loans and borrowings	0	0	0	10,000
Other non-current liabilities	0	0	0	0
Total non-current liabilities	0	0	0	10,000
Trade and other payables	1,664	2,040	1,895	2,358
Current loans and borrowings	0	0	0	0
Other current liabilities	0	0	0	0
Total current liabilities	1,664	2,040	1,895	2,358
Equity attributable to company	29,889	21,413	21,846	11,349
Non-controlling interest	0	0	0	0
CASH FLOW STATEMENT				
Profit for the year	(6,367)	(8,829)	(10,460)	(10,498)
Taxation expenses	(1,526)	(1,561)	(1,849)	(1,856)
Profit before tax	(7,893)	(10,390)	(12,309)	(12,354)
Net finance expenses	(88)	(41)	(39)	(28)
EBIT	(7,981)	(10,431)	(12,348)	(12,382)
Depreciation and amortisation	1,583	2,856	2,771	2,708
Share based payments	386	308	0	0
Other adjustments	11	161	(1)	(1)
Movements in working capital	(73)	336	(331)	(498)
Interest paid / received	88	41	39	28
Income taxes paid	1,745	1,261	1,261	1,261
Cash from operations (CFO)	(4,241)	(5,468)	(8,609)	(8,883)
Capex	(658)	(578)	(584)	(590)
Acquisitions & disposals net	0	0	0	0
Other investing activities	4,530	2,055	(1,945)	(1,945)
Cash used in investing activities (CFIA)	3,872	1,477	(2,529)	(2,535)
Net proceeds from issue of shares	14	45	10,893	0
Movements in debt	0	0	0	10,000
Dividends paid	0	0	0	0
Other financing activities	0	0	0	0
Cash from financing activities (CFF)	14	45	10,893	10,000
Currency translation differences and other	0	0	0	0
Increase/(decrease) in cash and equivalents	(355)	(3,946)	(244)	(1,418)
Currency translation differences and other	0	0	0	0
Cash and equivalents at beginning of period	9,521	9,166	5,221	4,976
Cash and equivalents at end of period	9,166	5,221	4,976	3,558

Source: Company data, Edison Investment Research

Contact details	Revenue by geography
Unit B, 1 Lion Works, Station Road East Whittlesford Cambridge – CB22 4WL UK 01223 75 0353 www.avacta.com	N/A

Management team

CEO: Alastair Smith	Chairman: Eliot Forster
Alastair Smith is founder of Avacta and since 2012 has raised over £50m for Avacta. Alastair has a degree and PhD in physics from Manchester University and, after working in the US for a period, took up a position at Leeds University in 1995. At the age of 38 he was awarded the chair of molecular biophysics.	Eliot Forster holds a PhD in neurophysiology from Liverpool University and an MBA from Henley Management College. He is chairman of the MedCity project that promotes the life sciences in the London/Cambridge/Oxford Golden Triangle and has held previous key roles at GSK and Immunocore (CEO).
CFO: Tony Gardiner	**CSO: Amrik Basran**
Between 2007 and 2011, Tony Gardiner was the chief financial officer of AIM-listed Fusion IP, an IP commercialisation company, which was subsequently acquired by IP Group in 2014. Tony has also held senior finance roles within Eversheds, KCOM Group, Eldon Electric and Hickson International.	Amrik Basran completed his degree and PhD at the University of Leicester and has a background in protein biochemistry/engineering. He then spent six years as a post-doctoral researcher at the Institute of Biotechnology, Cambridge University. He has held previous key roles at Domantis and GSK.

Principal shareholders	(%)
IP Group	17.08
JO Hambro	11.04
Ballie Gifford & Co	8.50
Lombard Odier Asset Management	7.90
Carlton Holdings International	7.24
Fidelity	5.74
Unicorn Asset Management	3.45

Companies named in this report

Bicycle therapeutics (BCYC), Harpoon Therapeutics (HARP), Molecular partners (MOLN), Pieris Pharmaceuticals (PIRS)

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