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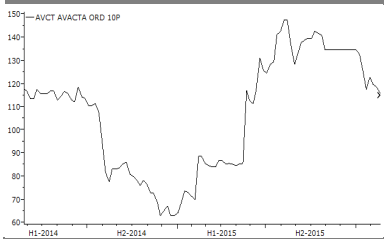
Pharmaceuticals & Biotech



Source: Fidessa

Market data	
EPIC/TKR	AVCT
Price (p)	115.0
12m High (p)	154.0
12m Low (p)	74.0
Shares (m)	67.5
Mkt Cap (£m)	77.6
EV (£m)	49.3
Free Float*	49%
Market	AIM

**As defined by AIM Rule 26*

Description

Avacta is a pre-clinical stage biotechnology company developing biotherapeutics based on its proprietary Affimer protein technology that benefits from near-term revenues from research and diagnostic reagents

Company information	
CEO	Alastair Smith
CFO	Tony Gardiner
Chairman	Trevor Nicholls
	01904 217 070
	www.avacta.com

Key shareholders	
Directors	0.5%
IP Group	25.1%
Henderson	12.4%
Aviva	10.0%
Baillie Gifford	7.8%
Ruffer LLP	7.2%
Fidelity	5.6%

Next event	
25 April	Interims
2Q'16	Opening Cambridge
3Q'16	New Wetherby site
October	Finals
Jan 2017	AGM

Analysts

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Avacta

Affimers – next generation therapeutic platform

Avacta is a life science company providing high quality and highly specific tools to the biopharmaceutical industry to help in the diagnosis and treatment of humans and animals. The group's Affimer technology is a revolutionary alternative to the established technology, antibodies, which dominates the drug industry despite its limitations. During 2015 Avacta focused all activities on the commercialisation of Affimers initially via a bespoke service and an on-line catalogue, with a longer-term view to develop its own bio-therapeutics for out-licensing. There is a clear mismatch between the EV of ca.£50m and the long-term potential of Affimers.

- **Strategy:** To commercialise the Affimer technology, initially by providing Life Scientists with high quality, powerful bespoke tools to accelerate the understanding of disease and improve diagnosis and treatment of humans and animals. Longer-term, Avacta aims to develop its own proprietary therapeutics.
- **Commercial opportunity:** Antibody technology is the accepted 'gold standard' in terms of research, diagnostic and therapeutic tools and have combined commercial markets in excess of $80bn per annum. Affimers may represent an important additional tool in the armoury especially where antibodies have limitations.
- **Valuation:** Avacta is trading on an EV of ca.£50m, having invested £11.0m to date in its proprietary disruptive technology. There is an under-appreciation in the market value derived from such assets. As the market better understands that Affimers can drive next generation therapies, Avacta's valuation will correct.
- **Risks:** Although Affimers have significant advantages over traditional antibody technology, the customer base might take time to realise these advantages and adapt to a new disruptive technology. Avacta is minimising this risk by initially focusing on areas where antibodies are unavailable or perform poorly.
- **Investment summary:** The enterprise value of Avacta does not reflect the value that big pharma is prepared to pay for new technologies and assets. The median up-front paid is US$17m and US$40m for pre-clinical and Phase I assets respectively. These figures were exemplified superbly by the deals that Molecular Partners has secured for its comparable DARPin technology.

Financial summary and valuation

Year end July (£m)	2013	2014	2015	2016E	2017E	2018E
Sales	2.70	3.18	1.81	2.15	3.02	4.17
EBITDA	-1.74	-1.33	-2.34	-3.30	-3.81	-3.89
Underlying EBIT	-1.83	-1.86	-2.91	-4.06	-4.57	-4.65
Reported EBIT	-1.87	-2.07	-5.57	-4.36	-4.90	-5.01
Underlying PBT	-1.80	-1.83	-2.89	-3.85	-4.40	-4.55
Statutory PBT	-1.85	-2.04	-5.54	-4.15	-4.73	-4.91
Underlying EPS (p)	-4.67	-3.07	-4.50	-4.68	-5.11	-5.03
Statutory EPS (p)	-4.82	-3.57	-9.84	-5.13	-5.59	-5.56
Net (debt)/cash	0.58	11.48	7.33	21.00	12.61	3.42
Shares issued	0.00	14.54	0.02	20.79	0.00	0.00
P/E (x)	nm	nm	nm	nm	nm	nm
EV/sales (x)	nm	nm	nm	nm	nm	nm

Source: Hardman & Co Life Sciences Research

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Executive summary

Background

Focused on commercialising its proprietary Affimer technology...

...through reagents and developing its own drug pipeline

Avacta is dedicated to providing scientists with high quality Affimer research tools that enable them to obtain a better understanding of biology and disease and is now also in the pre-clinical stages of its own therapeutic development programmes. The company came to the AIM market in 2006 with the intention of providing instrumentation, tools, consumables and reagents for scientific research and development. The group has now evolved, through acquisitions and disposals, to focus on commercialising its proprietary Affimer technology as an alternative to antibody technology, initially by providing a custom service and off-the-shelf reagents, but longer-term to discover and develop its own drug pipeline in the same way that many major drugs have been developed and marketed based on antibodies.

2015 – A transformational year

2015 was a transformational year for the group...

...with significant de-risking of the Affimer technology

The last 12 months have been transformational for the group. Affimers have evolved from being a new and interesting technology through to full commercialisation and therapeutic co-development. Initially, Avacta is focusing its reagents strategy on providing potential long-term licensing partners with a custom service for generating Affimers which have high specificity for their defined targets and which Avacta aims to get into the third parties' products. Following the proven and successful pathway trodden by Abcam (ABC.L), Avacta is also making its technology available to its customers via a small on-line catalogue with a focus on application areas that are difficult for antibodies. However, unlike Abcam, Avacta took the decision to embark on a discovery programme whereby it is generating its own therapeutic leads, which it can develop itself or in partnership, and move it further up the value chain. All these activities have contributed to a significant de-risking of Affimers.

In addition to technological and commercial advances, Avacta has invested in key personnel in senior management and Board positions, disposed of its non-core trading activity (Optim) and raised £22.0m of new capital via a share issue to fund its new therapeutics strategy.

2016 – Continuation of strategy

Well-funded to continue its strategy and make further progress in 2016

Progress made in 2015 has continued into 2016. An experienced Commercial Officer has been hired together with an expansion of the sales presence on the East and West Coasts of the US, and a new CFO has been appointed. In Wetherby, the Group is consolidating its two sites into a single facility on the same industrial estate which will be completed late summer. Avacta's therapeutic discovery activities will move from the Stevenage Bioscience Catalyst to new facilities based just outside Cambridge. In addition, the commercial traction for Affimers is likely to be enhanced through peer-reviewed publication of articles in reputable scientific journals.

From Antibodies to Affimers

18% of FDA approvals in 2015 were drugs derived from antibodies

Over the last 20 years, antibodies have laid the foundation for drug development, initially providing the tools for diagnosis and drug discovery, but eventually providing the therapeutics themselves. In 2015, eight (18%) of all new chemical entities approved by the FDA were derived from antibodies. However, while there are more antibody-derived drugs in late-stage development, it is now thought the low-hanging fruit (first generation antibody drugs) have been discovered and developed and a step-change (new generation of engineered biomolecules) is needed in order for there to be another wave of drugs – hence bi-specific antibodies, or alternatives to antibodies. Affimers represent a very credible alternative to antibodies and Avacta is the only company in the world with this proprietary technology.

Avacta's strategy is not to compete directly with well-established and competitive antibody products

Affimers are small, highly stable proteins that are engineered to display peptide loops which provide a high affinity binding surface for a specific protein target. As such, they provide powerful competitive advantages over antibodies and antibody-drug conjugates (ADCs). However, Avacta's strategy is not to compete directly with well-established and competitive antibody products. By targeting areas where antibodies are known not to work or are inaccessible to antibodies due to size, or lack of suitable targets, Avacta can carve its own niche for Affimers. This strategy is expected to provide both short – and long-term revenue streams.

Competitive advantages of Affimers	
Research & Diagnostic reagents	**Therapeutics**
Quick to develop	Quick to develop
High level of specificity	Wide range of potential targets
Small, robust & stable	High binding affinity/specificity
Consistent batch-to-batch manufacture	Easily formatted to suit application
Produced in laboratory, not in animals	Easy to manufacture – important
Easily modified to suit application	Intracellular activity
Functional within live cells	Small size – good tissue penetration
Clear, unencumbered IP	Clear, unencumbered IP
Easy to ship and store	Good shelf-life – stable over long periods

Source: Company reports; Hardman & Co Life Sciences Research

Commercial traction

Reagents

Affimers can be discovered and validated in 7-8 weeks…

…which, along with other performance advantages…

…makes them a very attractive alternative to antibodies

Affimers were first launched by Avacta in Autumn 2014. Avacta's primary commercial focus is on a bespoke custom Affimer service whereby customers provide Avacta with a specific target to which they require a strong and specific binding agent. Unlike antibodies which can take several months, Affimers can be discovered and validated in a matter of weeks (7-8 weeks), which, along with other performance advantages specific to each application, makes them a very attractive alternative to antibodies. Over the last 12 months Avacta has received orders from a mix of more than 30 major pharmaceutical, biotechnology and diagnostics companies. The custom service initially provides small quantities of Affimer to allow further R&D testing. Future commercial exploitation of the Affimer within the third parties' products such as diagnostic test or laboratory assay kits, for example, is a key part of the business model. Avacta would benefit through royalties from licensing the Affimers or from long term supply deals. Avacta is also providing a small number of Affimers to a wider range of customers at an accessible price point via an on-line catalogue to drive awareness, adoption and publications involving Affimers. The catalogue offers a relatively small – currently 50 – number of affinity reagents to provide scientists with new avenues of research and discovery.

Affimer therapeutics

Key objective is to have a therapeutic drug candidate ready for clinical trials within 3 years

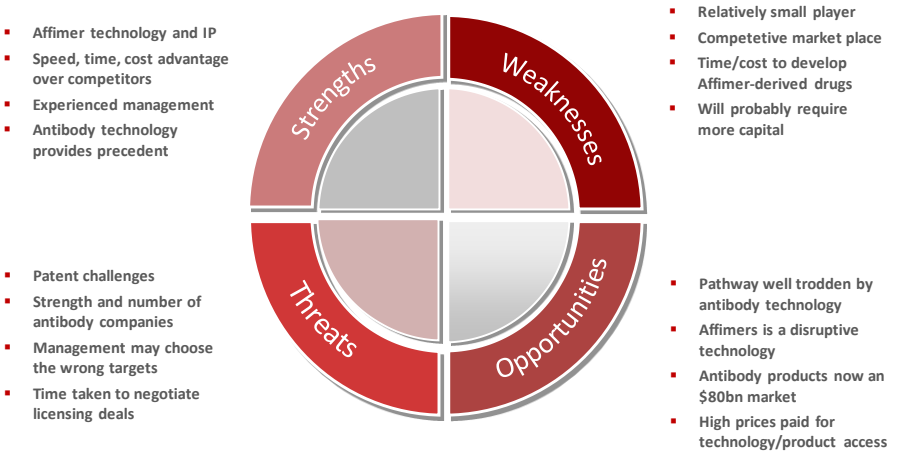
While the reagent business is developing its offering and increasing customer relationships, the therapeutics development team, currently based in Stevenage, is undertaking a discovery programme to identify Affimer leads that could be developed into therapeutics, either by itself, or in partnership with larger organisations. This would potentially take Avacta much further up the value chain. While there are numerous possibilities, Avacta is focusing on areas of unmet medical need, where the Affimer technology has competitive advantages compared with antibodies in terms of formatting for bi-specifics, tissue penetration and speed of development, eg oncology and blood clotting disorders. A key objective of the management team is to have a therapeutic drug candidate ready for early clinical trials as soon as possible, ideally within three years.

Commercial opportunity

Each of Avacta's markets is an attractive $bn commercial opportunity

Antibody-derived products are used as reagents in a number of research processes, as a component of diagnostic tests and directly as therapeutics. In 2015, these markets were estimated to be worth $2bn, $12bn and $80bn respectively (see pages 15-16). This is despite the known disadvantages and limitations of antibodies. Therefore, a technology that can redress any of these problems in a timely manner would have significant competitive advantages. Affimers have the potential to fill these gaps, both as reagents and as therapeutics. Moreover, drugs companies with successful portfolios of drugs based on antibody technology are looking for the next generation of technologies and platforms and are willing to pay handsomely to obtain exclusivity.

SWOT analysis



Source: Hardman & Co Life Sciences Research

Valuation

It's difficult to value a pre-clinical pipeline. A DCF valuation requires many far-reaching assumptions and an exhaustive analysis of the market opportunities, penetration rates, potential milestones and royalty payments that a partner might pay. Each programme then has to adjusted for the probability of success based on long-term industry benchmarks, which for pre-clinical candidates is less than 1%.

Big pharma has paid a median US$40m up-front for a Phase I asset

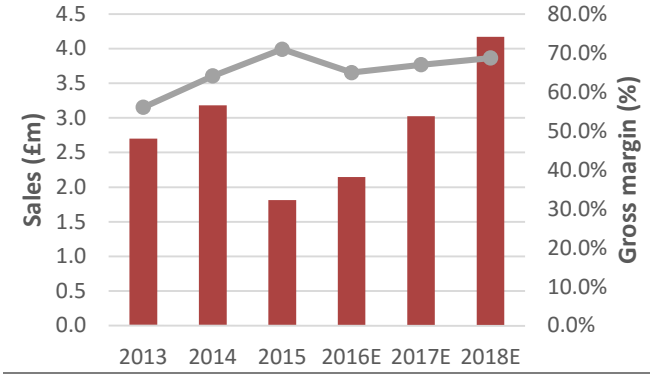
Moreover, pure financial analysis does not take account of the price that big pharma is willing to pay to gain access to disruptive technologies and products. We published a report recently that showed the median up-front deal value for immuno-oncology compounds to be US$17m for pre-clinical assets and $40m for Phase I assets. This is excellently demonstrated by the deals that Molecular Partners has signed with Allergan and J&J for its DARPin-derived targets with an average up-front of US$35m.

Investment summary & conclusion

Upside potential to forecasts on announcement of licensing partners

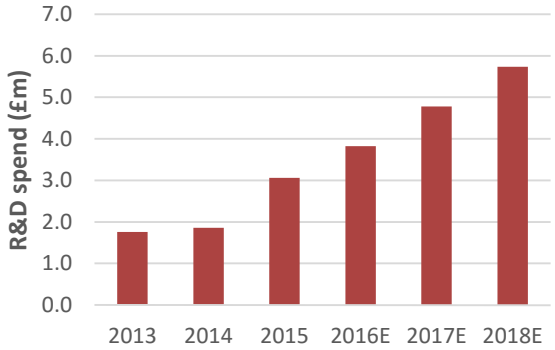
Our forecasts over the next three years assume a stable sales stream from the existing Animal Health business (an established veterinary diagnostics business within the wider Avacta Group) plus some revenues from Affimer reagents. By the end of the forecast period it is reasonable to expect that more licensing deals will have been signed. However, given the difficulty in concluding such deals leading to protracted timelines, we do not include such deals in our forecasts, which leads to upside potential when they are announced.

Sales & gross margin



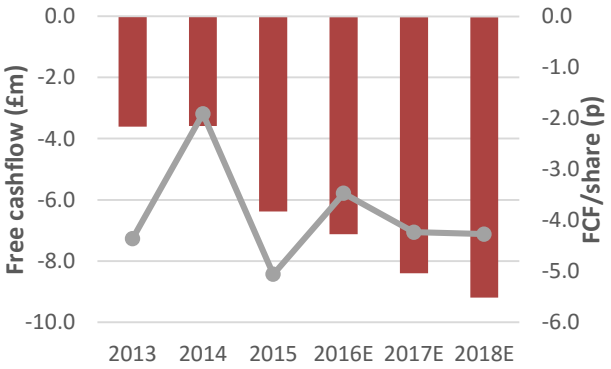
- Sales are derived from a stable Animal Health business and the growing contribution from Affimers (Life Sciences)
- Life Sciences sales are forecast to overtake the Animal Health sales in fiscal 2017
- Figures are based on reported sales. No correction has been made for disposal of the analytical business unit in 2015
- Forecasts do not include any contributions from licensing or milestone income which are lumpy and unpredictable

Capitalised R&D



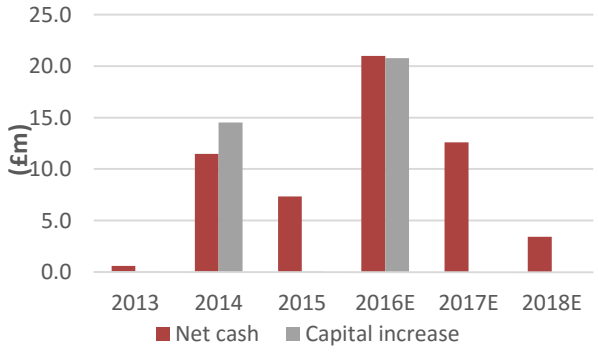
- Investment in R&D is capitalised, not written-off in the year incurred
- Increase in investment is directly linked to the Affimer development programme
- Total R&D spend on Affimer technology to date is estimated to have been £18m
- Some R&D investment may be recovered through partnership programmes

Free cashflow



- The forecast cash burn is approximately £0.6-0.7m per month
- Investment in senior personnel in 2015/16 has added to on-going cost structure
- Avacta has invested in improved infrastructure in Wetherby and Cambridge in 2015/16
- Cap-ex is expected to reduce down to maintenance levels in fiscal 2017

Net cash/capital increases



- Gross funds of £22.0m were raised in August 2016 to fund the development of its own Affimer-based drug pipeline
- Avacta is forecast to have sufficient cash resource for its internal development programmes for at least three years
- The net cash position would be positively affected by any announcements of partnerships/licensing deals

Source: Company data; Hardman & Co Research

Affimers

Next generation antibodies

Antibodies have paved the way...

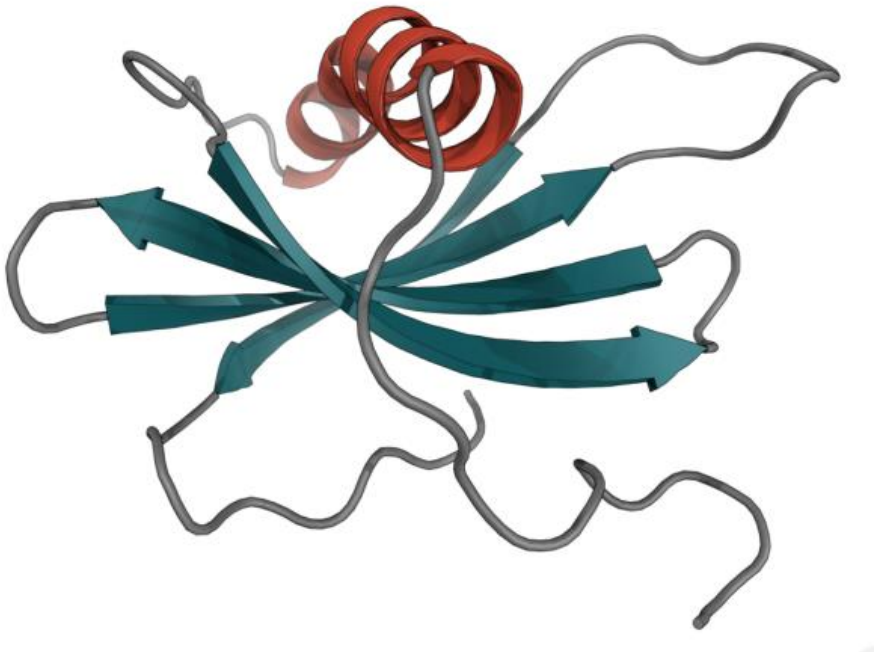
...but Affimers will be disruptive

Over the last 20 years, antibodies have become widely used reagents for research, diagnostics and therapeutics, generating a multi-billion dollar business despite some well-known disadvantages and limitations. Avacta has developed Affimers, which are engineered scaffold protein alternatives to antibodies, possessing all the positive attributes whilst overcoming many of the disadvantages. Therefore, they represent a major commercial opportunity.

What is an Affimer?

An Affimer is a relatively small (10x smaller than an antibody), highly stable protein that has been engineered to form loops that provide high affinity binding surfaces for a specific target protein in the same way that an antibody does. They were originally developed at the MRC Cancer Cell Unit in Cambridge and latterly, at the University of Leeds, from which the technology and IP was acquired by Avacta in 2012. During the recombinant engineering development process, these non-antibody scaffold proteins have become stable, non-toxic and biologically neutral.

What is an Affimer?



The Affimer protein scaffold – showing the two loops and the amino terminus where designer or random peptides can be inserted to create the binding surface

Source: Avacta

Large surface area for target proteins to bind with high specificity and high affinity

Affimers always contain two separate loop sequences, typically involving 18 amino acids, to create a potentially large surface area to which target proteins can bind with high affinity and high specificity. Consequently, Affimers can distinguish between proteins where there is as few as one difference in the amino acid sequence. They are not produced in animals so they do not rely on a host animal's immune response, which may not produce an antibody at all, and the batch to batch reproducibility is much better than with animal derived antibodies.

Affimers have a number of advantages and applications...

...and a validated target can be generated in 7-8 weeks

Key advantages of Affimers as research and diagnostic reagents

The main advantage of an Affimer is that their generation is controlled *in-vitro* so they can be made highly specific to a target, are quick to make and can be produced in situations where it is not possible to produce an antibody. Although they can also be produced against the same targets as antibodies, there is no point in employing resource to produce alternatives to adequately performing research antibodies since customers are unlikely to change their processes. The focus is to use the advantages of Affimers to satisfy the part of the market unsatisfied by existing technologies of which there are many due to the limitations of research grade antibodies which has been much discussed recently.

Key advantages of Affimers

- Speed of development – 7-8 weeks versus many months
- High degree of specificity, which can be controlled
- Relatively easy and reproducible manufacturing
- No reliance on an animal's immune system
- Relatively small, robust and stable

Source: Company reports; Hardman & Co Life Sciences Research

Applications and targets

Since launch, Avacta has greatly increased the number applications in which Affimers have been demonstrated. This means that they can be applied extensively to identify agents with high binding affinity and specificity against a host of targets.

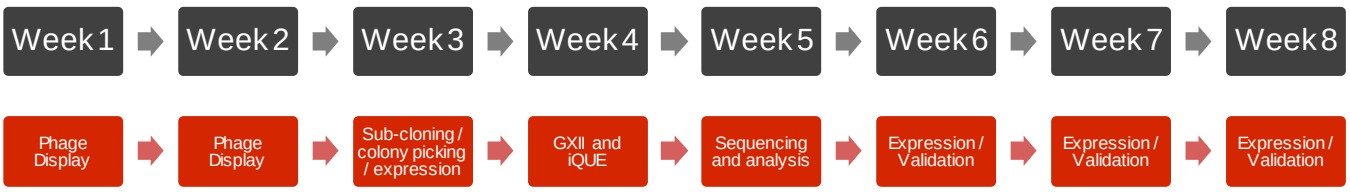
Uses of Affimers

Applications	Targets
Western Blotting	Proteins
ELISA	Peptides
Immunohistochemistry	Lipids
Immunofluorescence	Haptens
Microarrays	Small molecules
Flow cytometry	Whole cells
Drug target validation	
Chromatography – pull-down and affinity	
Super resolution microscopy	
Electrochemical sensors	
Biomineralisation catalysis	

Source: Company reports; Hardman & Co Life Sciences Research

The following schematic provides a broad outline of the timelines for producing a specific and validated Affimer from when a customer provides Avacta with a well-defined and high quality target.

Affimer development timeline



Source: Avacta

The key is for the customer to provide the company with the latter and under such circumstances, Avacta management believe that it has a 90% probability of success in the case of protein targets which make up the majority at the current time. Such a process represents a considerable time saving compared to that encountered for production of an antibody which may take up to a year.

Affimers versus antibodies

High quality lead candidates in a matter of weeks...

...with single digit nM effectiveness

On the simple premise that Affimers offer all the advantages that antibodies have to offer without the disadvantages, there are many applications for the technology – filling gaps in the range of available antibodies, replacing antibodies in routine laboratory tests and as purification agents.

Comparison of Affimers with antibodies

	Affimers	Antibodies
Affinity	nM per peptide; 3 peptides	pM - nM
Specificity – single amino acid change	Yes	Yes
Specificity – conformation	Yes	Yes
Size	13 kDa, 3nm	150kDa, >15nm
Expression in *E.coli*	Yes	No
Expression in human cells	Easy	Sometimes possible
Amenability to engineering	High	Low
Stability	High	Variable
ELISA, IF, IP, WB	Yes	Yes
Post-translational modifications required for proper function	No	Glycosylation, oxidation
Internal cysteine/di-sulfides	None	Multiple
Limited by immune system	No	Yes

Source: Avacta; Hardman & Co Life Sciences Research

Commercial traction – reagents

Being based on a small protein that can be engineered into a product that binds with high specificity and with high affinity to a wide range of protein targets, new Affimers can be produced easily in large volumes with no batch-to-batch variability, in just 7-8 weeks, which offers significant competitive advantages to laboratory, biotechnology and pharmaceutical industries.

Powerful competitive advantages of Affimers

Research & Diagnostic reagents	Therapeutics
Quick to develop	Quick to develop
High level of specificity	Wide range of potential targets
Small, robust & stable	High binding affinity/specificity
Consistent batch-to-batch manufacture	Easily formatted to suit application
Produced in laboratory, not in animals	Easy to manufacture – important
Easily modified to suit application	Intracellular activity
Functional within live cells	Small size – good tissue penetration
Clear, unencumbered IP	Clear, unencumbered IP
Easy to ship and store	Good shelf-life – stable over long periods

Source: Company reports; Hardman & Co Life Sciences Research

Avacta is focusing its business development and production efforts on providing a custom service to generate Affimer reagents on demand with a view to getting these Affimers into third parties' future products and generating royalty payments. During 2015, Avacta began commercialising the Affimer business opportunity:

- Demonstrated commercial traction through custom Affimer sales
- Formed strategic partnerships with pharmaceutical companies
- Achieved operational scale-up to underpin medium-term growth plan
- Grow the on-line Affimer catalogue
- Generated a therapeutic pre-clinical data pack to support licensing discussions

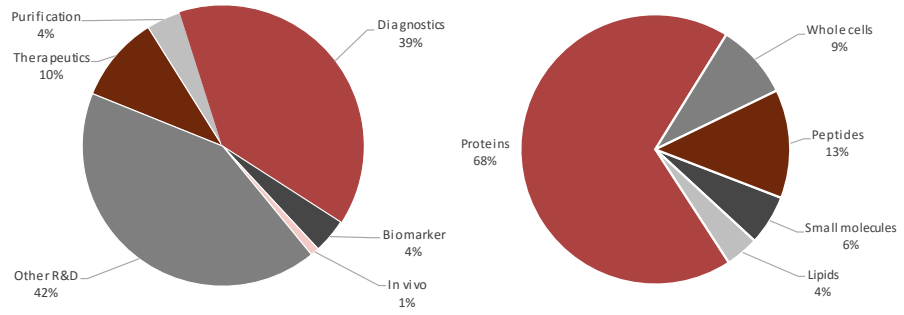
Avacta has achieved this by investing in and developing an experienced custom Affimer sales team. This will be expanded in 2016 with the appointment of a new Chief Commercial Officer – Philippe Cotrel – and with the addition of experienced sales people on both the west coast and east coast of the US.

Custom Affimer orders from 30 customers during 2015

During 2015, Avacta received custom Affimer orders of ca.30 from a number of well-known Pharmaceutical, Biotechnology and Diagnostic companies.

Avacta is also building a small catalogue of Affimers to make the technology widely available at a lower price point in order to drive awareness, adoption and publications involving Affimers.

Commercial traction – 2015



Source: Avacta reports

Commercial traction – therapeutics

Moderna deal is an excellent endorsement of the Affimer technology...

...and a desirable partner

Also during 2015, Avacta announced a significant research partnership with Moderna Therapeutics to provide a range of Affimers against a number of selected targets for messenger RNA therapeutics. This was an important endorsement that Avacta had generated sufficient early proof-of-concept data to support its claims regarding Affimers and attract a reputable drug developer. Moreover, Moderna is a desirable partner for Avacta as it has already strategic partnerships in place with other drug companies that are also commercialising antibody-derived drugs, including Merck & Co, AstraZeneca and Alexion (see page 16).

Therapeutic deals in 2015

Company	Activity
Moderna Therapeutics	Messenger RNA therapeutics
Blueberry Therapeutics	Antibiotic resistance
Phoremost	Phenotypic screening
D'Liver	CRO focused on liver metabolism

Source: Avacta announcements; Hardman & CO Life Sciences Research

Affimer therapeutics

As part of the long-term growth strategy, management is pursuing the development of bio-therapeutics based on Affimer technology, against selected targets, in the same way that antibody technology was developed into active drugs. The deal with Moderna demonstrated that there were three key advantages of the Affimer technology:

Rapid lead generation

- Affimers that can inhibit drug targets generated in a matter of weeks
- Good affinity and specificity straight from the early screens
- Targets not limited by an immune response in an animal

Ease of manufacturing

- High yields which is important for downstream manufacturing
- Production of high quantities (100s of milligrams) is a major advantage
- No aggregation in manufacturing
- No batch-to-batch variation

Drug delivery

- Bi-specifics for combination therapies can be generated
- Fc-fusions have been generated
- Intracellular functionality and survival – good tissue penetration

These attributes are attracting interest from pharmaceutical and biotechnology majors. The goal of Avacta is to create a portfolio of therapeutic assets derived from Affimer technology that can be taken into the clinic either alone or with partners depending on the therapeutic target. In our opinion, the successful advancement of an Affimer-based drug into the clinic would represent a significant value inflection point.

Selection of the right target is key

The opportunity for Avacta is quite significant because there is a wide range of therapeutic targets not adequately addressed by antibody proteins and non-antibody proteins (scaffolds). The risk is that management picks a target that does not progress as expected. The potential target space is very broad since Affimers can be generated to a wide range of both extra-cellular and intra-cellular protein targets. Management's strategy is to focus its in-house development programmes in: immuno-oncology where Affimers offer the benefit of easily producing bi-specific and tri-specific molecules hitting multiple drug targets at once; blood clot modulation where the company has a strong collaboration with a leading clinician providing the prospect of a potentially faster route to the clinic; being responsive to the requirements of potential partners in fully funded research partnerships.

Selecting the right targets for in-house therapeutic programmes is critical to maximise the chances of reaching the clinic and the value of licensing deals. To this end the company appointed Mike Owen, ex-Head of Biopharmaceuticals R&D for GSK as a non-executive Director late in 2015 and he is tasked with setting up a

Scientific Advisory Board early in 2016 to advise on the process and review development programmes in the future. Apart from selecting the right therapeutic target for in-house programmes, important in the decision process will be whether Affimer technology can improve the outcomes with existing therapies, or be the first to address a particular clinical condition. The importance of this is that the two approaches carry different degrees of risk.

Therapeutic targets

Best-in-class	First-in-class
Disease biology generally known	More speculative
Limitation of current therapies known	Biology less well understood
Commercial market understood	Potentially more valuable
Lower risk	Greater value/higher risk
Avacta could progress further	Need to out-license

Source: Avacta reports; Hardman & CO Life Sciences Research

Comparators

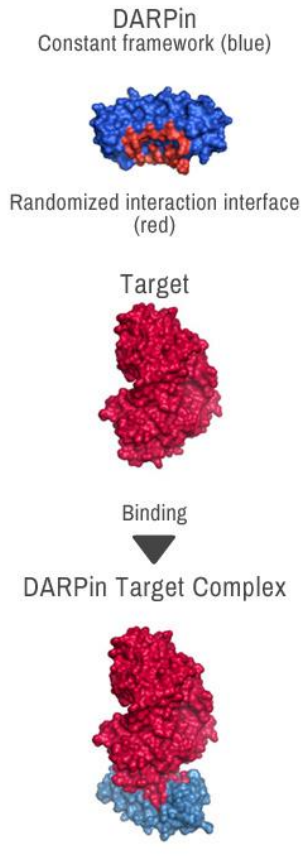
In our opinion, two useful comparators from a technology stand-point that both have non-antibody therapeutic molecules in the clinic are Affibody and Molecular Partners.

'Scaffolds'

Approach	Company	Product
Affibody	Affibody AB	Class of engineered affinity proteins with proven potential for therapeutic, diagnostic and biotechnological applications
Affimer	Avacta	Small, highly stable protein engineered to display peptide loops which provide a high affinity binding surface for a specific target protein
DARPins	Molecular Partners	Recognize targets with specificities and affinities that equal or surpass those of antibodies, but robustness & extreme stability allows more advanced applications

Source: Company websites; Hardman & Co Life Sciences Research

DARPin mechanism



Source: Molecular Partners

Affibody – www.affibody.com

Affibodies are a novel class of antibody mimetics which are claimed to have superior characteristics compared to monoclonal antibodies and antibody fragments. Again the aim of Affibody is to have the advantages of antibodies whilst overcoming the limitations. Affibody is taking the same approach to Avacta in that it has created an enormous library of more than 10 billion Affibody molecules from which binders to specific targets are selected. Avacta has several libraries of 10 billion in size from which it selects the Affimer binder to the specific target of interest. Like Avacta, Affibody also claims that its Affibody molecules are relatively small and inert and can potentially be used as bi-specifics. It has the advantage of being more advanced than Avacta having been tested in humans and with more commercial deals and published reports on the technology.

DARPins – www.molecularpartners.com

Design Ankyrin Repeat Proteins (DARPins) are also a novel class of small proteins which are engineered from ankyrin repeat proteins that are found commonly and involved in cell signalling and receptor binding. Molecular Partners claims that DARPins are small, highly potent and highly stable and bind with high affinity to specific targets and again can overcome the limitations of antibodies.

The approach of Molecular Partners is very similar to that of Avacta, with perhaps a little more emphasis at this stage on disrupting multiple pathways in a disease process in parallel (ie bi-specific and tri-specifics) in order to maximise the clinical response. It is more advanced, being in a Phase II trial in multiple myeloma.

Commercial strategy

Adopting a similar commercial approach to that successfully employed by Abcam...

Avacta is using the same commercial approach as that employed very successfully by Abcam (ABC.L), which led the way for antibodies to be used as affinity reagents for research, diagnostic and therapeutic markets that are now valued in excess of $2.0bn. However, there is one significant difference. Whereas Abcam focused solely on being the supplier of the necessary tools to enable its customers to generate commercial prospects, Avacta is aiming additionally to generate its own therapeutic leads. Therefore, management is operating a relatively straight forward business model: near-term revenues will be derived from reagents; longer-term revenues will be derived from therapeutics.

Reagents business

- Customer-driven bespoke Affimers
- Catalogue of Affimer reagents

Custom service

Avacta is focusing its efforts primarily on offering a custom Affimer service for bespoke development work for its OEM customers. Initially it will undertake custom synthesis of an Affimer for a defined target provided by the customer that will allow the customer to evaluate the product in its R&D process. The advantage to the customer is that the Affimer will be available relatively quickly and have high affinity and specificity for the target, and may be to a target for which previous attempts to find antibodies have failed. This service gives the customer R&D rights only and costs £15-20k/$25-40k.

In the event that the customer develops the Affimer into a commercial product, for example a diagnostic test for which it would want commercial protection, Avacta would license the Affimer to the customer, potentially on an exclusive basis, for which it would charge an upfront payment (which would be modest compared with therapeutic licensing deals ca.£50k/$80k) and receive royalties on end-product sales.

Affimer catalogue

The on-line catalogue currently has 50 products...

...mostly focused on gaps in the antibody market

Over the last decade, Abcam has developed a catalogue of antibodies/antibody fragments that are used, amongst other things, in cell signalling to become a business offering >100,000 products and worth $200m per annum. Avacta is also developing an on-line catalogue offering a small number – currently 50 – of Affimers that are focused on the many gaps that remain in the antibody market – there being no commercial logic in targeting replacements for established, commercially successful, antibodies that end users are unlikely to switch out of their processes. The emphasis for Avacta's catalogue is in getting Affimers into the hands of as many researchers as possible in order that they publish data using Affimers. Third party data has been shown by Abcam's experience to be the most effective form of validation and marketing for such products. Application areas where Affimers might find particular traction in the future include:

- Immunohistochemistry
- Flow cytometry
- Ubiquitin-proteasome system
- Live cell biology

Therapeutics business

...but additionally to discover and develop its own therapeutics

Cash raised in the share issue of August 2015 was to fund the discovery of therapeutic leads to the development of its own drug pipeline. The aim is to generate a putative drug which can enter the clinic ideally within three years. Whether Avacta develops the drug through clinical trials itself or with a partner is dependent of the disease target – large competitive diseases will certainly be licensed out. Even so, large pharma pays handsomely for such leads and Avacta could expect a decent up-front payment, milestones and royalties (see page 22).

Commercial opportunity

Reagents business

Abcam has established a strong position in the $2bn reagents market....

Abcam was born out of the need for researchers to source quality antibody reagents that came with a datasheet that genuinely reflected their uses and limitations. Today, the company has a catalogue of over 100,000 protein-based research tools, sales of £160m/$260m per annum and a market capitalisation of £1.25bn/$2.0bn. Abcam has stayed true to its core foundation of supplying quality reagents, the majority of which it sources from third parties, and has never moved into the drug discovery arena itself. There are now thought to be over 100 antibody reagents companies worldwide, supplying a reagent market estimated to be in excess of $2bn with:

- Monoclonal antibodies
- Polyclonal antibodies
- Antibody-based fragments
- Animal based libraries eg Camelids (derived from Camels, Llamas)
- Antibody-based scaffolds
- Tags and cell markers

...with antibodies fundamental to the $12bn clinical diagnostic market

In addition to the reagents business, antibodies are fundamental in much of the clinical diagnostics market, which is estimated to be worth in excess of $12bn per annum.

However, as well as being an extremely competitive field, all antibody companies suffer from the limitations surrounding antibodies described earlier, notably the lack of specificity in many cases, the size of the protein structures and the many months that it can take to derive an antibody specific to a target. This provides the opportunity for alternative technologies that can overcome these disadvantages.

Alternatives to antibodies

A number of approaches have been taken to provide alternatives to antibodies for research. However, in reality within the research reagents market, the only affinity molecules that have been commercialised are based on DNA and RNA (so called “aptamers”) and these have had very limited commercial success because of technical limitations. Affimers are the only major protein based technology to be addressing the reagents market with Molecular Partners, Affibody and others preferring to focus on the therapeutic opportunities.

With the significant competitive advantages offered by Affimers, together with management’s strategy of targeting segments of the market that are inaccessible to antibodies for whatever reason, Avacta has an excellent opportunity of expanding the current reagent market and taking a large share of this added portion. The key to driving this is making researchers and pharmaceutical customers aware of the role that Affimers can play in their discovery programmes, which should come through publication of articles by key opinion leaders in peer-reviewed scientific journals.

Therapeutics business

There are 60 approved drugs derived from antibodies...

Drugs derived from monoclonal antibodies now represent a large proportion of annual sales of prescription drugs. The first – ReoPro (abciximab) was launched in 1995 and there are now 60 regulatory approved monoclonal antibody drugs on the market with sales of just over $80bn in 2015. The table below shows the ranking of the top 10 drugs by ex-factory sales in 2015, with Humira (adalimumab) being the top selling drug in the world last year. The table also shows that drugs derived from antibodies have generated cumulative sales since launch approaching $560bn. These figures are expected to rise in coming years given that the FDA approved eight antibody derived drugs in 2015 and with a similar number under review in 2016. Therefore, the therapeutic opportunity is enormous.

...including the biggest selling drug in the world with annual sales of $14bn...

Drugs based on monoclonal antibodies have revolutionised the treatment of autoimmune disease such as arthritis (rheumatoid and psoriatic) and cancer. While arthritis drugs are the biggest sellers, 35 (58%) of the 60 approved drugs are for the treatment of different forms of cancer. However, it is thought that the currently approved and waiting for approval drugs represent the success of the first generation of antibody-based products and that a new generation of engineered antibodies based on a variety of biotech platforms is required to produce new therapeutics with enhanced mechanisms of action and/or improved pharmaco-kinetics and safety profiles:

- Bi-specific and Tri-specific antibodies
- Antibody-drug conjugates
- Alternative technologies
- Antibody and non-antibody scaffolds

....and cumulative antibody drug sales now approaching $560bn!

Avacta's proprietary Affimer technology represents one of these approaches. Avacta is focusing its discovery programmes on targets for which the benefits of Affimers such as formatting as multi-specifics and tissue penetration provide competitive advantages. The key to success for Avacta at the moment is to develop safe and effective therapeutic molecules which are able to compete with other therapeutic platforms to deliver best-in-class therapies that can be licensed. First-in-class therapies targeting new biology could be a high value future goal for Affimers. Unsurprisingly, drug companies that have developed a strong portfolio of antibody-derived drugs are showing particular interest in the next wave of technologies.

Top 10 antibody drugs – 2015

Rank	Drug	Generic name	Company	2014 ($m)	2015 ($m)	Growth (%)	Cumulative ($m)
1	Humira	adalimumab	AbbVie	12,543	14,012	+12%	78,609
2	Rituxan/MabThera	rituximab	Roche	7,541	7,333	-3%	73,539
3	Avastin	bevacizumab	Roche	7,013	6,948	-1%	57,205
4	Herceptin	trastizumab	Roche	6,858	6,796	-1%	59,756
5	Remicade	infliximab	Johnson & Johnson	6,868	6,561	-4%	59,532
6	Gleevec/Glivec	imatinib	Novartis	4,746	4,658	-2%	46,612
7	Soliris	eculizumab	Alexion Pharma	2,234	2,590	+16%	9,546
8	Stelara	ustekinumab	Johnson & Johnson	2,072	2,474	+19%	8,206
9	Lucentis	ranibizumab	Novartis	2,441	2,060	-16%	15,395
10	Orencia	abatacept	Bristol-Myers Squibb	1,652	1,885	+14%	9,170
				76,635	**80,513**	**+5%**	**558,382**

Source: Company reports; Hardman & Co Life Sciences Research

Financials & Investment case

Share capital

£54m of capital raised to fund working capital of the business to date

Since incorporation, Avacta has issued shares to the value of £78.1m, which is split £53.7m of working capital required to enact its strategy and £24.4m issued directly to the vendors as consideration for acquisitions. The most relevant of these share issues are shown in the table below.

In January 2012 (announced December 2011), shares were issued for the acquisition of Aptuscan Ltd through which Avacta obtained all the intellectual property rights to Affimer technology which is now the main thrust of the business.

The two most recent capital increases have been to provide the necessary working capital to invest in Avacta's strategy to strategy to develop the Affimer technology and commercialise it in the research reagents space and to fund the investment in Affimers to discover lead candidates that could be developed as therapeutics. First, the company raised £10.55m gross fund in May 2014; and secondly, it raised a further £22.0m gross in July 2015. Therefore, the company is well funded for the next three years even in the absence of any partnership or licensing deals.

Solid institutional support...

...with 75% held by top 8 shareholders

Avacta has always had a solid institutional support. At inception, the technology transfer group, IP Group (IPO.L), took a significant holding in the group and has supported management through each of its fund raises. Consequently, it remains the largest shareholder with 25.1%.

The last two funding rounds have brought in more institutions, such that the top eight shareholders together own 75% of the issued share capital. Directors own 0.5% of the group and, together with senior managers, are incentivised by the share option scheme, currently 1.43m outstanding.

Relevant Avacta share issues

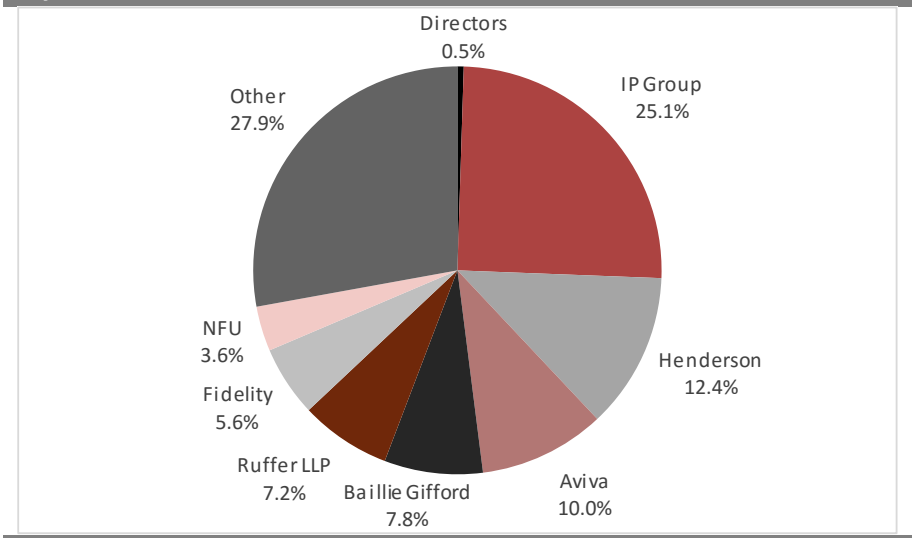
Comment	Date	Shares (m)	Price (p)	Raised (£m)	*Shares o/s (m)	Valuation (£m)
Placing	Aug-06	45.0	2.3	1.01	644.9	14.51
Placing at 2.5p per share	Apr-07	108.4	2.5	2.71	777.7	19.44
Issued for acquisition of Oxford Medical	Dec-07	22.0	5.0	1.10	800.4	40.02
Issued for acquisition of Oxford Medical	Mar-08	22.3	5.5	1.23	823.1	45.19
Issued for acquisition of Theragenetics	Jan-09	18.9	3.0	0.57	843.6	25.31
Issued for acquisition of Curidium Medica	Mar-09	274.7	2.3	6.18	1118.2	25.16
Issued for acquisition of Theragenetics	Jul-09	33.5	5.2	1.73	1151.8	59.43
Placing at 1.0p per share	Jul-10	143.4	1.0	1.43	1434.3	14.34
Placing at 1.05p	Jan-11	186.1	1.1	1.95	1633.2	17.15
Placing at 0.5p per share	Dec-11	1026.0	0.5	5.13	2693.6	23.75
Issued for acquisition of Aptuscan	Dec-11	228.0	0.7	1.48	2921.6	25.24
Joint share ownership plan	Dec-11	232.7	0.6	1.28	3156.8	26.53
Placing at 0.55p per share	Jul-13	855.1	0.6	4.70	4011.9	22.07
Placing at 1.125p per share	May-14	937.8	1.1	10.55	4967.6	55.89
Placing at 1.25p per share	Jul-15	1760.0	1.3	22.00	6739.4	84.25
Total	**Total**			**78.06**		

**On 25th January 2016, the company had a 100-for-1 share consolidation*
Source: Hardman & Co Research Life Sciences Research

100-for-1 share consolidation in January 2016

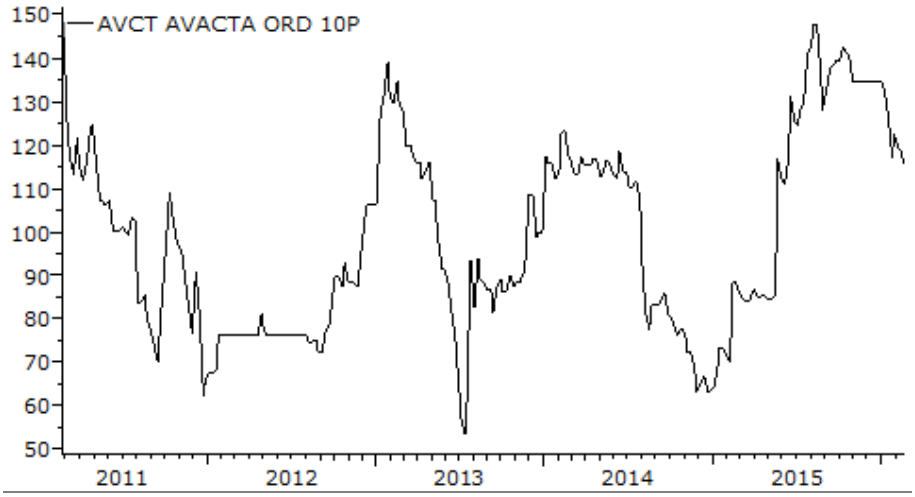
Subsequent to this, at its recent AGM, shareholders approved a resolution to consolidate 100 existing Ordinary shares of 0.1p each into 1 Ordinary share of 10p each and shares were quoted in the new form from 25th January 2016. At the time of going to press, there are 67.463million shares in issue and 1.426million options outstanding.

Key shareholders



Source: Company reports; RNS announcements

Share price performance



Source: Fidessa

Profit & Loss

The financial statements of Avacta are relatively straight forward and dominated by just three figures. First, the investment in R&D, which is capitalised, to generate Affimer products and therapeutic leads that could enter clinical trials. Secondly, the investment and on-going SG&A cost required to execute on the company's strategy. These, in turn, drive the cashflow which drive the third figure which is the net cash left in the balance sheet at the end of each financial year.

Sales

Over the forecast period, we envisage that Avacta Animal Health sales will grow broadly in line with inflation. Growth in group sales will be driven by increased Life Sciences revenues as the Affimer technology becomes even better understood and utilised. These sales will be largely in the form of custom Affimer sales with a small contribution from the reagent catalogue work. However, over this period, the Avacta story is not really about sales.

SG&A

Avacta has consistently added to the executive and senior management expertise over the last two years and this has continued again into fiscal 2016 with a new CFO and chief commercial officer. Such investment has been, and will continue to be, reflected in the SG&A line, which is the main driver of the P&L account after sales.

R&D

R&D is capitalised rather than being written-off in year incurred

R&D investment is capitalised and included in intangible assets in the balance sheet. We are forecasting rising expenditure between £3.0-5.0m each year from 2015-2018.

Profit & Loss account

Year end July (£m)	2013	2014	2015	2016E	2017E	2018E
Avacta Life Sciences	0.00	0.03	0.44	0.70	1.51	2.57
Avacta Animal Health	1.50	1.59	1.37	1.44	1.51	1.61
Sales	**2.70**	**3.18**	**1.81**	**2.15**	**3.02**	**4.17**
COGS	-1.19	-1.14	-0.53	-0.75	-1.00	-1.31
Gross Profit	**1.51**	**2.04**	**1.29**	**1.39**	**2.03**	**2.87**
Gross margin	**56%**	**64%**	**71%**	**65%**	**67%**	**69%**
SG&A	-3.25	-3.90	-4.20	-5.45	-6.60	-7.51
EBITDA	-1.74	-1.33	-2.34	-3.30	-3.81	-3.89
Depreciation & Amortisation	-0.09	-0.53	-0.58	-0.76	-0.76	-0.76
Licensing/Royalties	0.00	0.00	0.00	0.00	0.00	0.00
Underlying EBIT	**-1.83**	**-1.86**	**-2.91**	**-4.06**	**-4.57**	**-4.65**
Share based costs	-0.12	-0.21	-0.25	-0.30	-0.33	-0.36
Exceptional items	45.00	0.00	0.00	-2.41	0.00	0.00
Statutory EBIT	-1.87	-2.07	-5.57	-4.36	-4.90	-5.01
Net financial income	0.02	0.02	0.03	0.21	0.17	0.10
Underlying pre-tax profit	**-1.80**	**-1.83**	**-2.89**	**-3.85**	**-4.40**	**-4.55**
Reported pre-tax profit	-1.85	-2.04	-5.54	-4.15	-4.73	-4.91
Reported taxation	0.33	0.55	0.65	0.77	0.96	1.15
Tax rate	-18%	-27%	-12%	-18%	-20%	-23%
Underlying net income	**-1.47**	**-1.28**	**-2.24**	**-3.08**	**-3.44**	**-3.40**
Statutory net income	-1.52	-1.49	-4.89	-3.38	-3.77	-3.76
Period-end shares (m)	31.57	49.68	49.80	67.46	67.56	67.66
Weighted average shares (m)	31.57	41.82	49.73	65.90	67.46	67.56
Fully diluted shares (m)	31.57	31.57	42.85	51.16	67.33	68.89
Underlying Basic EPS (p)	**-4.67**	**-3.07**	**-4.50**	**-4.68**	**-5.11**	**-5.03**
U/l Fully-diluted EPS (p)	**-4.67**	**-2.99**	**-4.37**	**-4.58**	**-5.00**	**-4.92**
Statutory Basic EPS (p)	-4.82	-3.57	-9.84	-5.13	-5.59	-5.56
Stat. Fully-diluted EPS (p)	-4.82	-3.48	-9.56	-5.02	-5.48	-5.45
DPS (p)	0.00	0.00	0.00	0.00	0.00	0.00

Source: Hardman & Co Research Life Sciences Research

Upside potential on announcement of any licensing deals or partnerships

Licensing/milestone income

It can reasonably be expected that Avacta will sign some licensing and/or partnership deals during the forecast period. However, predicting the timing of such deals is notoriously difficult and our experience indicates that such income should not be included until such deals are announced. Obviously, the conclusion of any such deal would be positive for sentiment, cashflow and valuation.

R&D tax credits

Avacta undertakes R&D activities in the UK that qualify for tax credits from the UK government. As the company makes increased investment in R&D, so the tax credits, payable in arrears, will increase. The tax line is calculated on the basis that 20% of the R&D investment each year is accrued and received in cash during the course of the following year.

Balance sheet

- Avacta ended fiscal 2015 with £7.3m net cash, which was boosted immediately into the current financial year by the £22.0m (gross funds) Placing of shares
- R&D investment, shown in the cashflow statement, is capitalised and included under intangible assets in the balance sheet
- Based on current forecasts, Avacta has adequate cash resource for the next three years to identify Affimer therapeutic targets

Balance sheet

at 31st July (£m)	2013	2014	2015	2016E	2017E	2018E
Shareholders' funds	15.55	28.84	19.13	15.75	11.98	8.22
Cumulated goodwill	0.00	0.00	0.00	0.00	0.00	0.00
Total equity	15.55	28.84	19.13	15.75	11.98	8.22
Share capital	3.23	5.05	5.06	6.75	6.75	6.75
Reserves	12.32	23.79	14.08	9.00	5.23	1.47
Provisions/liabilities	0.47	0.82	0.86	0.86	0.86	0.86
Deferred tax	-0.29	-0.43	-1.07	-1.07	-1.07	-1.07
Long-term loans	0.00	0.00	0.00	0.00	0.00	0.00
Bank overdrafts	0.00	0.00	0.00	0.00	0.00	0.00
less: Cash & securities	0.58	11.48	7.33	21.00	12.61	3.42
less: Marketable securities	0.00	0.00	0.00	0.00	0.00	0.00
less: Non-core investments	0.00	0.00	0.00	0.00	0.00	0.00
Invested capital	**15.15**	**17.75**	**11.60**	**-5.45**	**-0.83**	**4.60**
Fixed assets	0.84	1.40	1.55	1.85	1.91	1.78
Intangible assets	14.58	16.29	10.36	14.19	18.97	24.70
Stocks	0.38	0.47	0.33	0.39	0.56	0.77
Trade debtors	0.63	0.47	0.21	0.21	0.21	0.21
Other debtors	0.35	0.51	0.55	0.60	0.84	1.16
Trade creditors	-0.07	-0.98	-0.66	-0.66	-0.66	-0.66
Tax liability	0.00	0.00	0.00	0.00	0.00	0.00
Other creditors	-1.56	-0.42	-0.74	-22.03	-22.66	-23.36
Debtors less creditors	-0.64	-0.41	-0.64	-21.88	-22.26	-22.65
Invested capital	**15.15**	**17.75**	**11.60**	**-5.45**	**-0.83**	**4.60**

Source: Hardman & Co Research Life Sciences Research

- Cap-ex in fiscal 2016 and 2017 will include ca.£1.5m of investment cap-ex as Avacta consolidates its two sites in Wetherby into a single larger premise and moves Stevenage into an expanded operation in Cambridge. Thereafter, cap-ex is expected to revert to maintenance levels
- In the event that Avacta identifies suitable therapeutic targets, increased R&D investment would be required depending how far down the clinical pathway the putative drug is taken. This could be in the form of licensing deals, collaborative partnerships and/or equity placing by the company

Cashflow

- The P&L account is largely driven by the investment in SG&A offset by any tax rebate on the R&D spend, which drops through to the cashflow statement
- Apart from the trading loss, the main driver in the cashflow statement is the investment in R&D which, unusually, is capitalised
- Cash resources were significantly boosted at the beginning of fiscal 2016 by the £22.0m capital increase, reduced to ca £21.0m by costs
- Based on our forecasts, Avacta has sufficient cash resource for its strategy for three years, even in the absence of any licensing income

Cashflow

Year end July (£m)	2013	2014	2015	2016E	2017E	2018E
Trading profit	-1.83	-1.86	-2.91	-4.06	-4.57	-4.65
Depreciation	0.28	0.36	0.52	0.70	0.70	0.70
Amortisation	0.09	0.17	0.06	0.06	0.06	0.06
Stocks	0.11	-0.09	-0.21	-0.06	-0.16	-0.21
Working capital	-0.62	0.14	0.25	0.22	0.18	0.16
Exceptionals/provisions	0.00	0.00	0.00	0.00	0.00	0.00
Disposals	0.04	0.00	0.03	0.00	0.00	0.00
Other	0.00	0.04	-0.29	0.00	0.00	0.00
Company op cashflow	**-1.92**	**-1.24**	**-2.55**	**-3.15**	**-3.79**	**-3.94**
Net interest	0.02	0.02	0.03	0.21	0.17	0.10
Tax	0.53	0.42	0.01	0.65	0.77	0.96
Operational cashflow	-1.38	-0.80	-2.52	-2.29	-2.86	-2.89
Capital Expenditure	-0.48	-0.92	-0.81	-1.01	-0.76	-0.57
Capitalised R&D	-1.76	-1.86	-3.06	-3.83	-4.78	-5.74
Sale of fixed assets	0.00	0.00	0.00	0.00	0.00	0.00
Free cashflow	**-3.61**	**-3.58**	**-6.38**	**-7.12**	**-8.39**	**-9.19**
Dividends	0.00	0.00	0.00	0.00	0.00	0.00
Acquisitions	0.00	-0.06	0.00	0.00	0.00	0.00
Disposals	0.00	0.00	2.21	0.00	0.00	0.00
Other investments	0.00	0.00	0.00	0.00	0.00	0.00
Cashflow after investments	**-3.61**	**-3.64**	**-4.17**	**-7.12**	**-8.39**	**-9.19**
Share repurchases	0.00	0.00	0.00	0.00	0.00	0.00
Share issues	0.00	14.54	0.02	20.79	0.00	0.00
Currency effect	0.00	0.00	0.00	0.00	0.00	0.00
Borrowings acquired	0.00	0.00	0.00	0.00	0.00	0.00
Change in net debt	**-3.61**	**10.90**	**-4.15**	**13.67**	**-8.39**	**-9.19**
Hardman FCF/share (p)	-4.4	-1.9	-5.1	-3.5	-4.2	-4.3
Opening net cash	4.19	0.58	11.48	7.33	21.00	12.61
Closing net cash	0.58	11.48	7.33	21.00	12.61	3.42

Source: Hardman & Co Research Life Sciences Research

Valuation

Discounted cashflow

The best approach to valuing biopharmaceutical companies is to prepare detailed discounted cashflow analyses of key products through to patent expiry and then to risk-adjust the NPV based upon industry standards for the probability of the product reaching the market. In the case of Avacta, while the real value is in therapeutic Affimers, these assets are at too early a stage to do a DCF valuation without far-reaching assumptions and exhaustive analysis of the market opportunities, penetration rates and potential milestones and royalty payments. Equally the probability of successfully reaching the market for pre-clinical assets is typically less than 1%.

Additionally, such analysis does not take into account the price that big pharma is willing to pay to gain access to breakthrough technologies and products, especially those assets that target markets of significant unmet medical need. Therefore, it is probably more relevant to look at recent transactions for similar stage assets.

Comparative valuation – M&A

Big pharma is willing to pay handsome prices for novel assets...

The Hardman Life Sciences Team published recently (Redx Pharma – Pipeline progress, 18th February 2016 available on www.hardmanandco.com[1]) a table of M&A activity which provided some indication of the value that big pharma and biotech put on novel assets even in early stages of preclinical development, including screening, discovery, lead optimisation, toxicology and IND enabling studies. Although the list is not exhaustive, it did analyse those transactions where financial terms were disclosed – there are many more deals where financial terms were not disclosed. We looked also at a number of transactions where the assets were already in clinical development to better illustrate the value inflection points on successful completion of pre-clinical phases and demonstration of safety in first-in-man studies.

The following is a summary of our findings:

- The median up-front license deal value of preclinical compounds in the Immuno-Oncology and oncology space is $17m per target compound with milestones of up to $357m
- A median deal value for Phase I assets of $40m

Molecular Partners shows the way

...exemplified by deals done by Molecular Partners

One of the best examples of licensing potential is the relationship between Molecular Partners and Allergan for its DARPin technology. In 2011, Molecular Partners licensed its lead asset, abicipar (MP0112), to Allergan when it had completed Phase I development for retinal diseases, for US$45m up-front and up to US$375m in milestones. Allergan has now progressed this DARPin-based product through to Phase III development for age-related macular degeneration. In 2012, Allergan expanded this relationship with two further agreements for the discovery, development and commercialisation of other DARPin-derived products, with further up-front payments of USD62.5m and potential success-based milestones and royalties up to $1.3bn.

[1] http://www.hardmanandco.com/docs/default-source/company-docs/redx-pharma--documents/redx-initiation-note---15-feb-2016

Also in 2011, Molecular Partners signed an agreement with Janssen Biotech (Johnson & Johnson) to develop immunotherapies based on DARPin technology. Molecular Partners received an upfront payment together with development and sales milestones of up to US$190m for each target.

Affibody partnerships

Affibody AB has also been active in out-licensing its Affibody and Albumod (efficacy enhancing) technologies. Being a private company the financial terms were not disclosed, but these deals demonstrate the attractiveness of new technology to the global industry.

Deals announced by Affibody AB

Date	Licensor	Technology	Up-front	Milestones	Royalties
24-Mar-09	Biovitrum AB	Inflammation & autoimmune targets			
5-Oct-10	Amylin	Albumod technology	✓	✓	✓
4-May-11	Algeta	2 x oncology targets	✓	✓	✓
6-Feb-12	GE Healthcare	Her2 specific PET imaging			
22-May-13	Daewoong Pharma	Albumod technology	✓	✓	
25-Jun-13	Daiichi Sankyo	Albumod technology – 1 x target	✓	✓	

Source: Affibody reports

Comparative valuation – Peer analysis

Additionally, we have constructed a table of comparable biopharmaceutical companies that are quoted on various stock exchanges. Given that there are over 100 companies worldwide involved with some form of antibody technology, this is clearly not comprehensive. Therefore, the table concentrates on a peer group that offers alternative technologies to antibodies, together with Abcam which is a useful UK peer. The share price used for the private company, Affibody Medical, is based on its last capital increase (2014) which might not be a true reflection of value if the company were to be listed today. However, the table shows clearly the potential for Avacta when it moves some of its assets into clinical development.

Comparative valuation

Company	Ablynx	Abcam	Affibody Medical	Avacta	Molecular Partners
	ABLX	**ABC**	**-**	**AVCT**	**MOLN**
	EUR	GBP	SEK	GBP	CHF
Share price	11.7	642	20.0	120	31.7
Shares in issue (m)	55.1	202.3	10.6	67.5	19.6
Market cap (lc)	641.9	1,298.9	211.6	81.0	621.3
Mkt cap (£m)	498.8	1,298.9	17.4	81.0	437.2
Cash	266.8	50.0	21.5	25.3	215.4
Debt	-105.7	0.0	0.0	0.0	0.0
EV (lc)	480.8	1,248.9	190.1	55.6	405.9
EV (£m)	**373.6**	**1,248.9**	**15.7**	**55.6**	**285.7**
2015 Sales	49.3	135.4	60.0	3.0	29.1
EV/sales	9.8	9.2	3.2	18.4	13.9
Stage of development	Phases I/II/III	-	-	Pre-clinical	Phase II/III
Licensing deals	>10	-	6	4	1/2

Prices/Currencies taken at close of business on 22nd February 2016
Source: Company reports; Hardman and Co Life Sciences Research

Company matters

Registration

Incorporated in the UK with company registration number: 04748597

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Board of Directors

Board of Directors			
Position	**Name**	**Remuneration**	**Audit**
Chairman	Trevor Nicholls	C	M
Chief Executive Officer	Alastair Smith		
Chief Financial Officer	Tony Gardiner		
Chief Operating Officer	Craig Slater		
Non-executive director	Michael Albin	M	M
Non-executive director	Alan Aubrey	M	C
Non-executive director	Mike Owen	M	

M = member; C = chair
Source: Company reports

The Nominations committee is convened on an 'as required' basis and chaired by the Chairman.

Dr Trevor Nicholls – Non-executive Chairman

Dr Nicholls has over 30 years of commercial experience building international businesses in the life sciences sector. He is currently Chief Executive Officer of the not-for-profit CAB International, an inter-governmental organisation owned by 47 member countries whose mission is to improve lives worldwide by providing information and applying scientific expertise to solve problems in agriculture and the environment. He is also Non-Executive Chairman of Activiomics Ltd, a UK biomarker discovery and drug profiling services business and was founder and CEO of Oxagen, a UK biotech company. Trevor brings great experience in commercial and corporate strategy, international sales & marketing and building life sciences businesses.

Dr Alastair Smith – Chief Executive Officer

Alastair has been Chief Executive of Avacta since its inception in 2005 and has been responsible for the management and strategic development of the company, led the IPO and the fund raising and M&A activities of the Group, and has overseen the product development programmes. He 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 a Chair of Molecular Biophysics and had, over ten years, grown one of the leading biophysics research groups in Europe. He left his academic career in 2007 to focus full time on delivering value to Avacta shareholders.

Tony Gardiner – Chief Financial Officer

Tony joined Avacta from AHR, an international architecture and building consultancy practice, where he has been Finance Director since 2011. Between 2007 and 2011, Tony was CFO of AIM listed Fusion IP plc, an IP commercialisation company, which was acquired by IP Group plc in 2014. There, he played a key role in supporting the Chief Executive Officer in growing the business and oversaw all finance activities as well as directly supporting life sciences and health technology companies in Fusion's portfolio. Tony has also held senior finance roles within Eversheds LLP, KCOM Group Plc, Eldon Electric Ltd and Hickson International Plc.

Craig Slater – Chief Operating Officer

Craig has more than 25 years' experience of commercial, operational and group management roles in manufacturing, construction, software and marketing groups. This experience is combined with strong finance and planning skills gained initially with Arthur Andersen and the completion of many corporate transactions including two IPOs, one delisting, a demerger and numerous acquisitions and disposals. Craig has worked with Avacta since June 2012 as Chief Operating Officer responsible for the commercial and operational development of the Group.

Dr Michael Albin – Non-Executive Director

Michael has over 30 years' experience in the development and commercialisation of technologies for the life sciences. With a Ph.D. in chemistry from Pennsylvania State University and postdoctoral research at the California Institute of Technology, Michael worked at SYVA diagnostics followed by 15 years at Applied Biosystems Inc rising to VP of Science & Technology, and then VP of Strategic Technologies of the parent company Applera Corp, an S&P 500 company. In recent years Michael has worked as a private consultant focusing on technical and strategic assessments and the positioning of a wide range of companies in the life sciences, molecular diagnostics, and personalised medicine sectors – areas of direct relevance to Avacta.

Alan Aubrey – Non-Executive Director

Alan was joint founder and CEO of Techtran Group Limited, the first company in Europe to offer a complete outsourced technology transfer function to universities. Techtran was acquired by IP Group in 2005. Alan is also Non-Executive Chairman of Proactis, an AIM-listed software company, and Energetix Group plc. From 1995-2002 Alan was a partner in KPMG where he specialised in providing advice to fast growing technology businesses. Alan holds a BA in Economics from the University of Leeds and an MBA from the University of Bradford. He is a fellow of the Institute of Chartered Accountants of England and Wales. Alan is also a member of the Department for Business, Innovation & Skills (BIS) Audit and Risk Committee.

Dr Mike Owen – Non-Executive Director

Dr Owen was SVP and Head of Research of GlaxoSmithKline's Biopharmaceuticals R&D Unit where, over a 10 year period, he was responsible for initiating and rapidly growing GSK's pre-clinical and clinical therapeutic antibody pipeline through in-house development and through acquisitions, such as Domantis. He left GSK in 2010 to establish Kymab which is developing biotherapeutics using its novel transgenic mouse platform. Dr Owen is an immunologist by training who had a highly successful scientific career at Imperial Cancer Research during which he was elected a member of the European Molecular Biology Organisation and a fellow of the Academy of Medical Sciences. Dr Owen is also an independent board member at Zealand Pharma and non-executive director of Ossianix Inc. and Blink Therapeutics. He sits on the scientific advisory board of Kymab and also advises the private equity CRT Pioneer Fund and HS Life Sciences.

Senior management team

As Avacta has grown and the Affimer technology has become a more important part of group strategy, so the senior management team has been strengthened.

Senior management team	
Name	**Position**
Amrik Basran	Chief Scientific Officer
Philippe Cotrel	Chief Commercial Officer
Matt Johnson	Chief Technology Officer

Source: Company reports

Dr Amrik Basran – Chief Scientific Officer

Dr Amrik Basran has over 10 years' experience of both the biotech and pharma industries. Before joining Avacta Life Sciences, he worked for GSK where he was Head of Topical Delivery (Biopharm Discovery Unit), supporting the development of biotherapeutics across the GSK portfolio. Amrik was Director of Protein Biosciences at Domantis, before the company was acquired by GSK in 2006 and prior to this had spent 6 years as a post-doctoral researcher at the Institute of Biotechnology, Cambridge University.

Dr Philippe Cotrel – Chief Commercial Officer

Dr Cotrel, a protein chemist by training, has over 20 years' commercial experience in sales, marketing and customer support in the life sciences sector having held senior positions in Amersham Pharmacia Biotech, Oxford Glycosciences, Affymetrix and Abcam. Whilst at Affymetrix, at that time the inventor and market leader of commercial microarrays, Philippe was appointed General Manager and Vice President of Commercial Operations in Europe with responsibility for European commercial operations, generating approximately £65m in sales made up of capital equipment, consumables and services. Philippe joined Abcam in 2008 as Commercial Director and has been responsible for significantly building up sales and marketing activities. He managed regional offices in Boston, Tokyo, Hong Kong and Shanghai, as well as business development activities for the custom service and *in-vitro* diagnostics divisions. Philippe joined Avacta from Abcam, where he held the role of Commercial Operations Director. Philippe leads the Group's commercial strategy and business development activities, and drives the commercialisation of Affimer technology, as both research reagents and biotherapeutics.

Matt Johnson – Chief Technology Officer

Matt studied Genetics & Microbiology at the University of Sheffield and stayed on to complete a PhD in Molecular Biology with Dr Anne Moir investigating novel surface proteins of the *B.cereus* endospore. As part of his PhD, he completed an EMBO fellowship at the Pasteur Institute with Dr Michele Mock looking at the same proteins in *B.anthracis*, the causative agent of anthrax. Matt undertook post-doctoral work in the Department of Biochemistry at Cambridge University with Professor George Salmond. Matt joined Abcam in 2005 as a development scientist producing and characterising antibodies through which the company grew to become the leading provider of research-grade antibodies in life sciences. Over 8 years and several roles he became Head of R&D, giving him a wealth of experience over a number of functions. As Head of R&D, he built and ran a research group with interests in recombinant antibody/binder technologies, alternative detection methodologies, immunoassay development and antibody characterisation. His other responsibilities included contributing to M&A strategy, licensing deals and technology scouting. To support this, he completed a Postgraduate Certificate in Intellectual Property Law at the University of Bournemouth in 2012.

Facilities

Avacta currently operates from two main sites. The HQ and laboratory facilities are centred in two buildings in Wetherby, where the Animal Health business and Affimer development work is performed. A second site is based at the Stevenage Bioscience Catalyst (www.stevenagecatalyst.com), which undertakes Affimer therapeutic development work. However, during fiscal 2016 and 2017, Avacta is investing in improved and larger facilities. The two sites in Wetherby are being consolidated into one larger site on the same Thorp Arch Industrial Estate. The new leased facility is currently being refitted and is expected to become fully functional and validated during the first three months of the 2017 financial year.

In addition, Avacta is moving its Life Sciences team from Stevenage to a new facility just outside Cambridge. This is also being kitted out and is expected to become fully operational by the middle of 2016. The overall investment in the new facilities is expected to be around £1.5m which will be split over two financial years, with the majority of the spend occurring in fiscal 2016.

Risks

General

Investments in small early stage companies carry a significant risk and investors must be aware of this fact. In our opinion, the following risks are particularly relevant. Each of them could have an impact on time to reach market, cash flow breakeven and profitability.

Intellectual property

Given that Affimer technology was first described in 2005 and there have not been challenges to the patents, the IP around this technology appears secure and Avacta has an ongoing strategy of further developing the core Affimer technology to expand continually its IP coverage. Moving forward, as the Affimer technology paves the way for the identification of specific therapeutic leads, each will need to be patented in order to protect the commercial rights to the putative drug. This will result in increased on-going costs. Should any patent be challenged for whatever reason, litigation costs are expensive and an unwanted distraction of management time.

Competition

Although Avacta has a unique position in Affimer technology, it does compete against antibody technology, which is more developed, much larger and commercially successful. Therefore, the company operates in markets dominated by large competitors, many of which have greater financial resources to fund development programmes, regulatory affairs and commercial activities.

Licensing agreements/partnerships

Avacta has already entered into agreements with third parties and its strategy is to enter into further arrangements for the development, production and commercialisation of its products. There is no guarantee that further deals can be signed in a timely manner which could influence the time to profitability and the cash balance of the group.

Regulatory

Development of a therapeutic lead through clinical trials requires different skills and close liaison with regulatory bodies in key markets. Avacta may need to invest in senior personnel that provide new skillsets, with the consequential increase in costs.

Dilution risk

In the event that Avacta identifies a good therapeutic lead that management decides to develop further through clinical trials by itself to maximise value for shareholders, it will most likely require additional capital to fund the increased R&D investment. This could be in the form of a Placing of shares which could be dilutive to existing shareholders if there is not an associated Open offer on a pro-rata basis.

Share liquidity

The last two share placings have increased significantly the number of shares in issue and the share liquidity. However, with 75% of the issued share capital tightly held by the top eight institutional shareholders there is limited daily volume. This is consistent with many small capitalisation companies listed on AIM, making it difficult to buy or sell shares in volume.

Glossary

ADC	Antibody-drug conjugates
Bi-specifics	Artificial protein composed of fragments from two different antibodies or affimers
DARPins	Design Ankyrin Repeated Proteins
Fc-fusions	Coagulation Factor IX protein involved in control and prevention of bleeding
OEM	Original equipment manufacturer
UPP/UPS	Ubiquitin proteasome pathway/system

The following websites have been visited regularly during the writing of this report:

www.abcamplc.com

www.affibody.com

www.antibodysociety.org

www.avacta.com

https://biopharmadealmakers.nature.com

www.cellculturedish.com

www.fda.gov

www.molecular partners.com

Notes

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