

Market data	
EPIC/TKR	AVCT
Price (p)	34.0
12m High (p)	98.0
12m Low (p)	28.0
Shares (m)	69.0
Mkt Cap (£m)	23.5
EV (£m)	15.2
Free Float*	60%
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. It benefits from near-term revenues from research and diagnostic reagents.

Company information

CEO Alastair Smith
 CFO Tony Gardiner
 Chairman Trevor Nicholls

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Key shareholders

Directors	6.1%
IP Group	24.8%
Lombard Odier	10.8%
Aviva	9.6%
Ruffer LLP	7.1%
JO Hambro	6.7%

Diary

Oct-18	Finals
Jan-19	AGM
1H'19	PD-L1/LAG-3 drug candidate selection

Analysts

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Avacta

In vivo expression of Affimers

Avacta (AVCT) is a pre-clinical biotechnology company and the proprietary owner of Affimer technology. Affimers represent a radical alternative to the established antibody technology, which continues to dominate the drug industry, despite its limitations. The significant technical and commercial benefits of Affimers is being recognised though increased corporate interest, on-going evaluations, and deal flow. The successful research collaboration with Fit Biotech provides evidence for the feasibility of using Affimer gene delivery *in vivo*. This represents an additional opportunity for Avacta to develop and partner Affimers as therapeutics.

- ▶ **Strategy:** AVCT is aiming to commercialise its Affimer technology through bespoke research tools, collaborative deals and by identifying and developing its own proprietary therapeutic leads. AVCT has sufficient cash resources to identify an Affimer lead to be ready for first-in-man trials in 2019.
- ▶ **FIT collaboration:** AVCT, together with its research collaborator, FIT Biotech, has completed successfully a proof-of-concept study showing that a single dose of Affimer DNA leads to clinically relevant levels of Affimer drug in mice. This opens up new opportunities for Affimer therapeutics.
- ▶ **Relevance:** In addition to being a major technical advance, the experiment reflects the versatility of the Affimer platform. A better expression of the Affimer was observed for up to a month following a single injection, with a significantly higher level compared to the antibody control.
- ▶ **Risks:** Affimers represent a new disruptive technology and the potential customer base might take time to recognise their advantages. While all new drug development carries a high risk, Avacta has hit a number of important milestones over the last two years which have reduced the risk profile.
- ▶ **Investment summary:** AVCT has made considerable progress towards its goal of having its own proprietary Affimer-based drugs and growing a profitable reagents business. By itself, the company has identified potential leads and completed both *in vitro* and *in vivo* pharmacokinetic pre-clinical, efficacy and immunogenicity tests. Awareness of the potential of Affimers is also being enhanced through the rising number of collaborative deals being signed.

Financial summary and valuation						
Year-end July (£m)	2014	2015	2016	2017E	2018E	2019E
Sales	1.81	2.17	2.74	3.15	3.60	5.49
R&D spend	-0.03	-1.50	-2.60	-3.40	-4.50	-5.50
EBITDA	-2.28	-4.79	-6.66	-8.13	-9.40	-9.25
Underlying EBIT	-2.85	-5.39	-7.60	-9.20	-10.47	-10.32
Reported EBIT	-5.51	-5.66	-7.98	-9.62	-10.94	-10.83
Underlying PBT	-2.83	-5.29	-7.51	-9.15	-10.48	-10.37
Statutory PBT	-5.48	-5.57	-7.89	-9.58	-10.94	-10.89
Underlying EPS (p)	-4.38	-6.46	-8.75	-11.74	-13.07	-12.55
Statutory EPS (p)	-9.72	-6.86	-9.31	-12.36	-13.74	-13.30
Net (debt)/cash	7.33	19.52	13.17	4.31	-6.22	-16.29
Capital increases	0.02	21.05	0.01	0.06	0.00	0.00
EV/sales (x)	17.7	14.8	11.7	10.2	8.9	5.8

Source: Hardman & Co Life Sciences Research

In vivo Affimer delivery & expression

Research collaboration with FIT Biotech

Back in October 2017, Avacta and the Finnish gene delivery specialist FIT Biotech Oy [FITBIO:HEX] entered into a research collaboration to assess the effectiveness of developing gene delivery using the Affimer technology and the gtGTU platform. FIT Biotech's gtGTU (Gene Transport Unit) vector was developed for gene delivery applications to ensure stable and prolonged expression of DNA-based therapeutics in a safe manner. The vector thus removes the requirement for frequent administration of protein therapeutics, which have limited half-life in the body.

The high degree of interest in the Affimer platform for gene delivery lies in its easy expression by cells given that they have a small size and simple structure compared with antibodies. It means that a clinically-relevant dose is more easily achieved.

The proof-of-concept study

The *in vivo* study was carried out in a mouse model and consisted of the injection of the DNA of two different Affimers into leg muscle tissue. The amount of Affimer produced in the muscle and entering the blood system was monitored over time. Key observations were made showing:

- ▶ The GTU platform delivered the genetic code of the Affimers into the host cells.
- ▶ An animal can be effectively dosed with an Affimer by gene delivery.
- ▶ No safety and tolerability concerns were observed during the experiment.
- ▶ Clinically relevant levels of Affimer drug in the bloodstream of mice for over one month following injection.
- ▶ Results were obtained following a single dose only of Affimer DNA into the leg muscle tissue.
- ▶ Due to the simple structure of the Affimer, the study showed significantly higher levels of Affimer production (between three and 12 times) when compared to an antibody used as a control in the study.

This approach will allow less frequent dosing because of the sustained production of the therapeutic by the patient's body. This should result in greatly improved patient compliance. In some cases, for example if the DNA of the Affimer is injected directly into a tumour, this may lead potentially to better efficacy. From a manufacturing point of view, the substantially lower cost of goods (DNA rather than protein) would be a significant commercial benefit.

Importance for Avacta

This study demonstrated for the first time the expression of an Affimer directly *in vivo* from the cell host. In addition to being a major technical advance, the experiment represents confirmation for another potential use of the Affimer technology in the therapeutic area. Avacta is looking currently at its options for potential patent protection of the technology further in the field of gene delivery. In addition of FIT Biotech, Avacta has currently additional research collaborations with other gene delivery specialist companies:

- ▶ **Moderna:** During 2015, Avacta announced a significant research partnership with Moderna Therapeutics (Cambridge, MA) to provide a range of Affimers against a number of selected targets for messenger RNA therapeutics. Several Affimers are currently in lead characterisation phase. The next step is for

Moderna to take a lead Affimer into its development programmes. The first milestone payment is due upon dosing of the first patient in a proof-of-concept Phase I trial, which is out of the hands of Avacta.

- ▶ **OncoSec Medical:** In January 2018, Avacta has signed a collaboration agreement with OncoSec Medical to investigate the use of ImmunoPulse – OncoSec’s gene delivery technology – as a means of injecting Affimers directly into tumours. The tumour then produces clinically-relevant doses of the Affimer drug highly targeted in the tumour microenvironment. Proof-of-concept data are expected in 1Q’19.

With the success of the research collaboration confirming Affimer expression *in vivo*, Avacta is considering its options to further explore the opportunities and take this forward collaboratively, and with a larger partner.

FIT Biotech and the GTU technology

Gene delivery

The gene delivery technology is the process of introducing a foreign genetic material (DNA or RNA) into a host cell with the aim of inducing the “gene expression” to make the protein therapeutic. The main challenge with the technology is to be able to stabilise the vector so that it is able to enter and transfer the genetic material to the host cell, allowing the potential production of the protein to occur.

FIT Biotech GTU technology

FIT Biotech (FIT) is a Finnish biotech company established in 1995 that develops and licenses its proprietary GTU vector technology. It is a non-viral platform with a DNA plasmid that encodes for a E2 protein system. The characteristics of the E2 protein allow the plasmid to be anchored to the cellular structure, without being integrated to the genome. This allows a smooth distribution during cell division and not to alter the genetic information of the host cell.

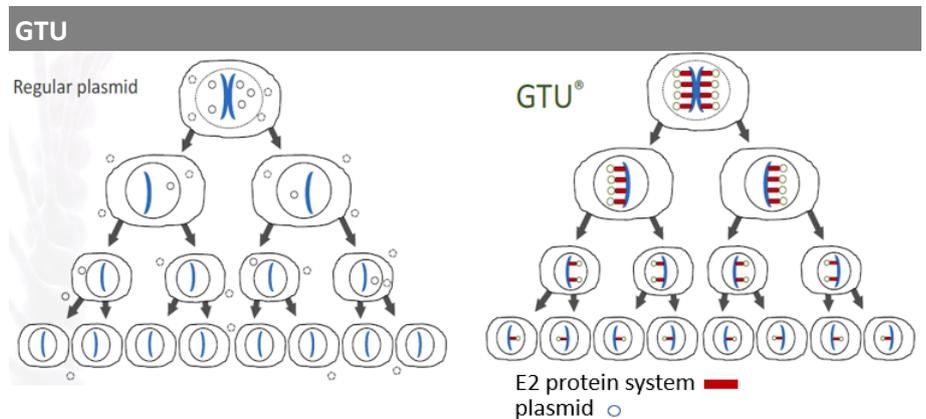
The gtGTU technology used in the expression of Affimers is an improvement of the GTU, designed to increase the expression level and duration of the gene-based medicines. The research collaboration with Avacta represents, for FIT, a validation of the technology by expressing protein other than antibodies.

Logo



FIT BIOTECH

Source: FIT Biotech



Source: adapted from Fit Biotech

FIT is part of a consortium of global institutes that are developing an HIV vaccine based on the GTU platform, currently in Phase I/IIa. Additionally, FIT has a portfolio of programmes in cancer and infectious diseases (in research & pre-clinical stages). The GTU vector been has shown to be safe, well tolerated, and did not create any immunogenicity issues in humans.

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The fact that we are commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

The full detail is on page 26 of the full directive, which can be accessed here: <http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf>

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