Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	AVCT
Price (p)	43.0
12m High (p)	64.4
12m Low (p)	21.0
Shares (m)	115.5
Mkt Cap (£m)	49.6
EV (£m)	34.6
Free Float*	78%
Market	AIM

**As defined by AIM Rule 26*

Description

Avacta (AVCT) 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	Eliot Forster
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	www.avacta.com

Key shareholders

Directors	3.9%
IP Group	18.2%
Baillie Gifford	8.5%
JO Hambro	7.5%
Carlton Int. Holding	7.3%
Fidelity	5.9%

Diary

14 Feb	AVCT science day
9 Apr	Interim results
1H'19	PD-L1/LAG-3 drug candidate selection

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AVACTA

A second wake-up call for the market

Avacta (AVCT) is a pre-clinical stage biotechnology company and the proprietary owner of Affimer technology. Affimers represent a radical alternative to the established antibody technology. The significant technical and commercial benefits of Affimers are being increasingly recognised, evidenced by corporate and academic interests, ongoing evaluations and deal flow. AVCT has just announced that, following a review period, Moderna has exercised its option to enter into an exclusive licensing agreement to further develop certain Affimer therapeutics for undisclosed targets. This is the second licensing deal with a major pharma player in the past few months.

- **Strategy:** AVCT is aiming to commercialise its Affimer technology through licensing for research and diagnostics, and by identifying and developing its own proprietary therapeutic pipeline for partnering. AVCT has sufficient cash resources to identify an Affimer lead and be ready for first-in-man trials in 2020.

- **Licensing deal:** Following the deal with LG Chem last December for a total value of up to $310m, Moderna has now exercised its option to develop certain Affimers against an undisclosed target. The financial terms have not been disclosed, but we expect AVCT to receive near-term development milestones.

- **Moderna:** Following its recent IPO in December 2018, which valued the company at $7.5bn, Moderna is a strong partner in the emerging field of therapeutic mRNA. With 11 compounds in clinical development, it represents a valuable partner that further supports and validates the Affimer platform.

- **Risks:** Affimers represent a new disruptive technology, and the potential customer base has taken some time to recognise their advantages. While all new drug development carries a high risk, AVCT has hit a number of important milestones over the last two years, greatly reducing the risk profile.

- **Investment summary:** AVCT has made considerable progress towards its goal of having a number of commercial partnerships for its Affimer technology, as well as developing its own proprietary Affimer-based drugs and growing a separate, profitable reagents business. The rising number of collaboration deals being discussed and signed is clear indication of the long-term value of its Affimer technology, which the market is currently only just beginning to recognise.

Financial summary and valuation

Year-end Jul* (£m)	2016	2017	2018	2019E	2020E	2021E
Sales	2.17	2.74	2.76	3.17	4.69	8.60
R&D spend	-1.50	-2.60	-3.78	-4.50	-5.50	-6.50
EBITDA	-4.79	-6.66	-9.15	-8.88	-8.72	-7.00
Underlying EBIT	-5.39	-7.60	-10.12	-9.85	-9.69	-7.97
Reported EBIT	-5.66	-7.98	-10.43	-10.19	-10.07	-8.38
Underlying PBT	-5.29	-7.51	-10.08	-9.82	-9.67	-7.99
Statutory PBT	-5.57	-7.89	-10.39	-10.16	-10.05	-8.40
Underlying EPS (p)	-6.46	-8.75	-13.07	-7.42	-7.12	-5.48
Statutory EPS (p)	-6.86	-9.31	-13.55	-7.72	-7.44	-5.83
Net (debt)/cash	19.52	13.17	5.22	7.75	-0.74	-7.32
Capital increase	21.05	0.01	0.05	10.92	0.00	0.00
EV/sales (x)	10.4	8.3	8.2	7.1	4.8	2.6

**AVCT has announced its intention to change its reporting date to December*

Source: Hardman & Co Life Sciences Research

Moderna exercises its option

Summary

In May 2015, AVCT announced a significant research partnership with Moderna Therapeutics (NASDAQ: MRNA) to provide a range of Affimers against a number of selected targets for messenger RNA (mRNA) therapeutics. At that point in time, the deal was of great significance for AVCT, as it was the first to be signed, and it represented a significant endorsement that AVCT had generated sufficient early proof-of-concept data to support its claims regarding Affimers and to attract a reputable drug developer. The deal with Moderna allowed AVCT to go back to the market, and it raised £21m to initiate its in-house therapeutic programme. AVCT has delivered the Affimer targets sought by Moderna and, following a period of review, Moderna has decided to exercise its option to enter into an exclusive licensing agreement for selected therapeutic Affimer candidates for clinical development as mRNA therapeutics, against a single potential therapeutic target. We expect AVCT to gain back the right of data generated against the other therapeutic targets, which could be used as commercial asset to forge future partnerships.

Moderna exercises its option to enter into an exclusive licensing agreement for selected therapeutic Affimer candidates for clinical development

This is the second full licensing deal with a major pharma/biotech to be announced by AVCT over the last two months. More are likely to follow as companies complete their validation work with the Affimer platform.

Terms of original agreement

No financial details have been provided yet

The collaboration, licensing and commercial agreement signed with Moderna in 2015 had all the components of a traditional pharma deal but was effectively separated into two parts by an option arrangement.

- Upfront: A payment of $500k on signing the original deal in 2015, together with undisclosed preclinical development milestones.
- Option: An option to enter into exclusive licensing agreements for clinical development of selected therapeutic Affimer candidates.

Other key features of the collaboration were:

- Clinical milestones: Milestone payments based on clinical development progress. It is believed that the total value of these payments could reach several tens of millions of dollars.
- Royalties: A small percentage of the net sales achieved by any drugs derived from the Affimer technology.

Following an initial two-year validation period, Moderna exercised its right to expand the agreement to include some additional targets. Although this should have resulted in further payments by Moderna, we believe that AVCT took the opportunity, instead, to adjust the original terms slightly.

Therefore, although the announcement does not provide financial details, the logical conclusion is that AVCT will not be receiving a further payment from Moderna at this point, but is likely to receive a milestone payment in the near future when an Affimer-derived product enters clinical trials.

Moderna Therapeutics

Moderna set the record for the biggest biotech IPO ever, valuing the company at $7.5bn

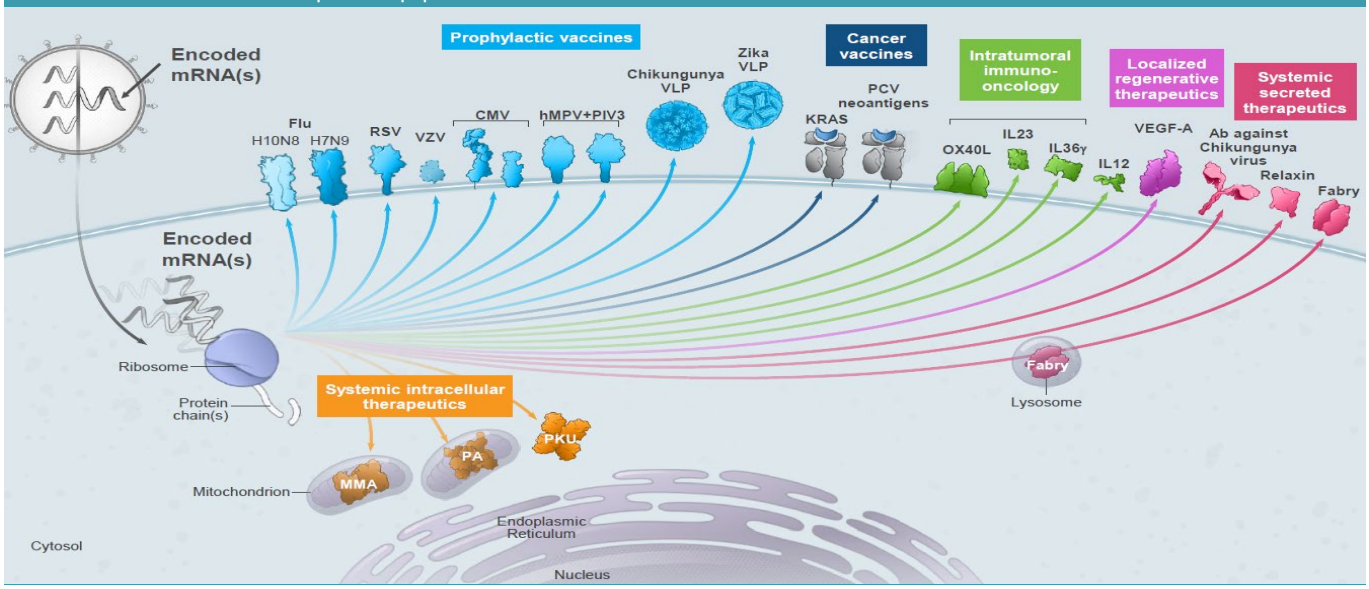
Until recently, it has been difficult to track the progress being made by Moderna, largely because it was a private and secretive company. However, in December 2018, the company hit the headlines when it set the record for the biggest biotech IPO ever, raising over $600m and valuing the company at around $7.5bn. The company also has$1.7bn in cash, cash equivalent and investments in marketable securities. Moderna is a pioneer of a new class of drugs based on mRNA, the '*software of life*', with potential in a variety of disease conditions.

Moderna is the pioneer of a new class of drugs based on mRNA, with a programme already in Phase II trial

Moderna has a development pipeline of 22 programmes, with 11 currently in the clinic; two have open Investigational New Drug (IND) submissions and one is IND-filed. Nine of those in the clinic are in Phase I and one is in Phase II (planning is under way for three additional Phase II studies). The programmes are split into six main modalities:

- prophylactic vaccines (nine programmes, six in Phase I);
- cancer vaccines (two programmes, one in Phase I);
- intra-tumoral immuno-oncology (four programmes, three in Phase I);
- localised regenerative therapeutics (one programme, in Phase II);
- systemic secreted therapeutics (three programmes); and
- systemic intracellular (three programmes).

Moderna – current development pipeline



Source: Moderna Therapeutics, corporate presentation

mRNA therapeutics

mRNA as a potential new class of medicines

mRNA therapeutic is a new approach in drug discovery that could prompt the body to make proteins, with potentials in many disease conditions

Used by all living cells in the process of translating genes in the DNA to proteins, mRNA technology is one of the new approaches in development in drug discovery. Moderna is leading the field and is building on the promise that the technology can be turned into a powerful treatment for genetic diseases, cancer, infectious diseases and others. In theory, the technology could prompt proteins to be made in the body, effectively implanting the drug factory within the body. mRNA therapeutics are currently in a multitude of clinical trials, and have so far proven to be safe and well tolerated. Other biotech companies working in the field include TranslateBio, Vertex and BioNTech, with many backed by big pharma companies.

In a nutshell, the DNA is a succession of gene sequences encoding proteins. When a gene sequence is expressed, its information is transferred to an mRNA molecule inside the cell nucleus by a process called transcription. The resulting mRNA is a single-stranded copy of the gene that moves outside the nucleus, which is next translated into a protein molecule. Moderna, with its platform, is bypassing the DNA transcription process, and the mRNA therapeutic will translate into an Affimer molecule inside the cell.

DNA vs. mRNA

Source: adapted from Translate Bio

Unlike DNA-based therapies, mRNA technology acts only during the period of treatment

The mRNA therapy is similar to DNA-based gene therapies, as both can produce therapeutic proteins within the body, but, while DNA's effect is normally permanent, the mRNA technology offers a temporary fix, which would alleviate some of long-term safety concerns surrounding gene therapy, as the drug would act only during the period of treatment. mRNA therapy has potential advantages, with broad application in multiple diseases, including:

- restoration of gene expression without entering the cell nucleus or changing the genome;
- enabling the treatment of diseases that were previously undruggable by using the cell's own machinery to produce natural and fully-functional proteins;
- drug-like properties that are familiar to healthcare providers, including the potential to repeat and adjust dosing in a chronic setting; and
- permits rapid development from target gene selection to product candidate.

Fit Biotech partnership

With respect to AVCT, it is worth noting that the collaboration with FIT Biotech confirmed the delivery and expression of clinically relevant levels of Affimer protein through the FIT's gtGTU platform. Results showed significantly higher levels of Affimer production when compared with an antibody used as a control in the study, and this was observed following a single dose only of Affimer DNA. (See our note '*In vivo expression of Affimer*', 31 May 2018).

Comparative valuation

One of the best ways to look at the value of the Affimer platform is to examine the different types of financial transactions in the area of antibody mimetics. The following table enumerates licensing deals in this space by three major competitors. It highlights that upfront payments are in line with general industry rates for products that have not yet reached the clinic, and also that partners are interested in utilising platforms by including options for additional products, bringing potential milestone payments above the $1bn threshold. Upfront and potential milestone payments are dependent on the type and number of projects involved, market potential and the number of reagents concerned.

Key M&As and licensing deals

Licensee	Licensor	Date	Upfront	Further payments	Comments
Pieris Pharmaceuticals	Seattle Genetics	9 Feb 2018	$30m upfront	Up to $1.2bn in milestone payments	Up to 3 programmes, low double-digit royalties
Pieris Pharmaceuticals	AstraZeneca	3 May 2017	$45m upfront + $12.5m when Phase I begins	$2.1bn in milestone payments	To progress PRS-060 with potential in asthma and four additional products
Pieris Pharmaceuticals	Servier	5 Jan 2017	$31.3m upfront	$338m in success-based payment for PRS-332 + 3 to 8 additional programmes for $201m in success-based payments	Double-digit royalties, PRS-332 is a dual checkpoint inhibitor
Pieris Pharmaceuticals	Aska Pharmaceuticals	27 Feb 2017	$2.75m upfront	Up to $80m	For PRS-080 (Phase Ib/IIa), inhibitor of hepcidin
Pieris Pharmaceuticals	Roche	8 Dec 2015	$6.4m upfront	Up to $409.3m in milestone payments	Undisclosed target, mid-single to low double-digit royalties
Pieris Pharmaceuticals	Daiichi Sankyo	12 Apr 2011	$7m upfront	Up to $200m	Two programmes, mid to high single-digit royalties
Pieris Pharmaceuticals	Takeda	10 Jan 2011	Undisclosed	Undisclosed	One programme
Pieris Pharmaceuticals	Sanofi	28 Sep 2010	€3.5m	€34.5m of milestone payments per target	Initially two targets and option for four additional targets
Pieris Pharmaceuticals	Allergan	15 Sep 2009	$10m upfront	Undisclosed	For the treatment of serious ocular disorders
Molecular Partner	Amgen	19 Dec 2018	$50m upfront	Up to $497m in milestone payments	For a preclinical molecule (MP0310) for immuno-stimulation
Molecular Partner	Roche	4 Dec 2013 (disc: 24 Jul 2015)	CHF55m upfront	CHF1bn in milestone payments	Deal on several programmes, double-digit royalties, deal discontinued due to Roche's toxin
Molecular Partner	Allergan	21 Aug 2012	$62.5m upfront	Up to $1.4bn in milestone payments	Two programmes and three options (exercised) for serious ophthalmic disease, low double-digit royalties
Molecular Partner	Janssen	8 Dec 2011	Undisclosed	Up to $200m per options	Four option agreements for the treatment of immunological disease, double-digit royalties, discontinued
Molecular Partners	Allergan	4 May 2011	$45m	Up to $375m	Licence agreement for MP0112 (Phase II) targeting VEGF for the treatment of retinal disease
Molecular Partners	Centocor R&D Inc	15 Jan 2008	$5m upfront	Undisclosed	Two programmes for inflammatory diseases
Ablynx	Sanofi	29 Jan 2018	€3.9bn		Acquisition
Ablynx	Sanofi	20 Jul 2017	€23m upfront + €8m R&D	Up to €2.4bn in milestone payments	Several targets plus options for more – low double-digit royalties
Ablynx	Novo Nordisk	25 Nov 2015	€5m upfront + €4m in R&D	€182m of milestone payments per programme	Up to two programmes
Ablynx	AbbVie	23 Sep 2013	$175m upfront	Up to $665 in milestone payments	To develop ALX-0061 (Phase II) to treat inflammatory diseases
Ablynx	Merck (MSD)	2 Oct 2012	€6.5m upfront + €2m R&D	Up to €448m in milestone payments	One programme (voltage gated ion channel) with the option for a second target
Ablynx	Merck KGaA	11 Oct 2010	€10m upfront	€15m in milestone payments	Extension of the 2008 agreement
Ablynx	Merck KGaA	4 Sep 2008	€10m upfront	Up to €325m in milestone payments	Two targets in oncology and immunology
Ablynx	Boehringer Ingelheim	Sep 2007	Undisclosed	$1.3bn in milestone payments	Research and licence deal
Ablynx	Boehringer Ingelheim	Jan 2007	Undisclosed	$265m in milestone payments	New therapy for Alzheimer's disease

Source: Company news flow, Hardman & Co Life Sciences Research

Pieris Pharmaceuticals

Pieris Pharmaceuticals develops anticalins in various therapeutic areas, which are based on naturally occurring proteins called lipocalins present in human plasma and body fluids. Three programmes are currently in Phase I (PRS-343, PRS-060/Phase Ib/IIa, PRS-80) clinical stage, with several partnership with major pharma companies. The first Phase I with PRS-050 (Angiocal), an anti-VEGF-targeted protein therapeutic, was initiated in June 2010 and successfully completed in November 2015, with no maximum tolerated dose reached, efficacy and lack of immunogenicity; but the product does not appear in their pipeline anymore.

Molecular Partners

Molecular Partners is developing the DARPins technology, which is based on the natural ankyrin repeat protein, one of the most common binding proteins in nature. The first-in-man trial started in April 2010, with two separate trials with VEGF-A inhibitor MP0112 for wet-related macular degeneration (wet AMD) and diabetic macular oedema (DMO). The programme is now in Phase III and Phase II for AMD and DMO, respectively, in collaboration with Allergan, with plans to file abicipar with the FDA in 1H'19 for wet AMD. Molecular Partners is also running four in-house programmes with its candidate product MP0250 in Phase I and Phase II in oncology.

Ablynx

The nanobody technology is based on a single domain antibody fragment. In December 2007, Ablynx disclosed the first clinical results of the bivalent nanobody ALX-0081 as antiplatelet agent, on 40 healthy male volunteers, and the study demonstrated no dose-limiting toxicity or serious adverse events. This is just two months after it undertook an IPO on Euronext, which was then the largest-ever biotech IPO, raising €86.2m (Ablynx also undertook an IPO in the US in October 2017, raising nearly $230m). ALX-0081, which is now known as caplacizumab, is in the filing stage in Europe for the treatment of acquired thrombotic thrombocytopenic purpura, and will be the first marketed nanobody. Remarkably, the drug has progressed from discovery to completion of Phase I in just over three years, a performance that AVCT is hoping to replicate with its first therapeutic Affimer. This has triggered a long list of research and licensing deals, with increasing upfront and milestone payments, with high single-digit to low double-digit royalties attached to future sales. Ablynx has more than 45 proprietary and partnered product candidates in development in various disease areas, with five Phase II currently running. Ablynx was acquired by Sanofi for $3.9bn in 2018.

Conclusion

The licensing agreement is the second deal signed with a major biotech company in the past few months

Confirmation that Moderna has exercised its option to enter into exclusive licence agreements for selected therapeutic Affimer candidates for clinical development is very positive for AVCT. It is a strong indication that AVCT delivers Affimers with activity against Moderna's targets to an extent that they are worthy of making a considerable investment in clinical trials. At this point, AVCT will start to reap some of the rewards.

This follows from the development and commercial agreement signed with LG Chem in December 2018, which is worth up to $310m. Moreover, a number of major pharma/biotech companies are nearing the end of a significant period of validation of Affimers against their specific targets, and it is likely that more deals will be announced in 2019.

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