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#### INITIAL COVERAGE EXPRES<sup>2</sup>ION BIOTECH November 21, 2019

Date: November 21, 2019

Analyst: Markus Augustsson, Carlsquare Niklas Elmhammer, Carlsquare

Company: ExpreS<sup>2</sup>ion Biotech Holding AB
Listing: FIRST NORTH STOCKHOLM

CEO: Steen Klysner
Chairman: Martin Roland Jensen

Market Cap: 64 MSEK
Current share price: 4.7 SEK

ExpreS<sup>2</sup>ion in brief: Expre

ExpreS<sup>2</sup>ion has developed a patented expression platform based on S2 cells with a proven ability to produce complex proteins with clinical potential. The main focus is on infectious diseases and cancer. The company's business model enables for recurring licensing revenue while at the same time being able to take part of the large potential upside in drug development companies through commercial agreements.

Opportunities and strengths:

The company has further developed the ExpreS<sup>2</sup>-platform, which broadens the market and opens for new opportunities. We believe this can contribute to good growth in the coming quarters.

The platform generates recurring revenue, which together with consulting fees and sales of platform related products is well on its way to cover the running costs and more. Through commercial agreements, the company can obtain royalty income without bearing development risk.

The jointly owned company AdaptVac consist of the project, AV001, a cancer vaccine for the treatment of HER2-positive breast cancer. In preclinical cancer models, the substance has a clear anti-tumour effect. The intention is to license the project even before the clinical phase. An out-licensing agreement is a trigger.

Risks and weaknesses:

The company currently lacks revenues that cover the costs of running the business.

AdaptVac is considered to be in need of additional funding to complete the preclinical development, which is likely to be required before an out-licensing deal becomes relevant.

 Valuation:
 Bear
 Bull

 3.9 SEK
 8.2 SEK
 16.5 SEK

**EXPRESZION BIOTECH** 

# Source: Thomson Reuters and Carlsquare 16.5 kg 8.2 kg 4.70 kg 3.9 kg

# Potential at reduced risk

ExpreS<sup>2</sup>ion provides a platform for the next generation of vaccines, including therapeutic vaccines. With an improved offering, license revenues with high margins may increase. The value in the jointly owned AdaptVac does not seem to be fully discounted.



ExpreS<sup>2</sup>ion Biotech Holding AB has developed a patented expression platform based on S2 cells with a proven ability to produce complex proteins suitable for vaccine and immuno-

therapy with clinical potential. The company generates revenue through consultancy fees, out-licensing of the right to use the platform as well as the sale of platform related products. Among the reference clients are well-known pharma companies such as Novartis and Roche, a demonstration of the platform's capacities. The company has further developed its offering, which has generated great interest among existing and potential clients. We believe that an improved offering will contribute to good growth in the coming years with a healthy margin.

As part of the business model, customers must enter into commercial agreements if they wish to proceed to clinical development with a protein developed and produced using the company's platform. This means that the company takes part of the potential upside that traditional drug development companies are often associated with, but without having to finance the development. Today, the company has several known "partner projects" of which a malaria-project with the Jenner Institute is the furthest progressed. A phase I/IIa study has been completed that demonstrated activation of the immune system and moderate but significant effect. Own projects are also run through the jointly owned company AdaptVac. The most advanced project, AV001, has shown clear tumour inhibitory effect in preclinical studies. AV001 is a therapeutic cancer vaccine for the treatment of HER2-positive breast cancer, a market that is expected to reach around USD 10 billion. With continued progress toward clinical trials, the project should become attractive to larger potential partners and we estimate that a licensing deal could amount to several hundreds of MUSD in total value. However, additional funding will be needed to complete the preclinical development.

By adding the value of the platform to the estimated values in the own projects (in AdaptVac) as well as known partner projects, a fair value in the base scenario is calculated to SEK 8.2 for the coming 6-12 months.

#### Key figures, base case

SEKm	2017	2018	2019P	2020P	2021P
Net sales*	10	9	13	23	36
EBITDA*	-8.6	-14.3	-13.4	-28.5	5.0
EV/Sales	6.9x	7.7x	5.2x	2.9x	1.9x
EV/EBITDA	-	-	-	-	13.6x

<sup>\*</sup> Excluding AdaptVac revenue and expenses. Source: ExpreS2ion Biotech and Carlsquare

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### **Temperature**

#### Management



Dr. Steen Klysner has over 30 years of experience from Biotech and the pharmaceutical industry and has been the company's CEO since 2016. Steen has previously held leading positions in companies such as Allergopharma (part of Merck Group), Nordic Vaccine and Pharmexa. Chairman of the Board, Martin Roland Jensen, is co-founder of the company together with COO, Dr. Charlotte Dyring, and CSO, Dr. Wian de Jong. People on the board and management complement each other well with various relevant areas of expertise.

Management is evaluated on a scale from 1-10, where grade 1 is the lowest and 10 the highest. Decisive for the grading is the management's experience, industry knowledge, business management skills. stock market confidence and previous accomplishments.

#### **Owners**



ExpreS²ion Holding ApS is the largest owner of the parent company ExpreS²ion Biotech Holding AB, which in turn owns 100 percent of ExpreS²ion Biotechnologies ApS, where the assets are located. Board member Dr. Allan Rosetzsky is privately and through his company ExpreS²ion's largest individual owner with an ownership share of 10.5 percent of the share capital. The management team has exposure to the share through warrants. This should give them a financial incentive to act in the interests of shareholders. Otherwise, the ownership is dispersed.

The owners are evaluated on a scale from 1-10, where grade 1 is the lowest and 10 the highest. Decisive for the grading are the owner's historical company procedures, financial strength, their representation on the board and from previous investments in similar companies or industries. Long-term preference and responsibility towards minor shareholders are also essential criteria.

#### Financial position



As of September 30, 2019, SEK 2.6 million was in the cash register. After Q3, the company has entered into an agreement for a bridge loan of up to SEK 8 million in the form of convertibles. This improved the financial position in the short term. We believe that the company need further financing for further development of AV001 in AdaptVac.

The financial position is evaluated on a scale from 1-10, where grade 1 is the lowest and 10 the highest. This decision criteria considers the company's profitability, financial situation, future investment commitments and other financial obligations, potential over- and under values in the financial statement and balance sheet.

#### **Potential**



The company's expression platform for complex proteins has a wide range of uses and is made even more attractive after recent developments with HighMan-S2™. The platform is proven, as demonstrated by ongoing collaborations with major commercial players such as Roche, Merch or Sanofi. It is our assessment that the company is well on its way to creating profitability, only through platform revenue. The joint venture, AdaptVac, adds further potential upside, which in our opinion is not fully reflected in today's share price. AdaptVac is looking for partners for its most advanced project, AV001. A license agreement is a potential trigger.

The company's potential is evaluated on a scale from 1-10, where grade 1 is the lowest and 10 the highest. Decisive for the grading is the size of the company's potential in terms of increased profit in relation to the company's trading share price today. In which market, the company operates and the prospects for that market are also decisive factors. A company can achieve a high grading even though the growth projections are modest, provided that the share price today is below the growth projections and vice versa.

#### Risk



The company has recurring revenue from consulting services, out-licensing of user rights to the platform and consumables. However, these revenues do not fully cover current costs. The risk is nevertheless reduced as funding for the partner-led as well as part-owned development projects often are financed with research grants. It also holds back the risk in relation to the "traditional biotech company". Transparency in the company's cooperation agreement and study results is limited, which increases the uncertainty in our assumptions.

The risk is evaluated on a scale from 1-10, where grade 1 is the lowest and 10 the highest. The risk is a combined assessment of all potential risks the company can be exposed to and that affect the share price. The grading is based on a combined assessment of the company's general risk level, stock valuation, the company's competitive situation and estimations of future environmental events that can come to affect the company





## About ExpreS2ion Biotechnologies

ExpreS<sup>2</sup>ion Biotechnologies ApS (ExpreS<sup>2</sup>ion or the company) was founded in 2010 as a spin-off from the Danish pharmaceutical company Affitech A/S. The business in ExpreS<sup>2</sup>ion revolves around the patented platform, ExpreS<sup>2</sup> (platform or technology). This uses S2 cells from insects to time- and cost-efficiently produce complex proteins especially suitable for vaccines, immunotherapy or diagnostics. With the platform as the foundation, the company offers its clients a variety of related services, such as cell line production and development and production of specific protein. The company also offers its clients to licensing usage rights to the platform and its related products, such as cell lines and expression vectors (platform revenue).

The ExpreS²-platform is well proven and has successfully produced over 300 proteins for customers, partner projects and part-owned development projects. The first client was signed already the same year the company was founded, 2010. Since then, the business has grown and today there are several customers and partners consisting of research institutes and pharmaceutical companies in Europe, North America, Australia as well as Asia. Reference clients include reputable universities and research institutes such as Harvard Medical School, Imperial College London and the Jenner Institute (University of Oxford) as well as pharmaceutical companies such as Idorsia, Roche, Janssen and Novartis.

In other words, ExpreS²ion is not a traditional drug development company but provides services, technology and products for early stage research and drug development. While the ongoing business generates recurring platform revenue, the business model enables the company to take part of the large potential upside that exists in traditional drug development companies, in many cases without demanding the company to provide funding. Thus, ExpreS²ion can be seen as a less risky investment than a traditional capital-demanding drug development company with high development risk.

#### Vaccine

Infectious diseases are caused by infectious agents often in the form of e.g. parasites, bacteria or viruses that are spread through e.g. animals, air or water. Influenza, malaria, hepatitis B, chickenpox, HIV and measles are examples of infectious diseases.



For many infectious diseases there are prophylactic vaccines. These make the body more or less immune to the infectious disease after vaccination has taken place. Conventional vaccines contain an active substance in the form of weakened or completely killed microorganisms or purified parts from bacteria or viruses. When the body is given the vaccine, the immune system is stimulated to act against the foreign substance. Following vaccination, the immune system recognizes the infectious agent and can thus quickly produce large amounts of antibodies in the event of a new (real) attack.

There are also therapeutic vaccines, a form of immunotherapy designed to cure or reduce symptoms in patients who have already become ill. This by injecting vaccine that activates the immune system and attacks the foreign agents. For example, therapeutic vaccines can be used to treat certain types of cancer, for example, Provenge (Dendreon) is used to treat disseminated prostate cancer.

## ExpreS<sup>2</sup>

As previously mentioned, conventional vaccines in many cases contain an active substance similar to a disease-causing pathogen but in the form of killed or weakened microorganisms. For example, the active substance in influenza vaccine is the whole virus, produced in chicken eggs, which is then killed in the laboratory. Preparing and modifying the infectious microorganisms is a time-consuming process (influenza vaccine takes up to six months). However, ExpreS<sup>2</sup>ion focuses on a more modern form of vaccine, so-called recombinant protein vaccine. When using recombinant techniques, only the immunogenic part of the harmful substance is used, which creates increased possibilities and many times makes the substances safer and more effective. Recombinant vaccines have emerged as an effect of advances in research and are considerably more time-efficient to produce.

ExpreS<sup>2</sup> is the company's expression platform for the production of recombinant protein. For development and production of recombinant protein for use in vaccines or other biological drugs, cell cultures from, for example, mammals or insects are used. The challenge is that in most cases are that these cells do not naturally produce the protein being sought after and that the desired protein cannot be recovered in sufficient quantity.

A recombinant DNA consists of DNA from two different organisms that are combined to encode the desired protein. These are produced in laboratories and inserted into the host cells by so-called vectors which are a carrier consisting of molecules that transport the recombinant DNA into a cell. In order for the cells to express (produce) the desired protein, the foreign DNA must contain sequences which allow it to be translated into various forms of RNA which in turn guide the synthesis (production) of the protein in the cell's ribosomes.

ExpreS $^2$  is based on the use of S2 cells derived from fruit flies (also called Drosophila Melanogaster). These cells in combination with the company's competence, patented expression vectors, reagents and culture media make the platform time-efficient while producing stable proteins with clinical potential. This is demonstrated not least by the established players among the company's reference clients who use the platform for both research purposes and in clinical development with a commercial purpose.



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#### In-licensed technologies and HighMan-S2<sup>TM</sup>

In order to maximize the potential of the platform, a license agreement with ERS Genomics has been signed. This gives the company the right to use and commercialize products on its own, or together with clients or partners based on ERS Genomics CRISPR/Cas9 gene editing technology. This technology enables users to precisely modify genes in a cell in new ways that widens the scope of use and allow the company to further develop the platform.

The in-licensing of CRISPR/Cas9 gene editing technology also helped the company to launch a brand-new cell line, HighMan-S2™ belonging to the GlycoX-S2™ product group in October 2019. HighMan-S2™ cell line is a modified S2 cell line with improved immunological properties. This creates new opportunities in both prophylactic and therapeutic vaccines, which increases the market potential of the platform. According to the company, interest among existing and potential clients has also been great.

Over time, the company intends to continue to develop new products to further improve its offering.

#### Patent situation

The company's patent application "Improved Protein Expression System" has been registered on the company's main markets, including North America, Asia (with China, India and Japan) as well as most countries in the EU. The patent covers the company's expression vector for S2 cells as well as the methods and processes related to ExpreS2, thus covering the platform as a whole. In the United States, the patent expires in year 2032. The company has also filed a patent application for HighMan-S2<sup>TM</sup>. Thus, through further development of the platform, patents can be extended.

#### A flexible business model

#### Platform-revenue provides stability...

The main source of revenue today is consulting fees, revenue from sales of consumables and recurring license revenue (platform-revenue). As the company is already an established player with clients generating recurring revenue, certain security/stability is created. Through further development of the technology (for example, HighMan-S2TM), the growth potential for platform-revenues increases, which should be able to cover the company's operating costs. It is also our assessment that the company is well on its way to break-even.

# ... but access potential good upside through agreements

As mentioned, there are also opportunities for the company to take part of the large potential upside that traditional drug development companies often are associated with. That is, when the customers who take on a substance developed and produced with the company's platform for clinical development must enter into agreements that give ExpreS<sup>2</sup>ion the right to milestone payments and/or royalties (2-5 per cent) with no counterclaim for funding.



With the above mentioned, the company business model can be divided into two steps. In the first step, the company acts as a consultant and delivers services such as producing demanded protein for a fixed or ongoing service charge. Alternatively, the customer licenses user rights to the platform and generates revenue on an ongoing basis from the use of related products.

#### Step one provides valuable recurring revenue

How the agreements are formulated when out-licensing the rights to use the platform varies. However, the company has three commonly used categories of agreements. In the "simplest" form of collaboration, a so-called "Material Transfer Agreement" is signed, which controls the customer's usage of the platform. In return, ExpreS<sup>2</sup>ion receives a fee for the ExpreS<sup>2</sup> test kit.

In a second form of agreement is a so called "Research License Agreement". This gives the client the right to conduct basic research on the cells that are part of the ExpreS<sup>2</sup> platform to produce proteins. In these cases, ExpreS<sup>2</sup>ion receives a license fee as well as compensation for associated consumables.

#### Step two with good potential upside

Given that the customer wants to move on to clinical development with protein produced with the company's platform, the second step is initiated. This means that a commercial agreement is entered with a much larger potential upside.

The third commonly used form of contract is thus a so-called "Commercial License Agreement" which gives the customer the right to carry out clinical development and commercialize products with the active substance consisting of protein developed and produced using the company's platform. Under this form of agreement, the company continues to receive platform-revenue, but there are also opportunities for development-related milestone payments and sales-related royalty income.

#### ...or by themselves

It should also be mentioned as an alternative that the company can develop a project on its own. This model increases the potential upside but is of course riskier as the development risk, including financing, lies with the company. Today, there are no self-managed projects, but this may be relevant in the future.

## Joint venture - AdaptVac

Another alternative is that the company takes direct ownership of patents or projects. The latter may imply an increased requirement for financing, but also gives the company a greater upside as a larger proportion of the potential value in the project(s) accrues to ExpreS²ion.

For example, co-ownership can come through a joint venture with the customer/partner where relevant assets are held. An existing Joint Venture company is AdaptVac, which ExpreS²ion established together with NextGen Vaccines ApS in 2017. ExpreS2ion's ownership interest in AdaptVac amounts to 50 percent.

The rationale behind the founding of AdaptVac was the combination of the



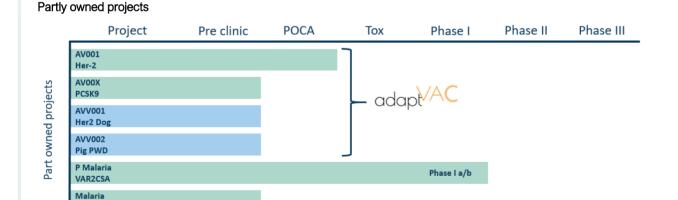
company's ExpreS<sup>2</sup>-platform with NextGen's virus-like-particle (VLP) technology to create specific antigens (in this case one in the form of a protein). It broadens the possibilities within vaccines, mainly focusing on immunotherapy and therapeutic vaccines for e.g. cancer and allergies.

Through AdaptVac, the company has its own (partly owned) project in breast cancer but also develops projects in cardiovascular diseases and veterinary medicine.

Three of four projects in AdaptVac are funded with grants of various kinds. Among other things, the company received a Danish InnoBooster grant of SEK 1.2 million in October 2019 as support for breast cancer studies in dogs. In February 2019, AdaptVac was awarded SEK 3.6 million by the Danish Innovation Foundation for participation in a vaccine project with the aim of preventing weaning diarrhea (PWD). The project can contribute to reduced antibiotic use in the farming (pig) industry.

## Project-pipeline and other possibilities

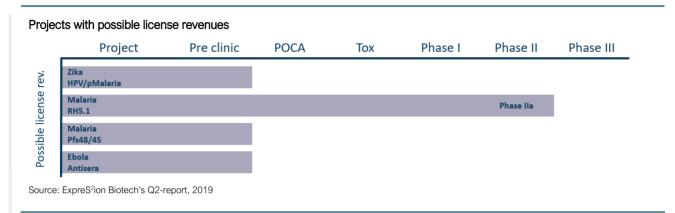
Today, the company has direct co-ownership in seven published and ongoing projects. The most advanced is VAR2CSA, a placental malaria vaccine. At the beginning of 2019, results from a clinical phase I a / b study were presented. See illustration below.



Source: ExpreS2ion Biotech's Q2-report, 2019

The company has three additional projects plus an unknown number of projects that have not yet been published that can generate revenue. That in the form of milestone payment and sales-related royalties (partner projects). See illustration on the next page.





We believe that AdaptVao's AV001-project has the greatest commercial potential and thus adds the most value for ExpreS<sup>2</sup>ion.

#### AdaptVac, AV001 – a potential cancer vaccine

Adaptvac's most advanced project is AV001, a cancer vaccine for the treatment of HER2-positive breast cancer. Patients with this form of breast cancer have tumors with a high expression of a protein called human epidermal growth factor receptor 2 (HER2). It causes an aggressive disease and these patients generally respond poorly to chemotherapy and anti-hormonal treatments. 20–25 percent of all breast cancer patients have HER2-positive breast cancer.

#### Major medical need...

The treatment of these patients received a major breakthrough when Genentech successfully developed an antibody trastuzumab (Herceptin) against a portion of HER2. Herceptin, which received market approval in 1998, is one of the most successful targeted cancer treatments ever. Nearly 50 percent of all tumors respond to treatment. Despite this, there is still a great medical need for these patients given that not everyone responds to trastuzumab and since the treatment is associated with the risk of serious side effects, including heart failure.

#### ...and a sizable market

The number of new breast cancer cases in the US, and the five largest markets in the EU, is expected to have reached 533,000 in 2018, of which an estimated 76,000 were diagnosed as HER2 positive (Source: Roche / Genentech). The market for HER2-positive breast cancer is expected to reach around USD 10 billion in 2025, compared with around USD 6.4 billion in 2015 (Source: Global Data). Although trastuzumab patents have expired, new potentially more effective HER2 antibodies such as antibody drug conjugates, as well as tyrosine kinase inhibitors, are expected to drive growth. As new treatments approach the market, interest in the area has increased. In March 2019, AstraZeneca and Daiichi Sanyo entered into a joint venture regarding an antibody conjugate called DS-8201 (trastuzumab deruxtecan) consisting of an anti-HER2 antibody and a cell toxin. AstraZeneca paid USD 1.35 billion in advance and up to USD 5.55 billion in possible milestone payments for a 50 percent share of the project.

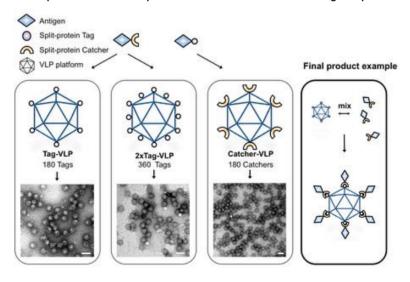


#### AV001, an antigen with VLP technology

Cancer vaccines of various types are also being investigated as potential treatments to create immunity to HER2. So far, only early clinical data are available, but promising observations have been made, for example, with a vaccine based on the patient's own dendritic cells being treated ex vivo and then returned to patients. The disadvantage is that autologous cell therapy is an expensive and complicated treatment.

AV001 means a simpler form of administration and is thus based on virus-like - articles (VLP). To these, a particular HER2-bearing antigen has been attached. When AV001 is injected into the body, the VLP portion acts as an adjuvant and starts an immune response and the body then creates its own antibodies against HER2. It is a challenge to produce VLPs with the capacity to carry large antigens such as HER2 proteins. To address this, AdaptVac utilizes a technology called SpyTag/SpyCatcher that enables larger antigens to bind to VLPs. Simplified, it is based on splitting a protein into two parts (tag and catcher) which are then fused with the antigen and VLPs, respectively. When the VLPs and the fused antigen are then mixed, the protein moieties bind to each other, causing the VLPs to have a dense surface of antigen.

#### Schematic illustration of AdaptVac's method for production of vaccine based on antigenic particles with antigen



Source: AdaptVac

There are approved VLP-based prophylactic vaccines for cervical cancer. AV001 is intended as a therapeutic vaccine, that is, for the treatment of patients already suffering from breast cancer.

#### Clear tumor inhibitory effect in preclinical cancer models

AV001 has shown promising preclinical results:

 Mice vaccinated with AV001 produce antibodies against HER2 that bind to human HER2-positive tumor cells.



- Prophylactic vaccination with AV001 in a so-called transgenic cancer model (mice carrying genes for human HER2) reduced the incidence of tumors by 50–100 percent and suppressed the growth of human implanted tumors in another model.
- Tests on cell lines from tumors resistant to trastuzumab suggest that AV001 inhibits their growth.
- In summary, the results give hope that AV001 can offer therapeutic benefits.

At present the intended use of AV001 is still open. New treatments are primarily aimed at patients who have relapsed after, or do not respond to, first-line treatment with trastuzumab plus chemotherapy. Below we report expected sales of a number of drugs / candidates either approved for or in late clinical development for second-line treatment for HER2-positive breast cancer.

#### Expected sales for second line treatments of HER2-positiv breast cancer

Treatment	Sales 2024P (MUSD)
DS-8201	1800
Kadcyla	1400
Tucatinib	268
Margetuximab	440
Nerlynx	697
Average	921
Median	697

Source: EvaluatePharma, Carlsquare

We calculate a median value of almost USD 700 million and use it as a preliminary assumption of peak sales for AV001 at this early stage. A potential use in the "first line" could multiply the potential. At the same time, competition in the area can be expected to be fierce.

AdaptVac's preferred strategy is to license projects even before the clinical phase. Below, we have listed a number of licensing deals targeting HER2-positive cancer or cancer vaccines:



#### Deal references for AV001

Company	Partner	Project	Indication	Phase	Value (MUSD)	Upfront (MUSD)
Puma Biotechnology	Pierre Fabre	neratinib	Cancer	Godkänd	405	60
Abclon	Henlius	AC-101/anti HER2	Solid tumors	Preklin.	ś	11
Zymeworks	BeiGene	ZW25/ZW49	Solid tumors	I	430	40
MacroGenics	Zai Lab	Margetuximab	Cancer	III	165	25
BioNTech	Roche	IVAC Mutanome	Cancer	Preklin.	310	
Advaxis	Amgen	ADX-NEO	Cancer	Preklin.	540	65
Mersana	Takeda	XMT-1522	Solid tumors	Preklin.	810	40
Inovio	AZN	INO-3112	Several cancers	I	727,5	27,5
Bavarian Nordic	BMS	Prostvac	Prostate Cancer	III	975	60
CureVac	ВІ	CV9202	Prostate-, Lungcancer	I	549	41,3
Pfizer	Puma Biotechnology	neratinib	Cancer	II	188	0
Rigontec	Merck	RGT100	Cancer	I	548	1 <i>37</i>
Merck Kga	Idera	TLR9-agonist	Cancer	I	400	40
Average					504	46
Median					485	40

Source: Carlsquare

We calculate a median value of USD 485 million. Given that AV001 is a preclinical project, we assume an up front payment of five percent or about USD 25 million.

# AdaptVac, AV00X - Vaccine to lower bad cholesterol

At the end of 2018, a vaccine project, AV00X, in cardiovascular disease was presented. AV00X targets an enzyme called PCSK9 that regulates LDL cholesterol levels, known as "bad cholesterol". LDL cholesterol is a major cause of atherosclerosis and cardiovascular disease. Antibodies that inhibit PCSK9 have been shown to lower LDL cholesterol by up to 60 percent and reduce the risk of "cardiovascular events" (such as death, heart attack and stroke) by about 15 percent.

Today's antibody treatments targeting PCSK9 are expensive, require recurrent injections, and many patients develop resistance. A vaccine could theoretically mean fewer treatments and thus a more patient-friendly alternative.

AdaptVac is not alone in this approach. The Austrian company Affiris has conducted a phase I study with a peptide-based vaccine. The treatment is said to have been well tolerated. The study achieved a statistically significant albeit rather modest LDL cholesterol-lowering effect (-13 percent compared to placebo).

According to Global Data, the market for PSCK9 antibodies is estimated to amount to USD 3 billion in 2024. Compared to other blood-fat-lowering drugs such as statins, this is a relatively low estimate. Presumably, expectations are dampened by the fact that today's anti-PSCK9 treatments are expensive and difficult to



administer, while no truly striking clinical effect has yet been demonstrated. Clinical development of cardiovascular drugs is very costly, making collaboration with major partners regarding AV00X a necessity.

# AdaptVac - Two projects for the veterinary market

AVV001 is a veterinary product targeting HER2-positive breast cancer in dogs. Although the veterinary market is significantly smaller than the market for human medicines, the requirements for clinical trials are, in contrast, significantly less extensive. The cost of taking a veterinary drug to the market can thus be limited.

AdaptVac is also developing a vaccine (AVV002) to counteract weaning diarrhea (PWD) in pigs when switching from milk to cereal-based diet and the piglet's immune system is not fully developed. This is a major problem for pig production as many animals that die suffer and the ailment is very contagious. Antibiotics and/or zinc oxide are currently treatments. Since neither of these methods is considered sustainable, there is a great need for new treatments. AdaptVac sees a sales potential of EUR 100 million for a PWD vaccine.

In our evaluation of AdaptVac, we only count for the AV001 project so far. Other projects are in early stage, and we still lack sufficient evidence and validation for a valuation approach.

# Partner project, VAR2CSA - Malaria infection in pregnancy with the University of Copenhagen

More severe forms of malaria are often caused by the single-celled parasites of the Plasmodium species. Infection is initiated when mosquitoes suck blood and simultaneously inject Plasmodium sporozoites via saliva. These then migrate to the liver where they multiply in the liver cells via multiple division into thousands of merozoites. This eventually causes the liver cells to burst and even more merozoites can attack further liver cells. In the next stage, merozoites enter the bloodstream and invade the red blood cells (erythrocytes), causing the first symptoms of the disease. After a certain period, the erythrocytes also burst, which means that the merozoites, together with toxic degradation products, enter the bloodstream and the disease will progress. The incubation period is between one and four weeks and causes nausea, vomiting, diarrhea and severe fever. Malaria can have a fatal outcome.

The disease is widespread especially in Africa but also in other tropical and subtropical areas. According to the World Malaria Report, published by the WHO in November 2018, the proportion of malaria cases was 219 million in 2017 in more than 90 countries. This is an increase of two million cases from the previous year. The total number of deaths recorded in malaria-affected regions in 2017 amounted to 435,000.

Despite the high prevalence of the disease in some affected regions, the market is relatively small. According to a report by analysis company Polaris Market Research, the global market in 2018 was valued at USD 12.3 million (approximately SEK 118 million). However, the market is expected to grow on average by 33.2 per cent per year until 2026.



Pregnancy malaria infection (PAM) affects as the name implies pregnant women. In PAM, the parasite establishes and spreads in the placenta. PAM is life threatening for both mother and the fetus as well as the newborn (low birth weight and prematurity). The capacity of the immune system to defend itself against malaria infection is reduced during pregnancy for unknown reasons. Thus, PAM can affect women who have already received a preventive vaccination. WHO estimates that around 35 million pregnant women in sub-Saharan Africa are in need of another vaccine.

VAR2CSA is an antigen that allows the Plasmodium falciparum parasite to establish and multiply in the placenta, which in turn gives rise to the disease state. Through a vaccine candidate PAMVAC, which is a CAR2CSA-based protein antigen, the intention is to create a preventive vaccine for women in vulnerable areas.

The development of PAMVAC has been facilitated by the University of Copenhagen in collaboration between several different parties including, Université d'Abomey-Calavi, European Malaria Vaccine Initiative and Institut de recherche pour le développement. ExpreS²ion, which together with the University of Copenhagen owns the patent on the vaccine technology, has contributed with the knowledge to produce the vaccine candidate PAMVAC and also participated in and developed the production cell line and the manufacturing process.

In mid-2016, a controlled and randomized phase la/b clinical trial was launched with the primary goals of evaluating safety and immunogenicity (PAMVAC's ability to stimulate specific antibody production against the antigen). In January 2019, the company was able to announce that PAMVAC was immunogenic in all participants. 292 adverse events were identified in the 36 patients. Of these, ten could be classified as a second on a five-degree scale, which means the incident or side effect was moderate. Two were classified as a third, which corresponds to a "severe" side effect.

The study was funded by the EU program FP7-Health-2012-Innovation, the Danish National Advanced Technology Foundation, the Independent Research Fund Denmark, the German Federal Ministry of Education and the Research Bill & Melinda Gates Foundation.

# Partner project, RH5.1 - Vaccine candidate, with Jenner Institute

RH5.1 is a recombinant malaria antigen developed based on a recombinant RH5.1 protein produced by the ExpreS2 platform. The development has been led by the renowned Jenner Institute, University of Oxford.

The RH5 antigen is expressed by the malaria parasite during infection and helps the parasite penetrate the red blood cells (erythrocytes). The intention of vaccines containing RH5.1 antigen is to induce the immune system's antibodies to block the invasion of red blood cells and thereby stop the progression of the disease.

In the fall of 2018, results from a phase I/IIa study were presented in which RH5.1 was administered together with an adjuvant (AS01B) from GlaxoSmithKline. A dose escalation study in healthy volunteers showed that the vaccine is safe. In



order to evaluate efficacy, a group of fifteen subjects were first injected with RH5.1 and then given a controlled malaria infection. The group was compared with another group (n=15) who received only controlled malaria infection. A moderate but significant effect on the parasite multiplication rate was observed, as was evidence of a persistent antibody response upon repeated infection.

The aim of the project is to initiate a larger phase II study to optimize the result based on the first study. In parallel or thereafter, any out-licensing business may become relevant.

#### Other projects in early stage development

The protein PfRips has a crucial role for the parasite's life cycle in the body and thus, the progression of the disease. With the help of ExpreS², the Walter & Eliza Hall Institute of Medical Research (WEHI) has developed a recombinant PfRips protein that, in animal models, shows that antibodies can prevent merozoites from invading red blood cells, which can also stop the course of the disease. The project is still in the early preclinical phase and is dependent on additional grant or other forms of funding.

ExpreS<sup>2</sup>ion is also the coordinator for the OptiFemVac project, which is run in conjunction with Abera Bioscience and the University of Copenhagen. The aim is to develop cost-effective vaccines that target women's reproductive and infant health. The main focus is on zika virus vaccine. In March 2017, the project received Eurostars funding totaling EUR 750,000. These cover project-related costs over a period of 36 months starting in April 2017. Additional grant funding will probably be needed to continue the project.

Another possible way to prevent malaria infection in humans is to prevent the establishment of infection in mosquitoes, which feed on infected people. Such a preparation can thus stop the transmission cycle. In this process, the surface protein Pfs48/45 plays an important role. By finding a formulation that causes the immune system to produce antibodies that bind to Pfs48/45, a new form of effective vaccine can also be created. Again, the project is in an early phase and is funded with research grants.

The company also today has a commercial out-licensing agreement with the French company Abivax, which runs the ABX544 program. It aims to develop into an antiserum containing neutralizing antibodies that are immunizing against Ebola antigen. The intention is that an antiserum should have an immediate effect, which is demanded in the outbreak of epidemics. The last Ebola epidemic took place in Africa in 2014/15 and harvested around 11,000 casualties. Abivax currently runs five projects in the clinical phase and four projects in the preclinical phase, of which the ABX544 program is the most advanced.

## Assumptions, forecasts and valuation

We have evaluated ExpreS2ion Biotech as the sum of the research activities (which generate what we call "platform revenue") as well as AdaptVac and the most advanced malaria projects. The valuation of the research activities is based on our forecasts as below



#### Research

#### Development creates growth opportunities

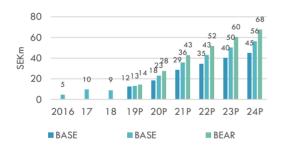
The third quarter report for 2019 was recently released. Net sales of SEK 3.2 million were reported for the quarter. This corresponds to a growth of 45 per cent on an annual basis, i.e. relative to the same quarter last year. During the first three quarters, the company generated net sales totaling SEK 10.2 million, corresponding to a growth of 37.5 per cent on an annual basis.

The current fourth quarter has historically been seasonally weak. We therefore model with sequentially falling revenues, which results in assumed net sales for the full year 2019 of SEK 13.2 million. This corresponds to strong growth of 48 per cent, which can be compared with a negative growth of about -9 per cent in 2018.

As mentioned, the company has further developed its offering with new products that make the platform more attractive. Among other things, the company has introduced HighMan-S2™, which facilitates scalable production of proteins with improved immunological properties for both preventative and therapeutic vaccines. According to the company, this has created an increased interest in the company's platform in the market and should be able to drive growth in the coming quarters. It is also the company's intention to continue to develop the new platform in order to maintain an attractive position. Therefore, in the base scenario, we model net sales (from platform revenues) of SEK 23.0 million, a strong growth of high 75 percent in 2020.

Below are our projections for platform-related revenues until 2024.

# Estimated platform revenue on an annual basis in three scenarios and assumed platform revenue on a quarterly basis in the base scenario





Source: ExpreS2ion Biotech and Carlsquare

In the base scenario, we have assumed an average annual growth rate of 36 percent during the period 2019-2024. The corresponding figure in the bear and bull scenarios is 27 percent and 40 percent respectively.

#### A bit left before Break-even

For the third quarter of 2019, a gross margin of 77 per cent was reported. This has varied between 57 per cent and 87 per cent during the first three quarters of the year and is reasonably affected by the product mix. A high proportion of license



revenue can be assumed to increase the gross margin, while consulting services that involve material consumption hold back the gross margin.

Including the item "Profit in jointly controlled companies", ExpreS<sup>2</sup>ion reported an EBITDA result of SEK -2.6 million during the third quarter of 2019. This is a clear improvement compared to the same period last year and is mainly due to increased revenue. Also, we do not expect any major changes in the cost base in the coming quarters. Over time, however, we anticipate an increase in staff.

Given licensing revenues with a high gross margin, it is also not unreasonable for the company to report margins above industry standards over time. In our base scenario, the company makes a positive EBITDA result in 2021, when it only included platform revenue and excluded the item "Profit in jointly controlled companies" (to avoid double counting these in the valuation. In the same scenario, we have adopted a sustainable EBITDA margin over time of about 30 percent. In the bull and bear scenario, we expect a sustainable EBITDA margin of about 35 per cent and about 20 per cent, respectively.

The graph below shows forecasts for EBITDA results excluding "Profit in jointly controlled companies".

# Assumed EBITDA results, excluding "results in AdaptVac" on an annual basis in three scenarios and projected platform revenue on a quarterly basis in the base scenario





Source: ExpreS2ion Biotech and Carlsquare

#### **DCF-valuation**

In an approach to evaluate research activities, we have applied a DCF model. With this method, an enterprise value in the base scenario is estimated at approximately SEK 44 million. In the bull scenario, the total enterprise value is estimated at approximately SEK 76 million and in the bear scenario at approximately SEK 10 million. See table below:



#### DCF-valuation

	BEAR	BASE	BULL	
Wacc	14.3%	14.3%	14.3%	
CAGR, 2019P - 2020P	31.1%	36.1%	40.3%	
Growth, perpetuity	2.0%	2.0%	2.0%	
Long term EBITDA-margin	20.2%	30.4%	35.1%	
Enterprise value, SEKm	9.8	44.2	76.1	
Shares, million	13.6	13.6	13.6	
Per share, SEK	0.7	3.3	5.6	

Source: Carlsquare

We have used a discount rate of 14.3 percent. This is based on a risk-free interest rate of zero percent, a beta value of 1.3 and a risk premium of 11 percent. The latter is based on PwC's *Risk Premium Study 2019* and consists of a market risk premium of 6.8 percent and a size-specific risk premium of 4.2 percent. The beta value is a cut for the biotech industry according to Damodaran Online.

#### AdaptVac

#### Cancer project, the main value driver

In our evaluation of AdaptVac, as mentioned above, we have so far only taken into account the cancer project AV001. We have assumed that an out-licensing takes place after preclinical phase to a value corresponding to USD 485 million of which USD 25 million in an upfront payment. We have assumed that AdaptVac is entitled to royalty payments corresponding to 7.5 per cent of sales. We have calculated a probability of launch of just over three percent, given a fairly low historical probability of launch for cancer projects and since regulatory toxicological studies have not yet begun.

#### Malaria project

#### FDA program can drive interest

The market for malaria vaccines is expected to amount to about USD 135 million in 2026 (Source: Polaris Market Research). If we assume a market share of 25 per cent for RH5.1, this corresponds to sales of USD 34 million.

- In our valuation of RH5.1 we have assumed that the project can be outlicensed to a value of MUSD 13.5 in possible advance and milestone payments, of which ExpreS2ion receives 35 percent. We also assume that ExpreS2ion will receive 3.5 percent in royalties on future sales.
- For VAR2CSA (pregnant women), we have adopted a target population
  of 35 million pregnant women in regions of sub-Saharan Africa (WHO)
  and a potential market of MUSD 70. An assumed penetration of 50
  percent renders sales of USD 35 million. We assume that the project
  can be out-licensed to the value of USD 7 million in possible advance
  and milestone payments. Like RH5.1, we assume that ExpreS²ion
  receives 3.5 percent royalties and 35 per cent of down payment and



milestone payments.

For the malaria projects, we have assumed a probability of launch of 28
per cent. This is in light of the fact that these have advanced to the early
clinical phase and, in addition, a relatively high historical probability of
launching drug projects for infectious diseases, compared with, for
example, the cancer field.

Although the commercial market for malaria is relatively small compared to other indications in the vaccine market, there are several incentives that can attract potential partners. In the US, for example, there is a program where drugs for a number of "neglected" diseases, such as malaria, at FDA approval give the developer a so-called "priority review voucher". It is a right to a priority review of an individual new drug application. This right can be resold. About fifteen such transactions have been made in the last five years to the value of USD 68 to USD 350 (Source: www.prorityreviewvoucher.org). In addition, efforts to develop treatments for diseases that are endemic in developing countries can provide significant goodwill, and there is also the possibility of extensive financial support from state and private charities.

#### Summary, valuation

Below we summarize our valuation of the sum of the parts in ExpreS<sup>2</sup>ion Biotech:

#### ExpreS2ion Biotech Sum-of-the-parts, BASE

	Top sales (MUSD)	Risk adjusted NPV (MSEK)	Per share (SEK)	Assumption
ExpreS2ion AB		44	3,3	See above
AdaptVac, AV001	700	85	6,2	50 % share
Malaria-project	70	14	1,0	RH5.1, VAR2CSA
Net cash/-debt		-5	-0,4	Sep 30th, 2019
Total		138	10,1	13.6 m shares
Assumed financing		18		
After delution		156	8,2	

Source: Carlsquare

In total, we calculate a risk-adjusted motivated value of SEK 138 million for ExpreS2ion in the base scenario.

As of September 30, 2019, cash was SEK 2.6 million. After the end of the period, the company has entered into a bridge financing agreement of up to SEK 8 million with a maturity of 31 May 2020. In addition, there are 1.6 million outstanding warrants with a strike price of SEK 6 per share, which can bring in SEK 9.6 million before full utilization costs. However, as the share is traded below the strike price, this source of financing is uncertain at present.

We believe that there is a need for financing in the coming years for working capital and to drive AdaptVac's AV001 project further in the preclinical development. To take this into account, we have assumed a capital requirement of the same size as the most recent rights issue 2018. Adjusted for the estimated dilution, we calculate



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a fair value of SEK 8.2 per share.

In addition to higher projections for platform revenue, in our bull scenario we have assumed that the company will enter into an out-licensing business with AV001 in six to twelve months term. We also assume that the warrants are exercised, which reduces the need for financing. In this scenario, the motivated value rises to approximately SEK 290 million or SEK 16.5 per share after the dilution assumed.

In our bear scenario, in addition to lower platform revenues, we have assumed that no out-licensing deal is reached for AV001 after preclinical phase and that the company needs to do a phase I study on its own. We also assume less favorable terms in a future out-licensing deal. Furthermore, we have assumed that the malaria projects will not advance further. In this scenario, the fair value per share falls to SEK 3.9 per share.



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