

# Ever-changing landscape

## Bavarian Nordic payment to AdaptVac in 2023

Recruitment of elderly subjects in the 4 000-patient registrational phase 3 study with ABNCoV2, initiated in September last year, has been slower than anticipated. Vaccination rates are running low in Europe, probably contributing to a slow progress.

A first read-out from the study is now expected in mid-2023. According to Bavarian Nordic's annual report, following a positive readout and filing this year, it expects to pay up to DKK 300m to AdaptVac in 2023.

## New share issue resolves financing of ES2B-C001

Expres<sup>2</sup>ion Biotechnologies has seen R&D costs rising to SEK 36m in the last quarter of 2022, up from SEK 1,6m in the first quarter of 2022. With the proposed new share and warrant issue of around 200 MSEK, the company can continue to drive investments in the vaccine candidate ES2B-C001 and transform into a pipeline driven organization. We expect first patient in a future phase 1 trial with ES2B-C001 to be treated in mid-2024, a minor delay compared to our previous assumptions.

## FDA proposes new vaccination procedures

On January 26 an FDA advisory committee meeting was held discussing Covid-19 vaccination procedures. The experts invited to the meeting voted in favor of the idea that both primary and booster vaccinations should be carried out with the same vaccine composition. The panel and the FDA officers preferred the recently launched bivalent mRNA vaccines over the monovalent versions, which were introduced in 2021 and now likely to be phased out.

Such a decision should not directly impact the ongoing Bavarian Nordic phase 3 program with ABNCoV2. However, it remains to be understood if new Covid-19 procedures in the US will raise hurdles for approval of next-generation Covid-19 vaccines.

## Major dilution from new rights issue

The proposed new share issue at a price of SEK 4,90 per share with a subsequent warrant issue will more than double the number of shares in 2023, assuming full subscription. Given the dilution and a lowered projected number of Covid-19 vaccinations in 2025-28 in EU and US, we cut fair value of Expres<sup>2</sup>ion Biotechnologies to SEK 12 (25).

Topline phase 3 data on ABNCoV2 and 12-month durability data in phase 2, together with the advancement of the ES2B-C001 program, make up potential near-term share price triggers in 2023.

## Expres<sup>2</sup>ion Biotech

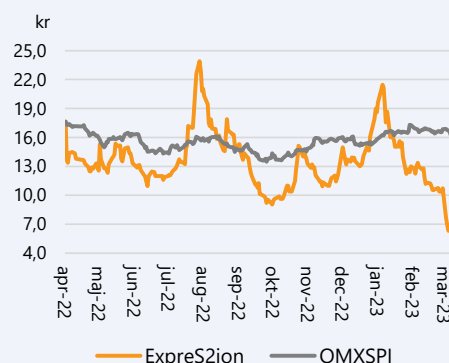
Date 15 mars 2023  
Analyst Sten Westerberg

### Facts

Industry Vaccine Development  
Chairman of the Board Martin Roland Jensen  
CEO Bent U. Frandsen  
Year of Listing 2016  
Stock List First North Growth Market  
Ticker EXPRS2  
Share price SEK 6,2  
No. of shares, mln. 37,6  
Market cap, SEKm 232  
Cash 2022, SEKm 111

Web site [www.expres2ionbio.com](http://www.expres2ionbio.com)

Kursutveckling senaste året



Source: Refinitiv

### Forecasts & Key ratios, SEKm

	2021	2022	2023p	2024p
Revenues	14	6	13	46
R&D expenses	-10	-69	-100	-120
Net income	-44	-119	-151	-139
Earnings per share	-1,5 kr	-3,2 kr	-4,0 kr	-3,7 kr
Revenue growth	-10%	-57%	117%	250%
Cash	139	111	267	128
New share issue	83	76	205	0

Source: Company, Analysguiden forecasts

## Infection diseases advisory board

ExpreS<sup>2</sup>ion Biotechnologies has announced the formation of a four-person scientific advisory board which will strengthen its efforts in preclinical development in areas such as antigen selection and relevant in vivo models. Two of the members, Drs Plotkin and Schleiss, are renowned experts in infection disease areas such as cytomegaloviruses (CMV). This area has become a preclinical focus in the recent partnership with Evaxion Biotech, another Danish vaccine development company.

The collaboration with Evaxion will combine ExpreS<sup>2</sup>ion's technology platform for vaccine development with Evaxion's artificial intelligence platform for vaccine candidate discovery and preclinical models. The aim of the collaboration is to pick a novel CMV lead vaccine candidate before the end of 2025, when ExpreS<sup>2</sup>ion has the exclusive right to license the program under a Development and Commercialization Agreement.

## Two advisory boards underscore commitment

In November the company also formed a six-member oncology advisory board to back up investment in its breast cancer vaccine candidate ES2B-C001. The two advisory boards will also function as advisors, potential contributors to future clinical studies and as participants in Key Opinion Leader events. These actions underscore management's commitment to transform ExpreS<sup>2</sup>ion into a pipeline-driven company, advancing its position in the pharmaceutical industry value chain.

## Research fund in mucosal vaccine program

ExpreS<sup>2</sup>ion Biotechnologies also announced recently that it is investing in a preclinical program in the development of vaccine delivery over the mucosa. The program is a collaboration between ExpreS<sup>2</sup>ion and the Department of Immunology and Microbiology at the University of Copenhagen.

A major part of the investment will be covered by a public fund, IFD Investments. The awarded funding amounts to 29 MDKK over a 5-year period. The project seeks to combine the protein expression capabilities of ExpreS<sup>2</sup>ion with vaccine approaches and animal models at the University of Copenhagen, aiming to develop a recombinant general vaccine platform to treat influenza viruses.

In another program, the INDIGO consortium, the company is involved in another development of an influenza vaccine. The consortium is led by the University of Amsterdam. Pending further grants from EU, this project is expected to enter preclinical development in 2023.

## Minor delay for Bavarian Nordic

Bavarian Nordic recently updated the timeline of the phase 3 trial of ABNCoV2, which is ongoing in US, Denmark and Belgium. The trial is funded by the Danish state and will enroll 4 000 subjects, out of which 3 000 will be in the safety-check, non-randomized Part B

carried out in the US. According to the company it has been difficult to recruit +65 years old subjects to the trial. Topline results on immunogenicity will thus be released mid-2023, compared to a previous ambition of a topline announcement by early this year.

This is the third time that the anticipated topline read-out is delayed. Falling vaccination rates for Covid-19 certainly should make it difficult to operate a registrational phase 3 trial in this area and this should be no surprise to the stock market. On top of this we also would point to a complicated regulatory environment, which has contributed to some of the previous delays.

### Payments to AdaptVac in 2023

According to Bavarian Nordic Annual report of 2022, management expects to pay up to 300 MDKK (40 MEUR) in milestones to AdaptVac in 2023. We assume this would be the result of both a positive topline read-out and a subsequent filing for approval before year-end. Potentially, Bavarian Nordic will pay another 92 MEUR to AdaptVac, excluding this year's milestones and the 4 MEUR milestone paid in 2020 at the signing of the deal with AdaptVac.

This makes the agreement front-end loaded and at this stage we expect a total of 96 MEUR to be shipped to AdaptVac in 2023-28. Bavarian Nordic has so far capitalized around 72 MEUR of deferred payments to AdaptVac in its balance sheet, thus a lower number than the potential number announced in 2020.

Through its CMO, Bavarian Nordic has started to manufacture commercial batches of the vaccine candidate and booked to the Bavarian Nordic balance sheet at a cost of 132 MDKK. We estimate this batch to equate around 1 million doses, assuming a price per dose of around EUR 40. In total we expect ABNCoV2 to have the potential to reach 57 million doses sold 2024-28.

### A longer-lasting vaccine

The aim of the ABNCoV2 program is to “create a longer-lasting vaccine protection with broader efficacy that obviates the need for continuously adapting” to new variants of the virus. An important piece of information will be provided around mid-2023 when 12-month data on the durability of immunogenicity from a subgroup in the phase 2 program will be released.

Unpublished 6-months data from 39 subjects in the phase 2 study suggest a slower waning of SARS-CoV2 antibodies elicited by ABNCoV2 compared to data shown in published studies on the marketed mRNA vaccines. Due to the nature of the treatment procedures, it may be expected that 12-months data is limited to an even smaller population than the 6-months data.

### Program financed by Danish government

The phase 3 study is financed through a DKK 800m grant by the Danish government. It is divided in two groups, one randomized part including 1 000 Danish and Belgian subjects (Part A) and another non-randomized part of 3 000 US patients (Part B).

Part A will evaluate the non-inferiority of ABNCoV2 (at least not inferior) to Pfizer's market leader Comirnaty, either in participants previously treated with a primary vaccination (two doses) or with a booster injection after primary vaccination (three doses). Part A will have a primary endpoint based on neutralizing antibody titers to the wildtype Wuhan strain, the ancestral dominating strain in the initial phase of the pandemic.

The primary endpoint in part A is measured two weeks after administration of ABNCoV2. Secondary endpoints in parts A and B will look at different safety parameters and biomarkers, such as the number of neutralizing antibodies to the different Sars-CoV2 strains, specifically the dominating omicron variants.

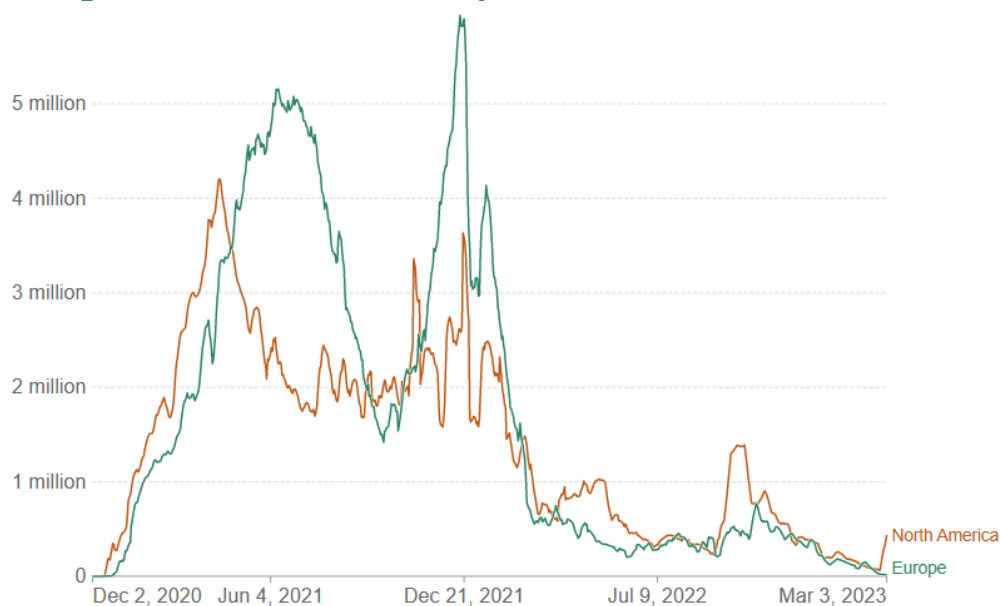
Establishing the safety profile of ABNCoV2 is the priority at this stage, but hopefully phase 3 results may also allow for therapeutic claims, such as trending superior immunogenicity and durability. The absence of an added adjuvant may also prove to be a selling point. Otherwise, the unique selling point at launch point may be limited to pricing and the convenience of storage in room temperature. The phase 3 program will include a pivotal long-term follow-up of immunogenicity durability of ABNCoV2. Assuming a rolling submission of data, 12-months durability may be ready in time to a launch late 2024.

## Sharp decline in vaccinations

According to data from Our World in Data, a public database, the daily number of global vaccinations has fallen well below 1.0 million doses per day from a peak in 2021 at 44 million doses per day. If the current vaccination rate is extrapolated into 2024, we should expect total volumes for next year to dwindle down to below 400 million doses compared to around 8 billion in 2022.

This compressing scenario can be turned over by new outbreaks and difficult to treat mutations. However, our best guess is that volumes will continue to suffer as the pandemic moves to an endemic phase in 2023, where governmental reimbursements are wound down.

## Falling vaccination rates in Europe and N-A



Source: Our World in Data, based on official data

We expect Bavarian Nordic to launch in North America and Europe, which are making up a minor part of the possible 400 million global vaccination doses in 2024. A rough estimate would be 100 million annual doses, primarily in the US. In Europe the current vaccination levels are close to 20 000 per day, making a market estimate for 2024 difficult, mostly depending on if Covid-19 will be dealt with as an influenza requiring annual revaccination.

Since we expect ABNCoV2 to be launched in mid to late 2024, after regulatory review of 10-12 months, we expect it to be targeting a market over the period 2024-2028 of some 400 million doses accumulated. Our best guess is that ABNCoV2 will sell 57 million doses during this period, corresponding to a market share of 15 percent.

This scenario assumes that ABNCoV2 will be able to differentiate itself from the dominating products from Pfizer and Moderna, mainly by longevity of antibody titers, but also from the current inflow of new vaccines, such as vaccines from J&J, Novavax and Sanofi/GSK. We have assumed a EUR 40 per dose selling price for ABNCoV2 (EUR 35 in previous report), well below the mRNA vaccines which are expected to sell at prices around EUR 100 per dose in 2023.

In 2021, Pfizer launched Comirnaty at USD 19.50 per dose to the U.S. government, increasing to about USD 30 per shot in June this year. The company has recently said that next year private payers may be charged as much as USD 130 to compensate for falling volumes.

## Panel recommendation to FDA

On January 26 the Vaccines and Related Biological Products Advisory Committee held a meeting to address a question from the US Food and Drug Administration how to simplify the current procedures of

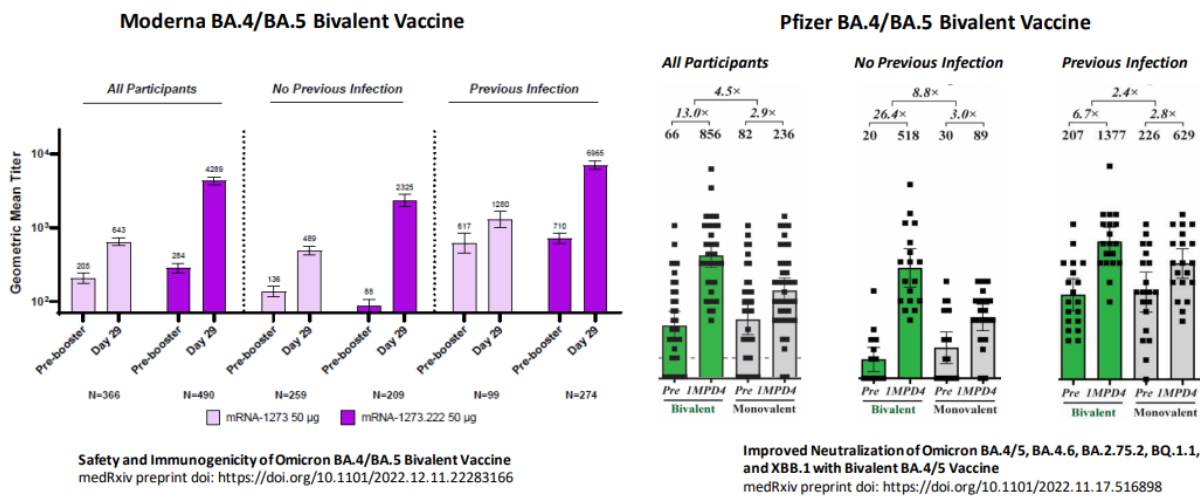
Covid-19 vaccination. The invited experts supported plans at the FDA to harmonize the different vaccine types and doses approved.

We interpret this recommendation so that the monovalent vaccines, which were originally approved in 2021 based on the ancestral Wuhan strain of the SARS-CoV2 virus, will be phased out in favor of more recently approved bivalent products. This decision would be based on data implying superior immunogenic efficacy with the bivalent mRNA-based products, which have recently been launched by Pfizer and Moderna.

The Committee voted unanimously to recommend that the FDA moves toward currently approved bivalent vaccines which have been construed to raise an immune response both to the ancestral Wuhan strain as well as to the Omicron B4/B5 strain. A consequence of such a decision would be that both primary and booster vaccinations would be carried out with the same products.

At this point in time, it is unclear to us how FDA will deal with the older monovalent Covid-19 vaccines. In the figure below it can be seen that the bivalent Pfizer and Moderna products (violet and green bars) appears to raise a superior immunogenicity to the Omicron BA.4/BA.5 variant compared to the monovalent precursors (light violet and grey bars).

### Omicron BA.4/BA.5 Neutralization – Data from vaccine manufacturers



Source: FDA presentation at January 26 advisory committee meeting

At the FDA meeting a medical officer presented data suggesting an advantage in immunogenicity of the bivalent versions from Pfizer and Moderna compared to the monovalent versions (chart above). Data is obtained from manufacturers Pfizer and Moderna, but invited experts stressed that there have been no randomized trials comparing monovalent BA.4/BA.5 vaccines to the approved bivalent products.

### Shifting landscape for Bavarian Nordic

In the ongoing phase 3 trial of ABNCov2, Bavarian Nordic is comparing its vaccine candidate to the monovalent version of Pfizer's Comirnaty. It is possible that a change in the first-line vaccine procedure to a bivalent product, in theory, may raise the bar for an

US approval. However, in the phase 2 trial with ABNCoV2, it showed a broad and promising immune response of neutralizing antibodies to all principal variants of SARS-CoV2, such as the ancestral Wuhan strain, a Delta variant, and the Omicron BA.1 variant, even if the response to Wuhan appeared to be more pronounced than to Omicron BA.1.

ABNCoV2 is also a monovalent vaccine since its antigen part is strictly based on the Wuhan spike protein. At this point in time, it is unclear if an expected change in the vaccination procedure in the US will have a regulatory impact on the expected approval process for ABNCoV2.

### Advisors call for broader and longer protection

At the FDA committee meeting on January 26, which included twenty-one invited specialists, non-voting comments of importance to the industry pleaded for new protein-based vaccines. Experts characterized the approved mRNA vaccines as having a short duration. There was a call for new vaccines developed by other technology platforms than mRNA, such as the Novavax monovalent vaccine Nuvaxovid, which later can be changed to a bivalent form. In this context, there should be an interest also for the protein-based ABNCoV2 vaccine candidate. This product is based a nanotechnology structure called capsid virus-like particle (cVLP), while the attached antigen spike protein should be identical to the Novavax product.

We believe that the recommendation at the advisory committee meeting should not be seen as a ban of developing monovalent vaccines. On the contrary, requests following the vote encouraged development based on new protein-based technologies. As long as a new vaccines can prove non-inferiority in the short run and later also a more long-lasting immunogenic duration compared to the mRNA products, there will a clear commercial path forward for such a products.

It was also concluded at the meeting that by simplifying the vaccination procedure it will be easier for platforms competing with the mRNA platform to reach the market. At the meeting FDA also made clear that it expects to see regular product updates of the spike-protein used in the vaccines as new variants of the SARS-CoV2 virus surge.

## Investment in ES2B-C001

The proposed rights issue in 2023 is primarily aimed at investments in the breast cancer vaccine candidate, ES2B-001. Later this year, management expects to release toxicology findings in primate models. An Investigational New Drug application is expected to be filed beginning of 2024, a minor delay from the previous timeline in the Q4 report, when the IND was expected to be sent in end of 2023.

We expect first patient to start testing in mid-2024. However, this program has been delayed a few of times since ExpreS<sup>2</sup>ion Biotechnologies acquired rights to the program in 2021 from AdaptVac, where it swapped a 16-percent stake for the rights. ExpreS<sup>2</sup>ion Biotechnologies now holds a 34 percent stake in AdaptVac.

## Financial discussion and valuation

Expres<sup>2</sup>ion Biotechnologies holds an approximate 1 percent stake in future Bavarian Nordic sales of ABNCoV2 and more importantly a 34 percent stake in AdaptVac, which in turn holds a +10 percent share of ABNCoV2 income. The 34 percent stake in AdaptVac is, in our opinion, continuing to be the most valuable asset of Expres<sup>2</sup>ion. After a potential launch of ABNCoV2 in 2024-25 AdaptVac may end up as a pile of royalties and milestones from Bavarian Nordic.

The distribution of this potential cash pile remains to be decided, but in the press release on the proposed rights issue, management says that Expres<sup>2</sup>ion could potentially “monetize its 34% stake in AdaptVac through e.g., dividend pay-out.....”.

According to the Bavarian Nordic annual report the company may pay milestones of up to 300 MDKK, or approx. 40 MEUR, to AdaptVac in 2023. We expect a part of this, to be distributed to shareholders in 2024. We have assumed a 50 percent distribution of free cash flow, which may prove to be both reasonable or optimistic. The control of AdaptVac lies with NextGen Vaccines, holding the 66 percent of the AdaptVac shares.

In our long term valuation of AdaptVac we speculate that a 80 percent of the cash pile will be distributed to shareholders over the period 2025-29. It may also be speculated that Bavarian Nordic has a unique possibility to gauge the success of the vaccine candidate ABNCoV2 and that it may decide to launch a bid for AdaptVac in case the program develops in a favorable direction.

### Milestones beyond 2023

AdaptVac may receive a remaining total of up to EUR 132 million in development and commercial milestone payments from Bavarian Nordic, according to the agreement from 2020. Given our sales scenario for ABNCoV2 we expect milestones of EUR 96 million to be paid in milestones over the period 2023-29.

By the end of 2022 Bavarian Nordic had booked a deferred liability to AdaptVac of DKK 533 million, or EUR 72 million, as a net present value of future development and commercial milestones, a lower number than the total value at EUR 132 million. We speculate that EUR 72 million may be paid to AdaptVac in the course of 2023-26 and the remainder is yet to be concluded depending on the sales performance of beyond 2026.

We have assumed AdaptVac to receive a 11 percent royalty on sales of ABNCoV2. Out of this revenue stream we expect Expres<sup>2</sup>ion to catch 11 percent, i.e., about 1 percent share of sales of ABNCoV2. On top of this Expres<sup>2</sup>ion is entitled to receive EUR 2 mln in commercial milestones from AdaptVac when ABNCoV2 is launched, which we expect to happen in 2024.

## SOTP lowered to SEK 12 (25)

Our NPV calculation of AdaptVac ends up at SEK 1,2bn out of which Expres<sup>2</sup>ion Biotechnologies holds 34 percent. In our valuation of the



AdaptVac holding we expect 80 percent of the cash pile in AdaptVac to be distributed to its shareholders in 2023-29. At this point in time, we value ExpreS<sup>2</sup>ion's holding at 4,1 SEK/share, which is on top of the 1,7 SEK/share coming from the royalty stream.

Our sum-of-the-parts valuation of ExpreS<sup>2</sup>ion Biotechnologies is SEK 12/share, down SEK 13 since our previous report. The reduction is primarily a result of dilution and lower Covid-19 vaccination forecasts. We have raised the assumed price per dose of ABNCoV2 to EUR 40 (35).

### Sum-of-The-Parts valuation of ExpreS<sup>2</sup>ion Biotech

	<b>Project value (MSEK)</b>	<b>Value / share (SEK)</b>	<b>Peak sales (MEUR)</b>	<b>LOA*</b>	<b>WACC</b>	<b>Share of NPV</b>	<b>Comments</b>
ES2B-C001	254	3,2	2 412	16%	14%	100%	Phase 1 in 2024
Royalty, ABNCoV2	137	1,7	2 415	64%	9%	100%	11% of Adaptvac
Adaptvac holding	325	4,1		64%	9%	34%	of DCF value
Platform	50	0,6	0,9	100%	7%	100%	cash flow based
Malaria project	110	1,4	175	21%	14%	10%	of consortium
Indigo (influenza)	30	1,0	952	5%	12%	10%	of consortium
Sum	906	12,0					<i>based on no. of shares end of 2023, mln 79,4</i>
							<i>*) Likelihood of approval current number of shares, mln 37,6</i>

Forecasts by Analysguiden

### ExpreS<sup>2</sup>ion exposure to ABNCoV-2, three scenarios

	<b>Slow scenario</b>	<b>Main scenario</b>	<b>Strong scenario</b>	<b>Comments</b>
Aggregated sales , EURm	1 000	2 415	4 500	57 mln doses sold in main scen
EUR per dosis	40	40	40	Our assumption
Adaptvac royalty from Bavarian	7%	11%	13%	Single digit to double digit
ExpreS <sup>2</sup> ions royalty from Adaptvac	11%	11%	11%	Double digit number
<i>royalty of vaccine net sales</i>	<i>0,8%</i>	<i>1,2%</i>	<i>1,4%</i>	
ExpreS <sup>2</sup> ion revenues, EURm	8	29	64	Over period 2023-2028
<i>in SEKm</i>	<i>85</i>	<i>321</i>	<i>708</i>	
Milestone from Adaptvac, SEKm	20	20	20	EUR 2m on first sales in 2024
ExpreS <sup>2</sup> ion revenues, SEKm	105	341	728	
SEK/share	1,3	4,3	9,2	
Tax rate	18%	18%	18%	Assuming full taxation
Likelihood of Approval (LOA)	64%	64%	64%	80% phase 3, 80% regul.risk
Risk-adjusted after tax, SEK/share	0,7	2,3	4,8	Not discounted, see SoTP

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Assumptions in Net Present Valuation of ExpreS<sup>2</sup>ion Biotech

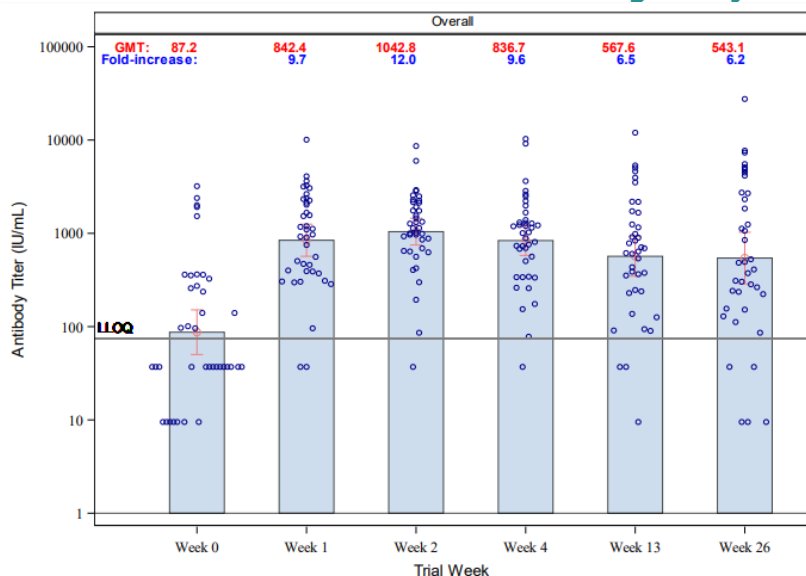
SEKm	2021	2022	2023p	2024p	2025p	2026p	2027p	2030p
Operating income	14	6	13	46	42	144	56	0
<i>ABNCoV-2</i>	0	0	7	41	34	48	47	0
<i>ES2B-C001</i>			0	-3	0	87	0	153
<i>platform/services</i>	5	6	6	7	8	9	9	9
EBIT	-48	-127	-151	-138	-72	2	3	
Cash	139	111	267	128	55			
ABNCoV-2 (EURm)	2021	2022	2023p	2024p	2025p	2026p	2027p	2030p
Net sales		0	0	206	395	569	546	
<i>EUR/dosis</i>		40	41	41	42	42	42	
<i>No. of doses, mln total of 41</i>		0	0	5	10	14	13	
ExpreS <sup>2</sup> ion milestones, EURm	0	1	0	0	0	0	0	
Royalty, MEUR		0	0	2	5	7	7	
<i>Royalty rate</i>			#####	0,8%	1,2%	1,2%		
Expres2ion revenues, SEKm	0	11	0	17	53	76	73	
<i>Risk-adjusted</i>	1,00	1,00	0,80	0,80	0,64	0,64	0,64	
Risk adjusted revenues, NPV (SEKm)		0,0	0,0	11,2	33,7	48,5	46,5	
WACC	9%							
NPV, royalty (SEKm)	137							
NPV/share, SEK	1,7							
LOA	64%							
ES2B-C001 (SEKm)	2021	2022	<i>Licens</i>	2024p	2025p	2026p	2027p	2030p
Costs, preclinical / clinical	-40	-24	-20	-14	0	-50	0	-75
<i>incl milestones to Adaptvac</i>	-3,5	-3,5	0	-14	0	-50	0	-75
Sales, EURm							0	946
Milestones, licensing partner	600		0	0	0	100	0	150
<i>Royalty 15%</i>							0	142
Expres2ion revenues, SEKm			0	-14	0	1050	0	3136
<i>Risk-adjusted</i>	0,95	0,71	0,71	0,32	0,18	0,16	0,16	0,16
Risk adjusted revenues, NPV (SEKm)			0	-3	0	87	0	153
WACC	14%							
Net present value (SEKm)	254							
NPV/share, SEK	3,2							
LOA	16%							

Forecasts by Analysguiden

## Appendices - Immunogenicity duration in phase 2

During 2022 Bavarian Nordic announced phase 2 six-month data on immunogenicity of ABNCoV2, its unadjuvanted recombinant protein vaccine candidate. The largest cohort in this booster study was made up of 103 seropositive participants, subjects previously vaccinated or infected by the virus. Out of these 103 patients 41 showed up at a six-months check, where two of them were found reinfected by the virus. In the remaining sample of 39 uninfected patients, antibody titers were measured and showed a certain loss of immunogenicity from baseline and 1 month data. In the table below we interpret this loss as a 48 percent decline, a geometric mean titer going from 1 042 IU/mL at the week 2 post shot peak to 543 IU/mL at week 26. This waning of antibodies over a 24-week period is commented by the company as suggesting a slower waning than compared with market leading mRNA products.

### Six-months data on Wuhan virus immunogenicity



Source: Bavarian Nordic Q3 presentation

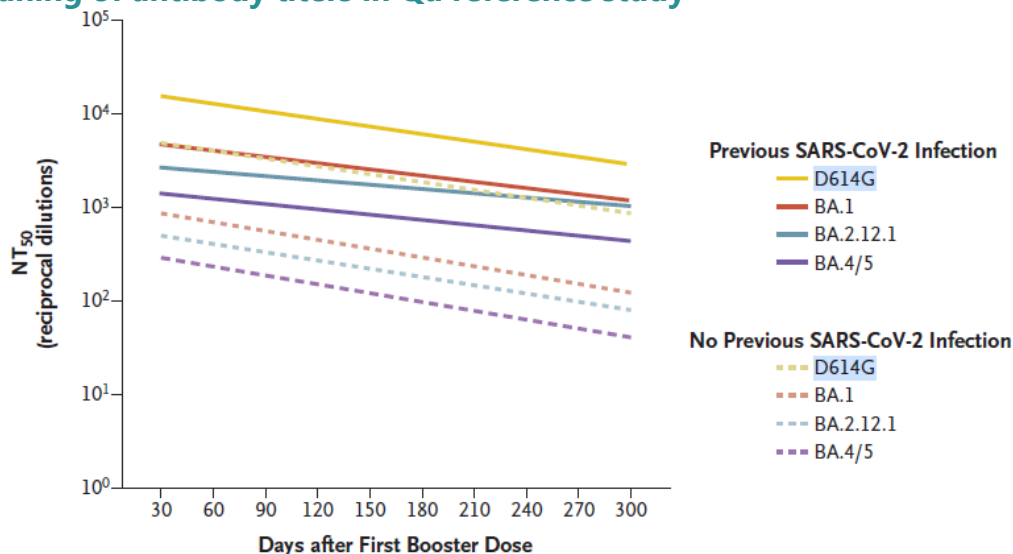
In one of the references provided by Bavarian Nordic, the authors discuss their results of waning of antibodies of different targets in a cohort of 46 health workers at the Ohio State University Hospital. Overall, the authors conclude that titers of neutralization antibodies were on average 1,7 times higher during months 1-2 compared to months 7-9<sup>1</sup>.

This study did not look at the specific wildtype Wuhan variant. It also concluded that the decline was more rapid in subjects not previously infected by SARS-CoV-2 (seronegative) subjects, while the Bavarian study is made up of seropositive participants. This group is referred to hybrid immunity subjects, having both been infected and

<sup>1</sup> Qu et al. Durability of Booster mRNA Vaccine against SARS-CoV-2 BA.2.12.1, BA.4, and BA.5 Subvariants (letter to New England Journal of Medicine)

vaccinated. Other studies have pointed out age as a decisive factor of the rate of decline for neutralizing antibodies

### Waning of antibody titers in Qu reference study



Source: Qu et al, NEJM 387;14

Looking more closely at the seropositive patients in the Qu et al study, data showed a monthly decline in the range of 10-15 percent, depending on the virus type. A 10 percent decline over a 24-week period would correspond to a 53 percent decline, not markedly inferior to the numbers reported by Bavarian Nordic, while a 15 percent monthly decline would make ABNCoV2 look clearly more potent.

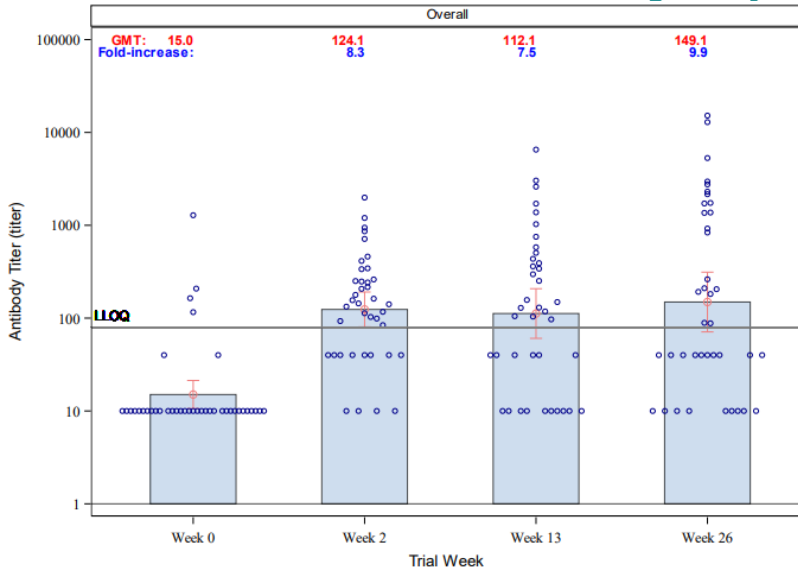
In another reference provided by Bavarian Nordic<sup>2</sup>, the decline of neutralizing antibodies to the Wuhan variant in patients with hybrid immunity after a booster with mRNA vaccine was 42 percent during a three-months period, which suggests a faster runaway than in the other reference.

The most surprising information in the Bavarian presentation in our eyes is perhaps the antibody data for the omicron BA.1 variant (see table below). These data suggest there was no waning of the antibody titers. This finding should partly be seen in the light of very low baseline titers which makes the data difficult to interpret.

Since the Bavarian Nordic releases is based on a small uncontrolled cohort, we must conclude that six-months data looks very promising but will have to be repeated in a larger setting before any firm conclusion can be drawn. It remains unclear to us if ABNCoV2 by the time of its approval, possibly early in 2024, will be able to make substantiated claims as to superior longevity or durability of the product's immunogenicity to the omicron strains.

<sup>2</sup> Bellusci et al. Antibody affinity and cross-variant neutralization of SARSCoV-2 Omicron BA.1, BA.2 and BA.3 following third mRNA vaccination

## Six-months data on Omicron BA.1 immunogenicity



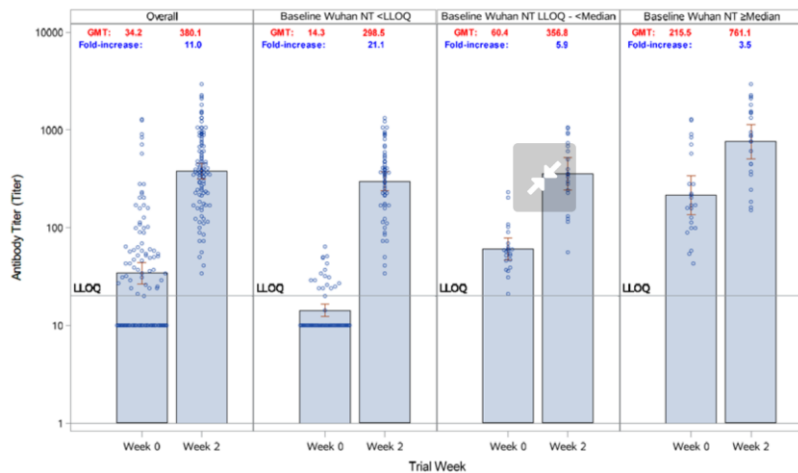
Source: Bavarian Nordic Q3 presentation

In the literature it is also stressed that a decline in neutralizing antibodies should be an expected immune response once a person is recovered from an infection. Some authors also claim that it is not necessary a negative finding if circulating memory B cells are present in blood stream.

First results from the phase 2 study of ABNCoV2 were presented in late 2021. Results for the three virus variants Wuhan (the wild type), Alpha and Beta were showing strong antibody responses (2- to 40-fold higher levels compared to Wuhan baseline) two weeks after the booster shot.

As for the currently dominating Delta variant a slightly less potent booster effect was recorded, a 4 to 21-fold increase in levels of neutralizing antibodies (highlighted in blue in graph below). These levels still qualify for a highly potent immunization to the virus.

## ABNCoV2 immunization to SARS CoV2 Wuhan variant



Source: Bavarian Nordic

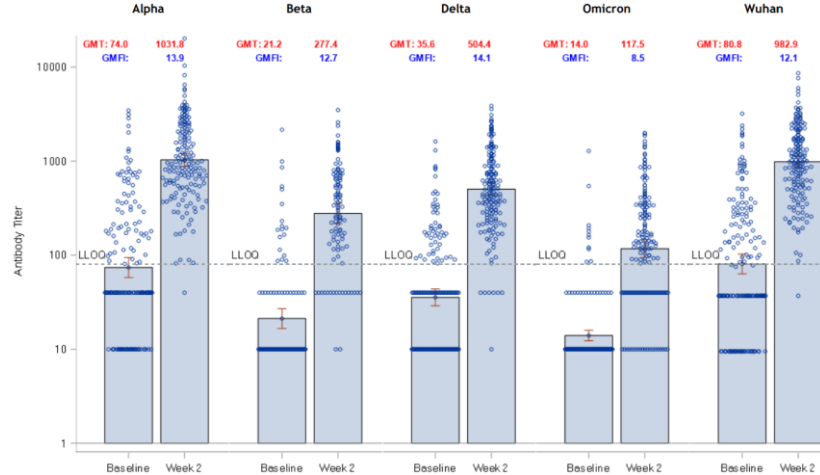
Moderna's Spikevax 50 µg dose has shown equally strong immunization boost to Delta as to Beta and Gamma (see below).

These relative computations of increases of antibody levels have to be made carefully as they are entirely dependent on the baseline values, which makes it very difficult to compare this phase 2 trial to other phase 2 trials. In general, we believe that Bavarian Nordic has set itself a difficult comparison, with a shorter interval down to 90 days after the prime vaccination.

### ABNCoV2 vaccination grade below 96 percent

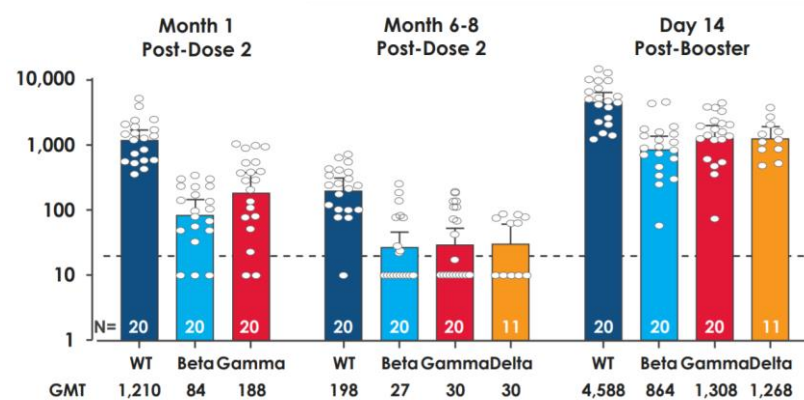
However, when looking at the absolute levels of neutralizing antibodies in subjects infected with the Delta variant, the currently dominating variant, they are trending well below the 1 000-mark (see graph above). This mark believed to correspond to a 96 percent vaccination effect. In Moderna phase 2 data we still read the mean titers as being well above the 1 000 mark, corresponding to a vaccination grade above 96 percent (see graph below). Again, the ABNCoV2 values for the Delta variant are retrieved with a different assay than the 50 percent neutralizing titer assay which is the standard in the industry.

### Antibody levels with ABNCoV2 in phase 2 study results



Source: Bavarian Nordic

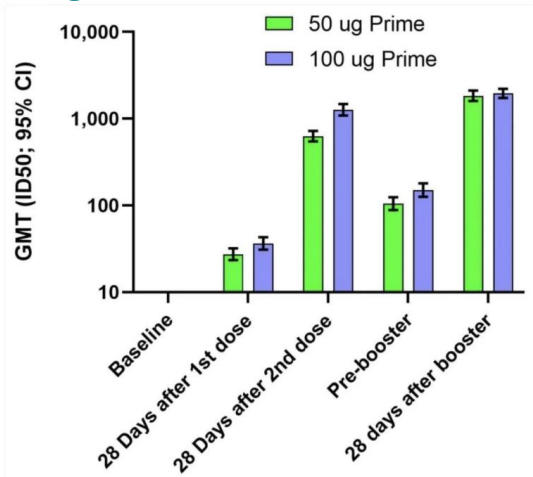
### Moderna shows 23 to-40-fold antibody increase



Source: Moderna study 201B, CDC presentation, October 21

Both Moderna and Pfizer claims higher neutralizing titers one month after the booster dose compared to one month after the prime vaccination. Pfizer-BioNTech Comirnaty (BNT162b2) booster dose at 30 µg shows a 99,5 percent seroresponse rate one month after the booster injection. The mean neutralizing antibody titers with Comirnaty were 2 455 at that point, substantially higher than seen in the Bavarian Nordic trial, but again based on a different assay for measuring the immunization boost.

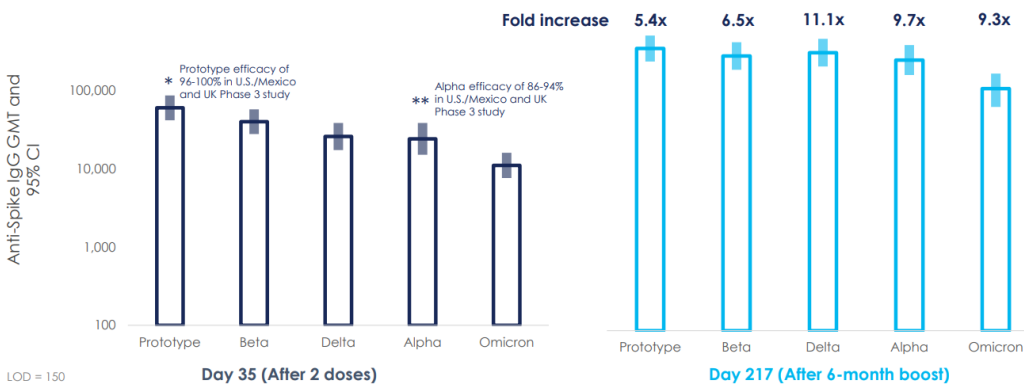
### Strong reneutralization with Moderna 50 µg boost



Source: Chu, L.(2021). Immune Memory Response After a Booster Injection of mRNA-1273

In the chart above we show data from another Moderna study of the booster properties of Spikevax to Wuhan and Delta strains. Participants immunized 6-8 months earlier with a primary series of two doses of 50 or 100 µg of mRNA-1273 were administered a booster injection of 50 µg of mRNA-1273. A single booster dose of Spikevax was shown to result in a geometric mean fold rise (GMFR) of 13,0 (95% CI: 11.04, 15.29) in neutralizing antibodies from pre-booster compared to 28 days after the booster dose.

### Booster responses to Nuvaxovid (Novavax)



Source: Novavax investor presentation

### The Danish financing agreement

In August 2021 Bavarian Nordic entered a funding agreement, valued at up to DKK 800 million, with the Danish Ministry of Health to provide the full financing of ABNCoV2 development towards

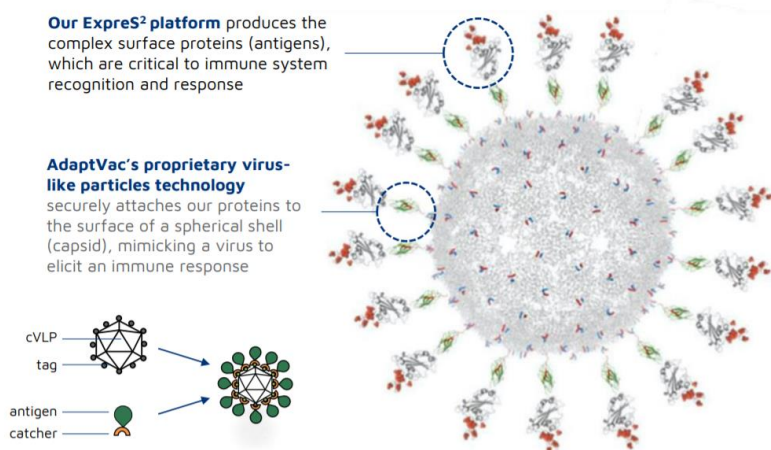
approval. The agreement included an upfront payment of DKK 80 million in October, in addition to payments of up to DKK 720 million. The additional payments are contingent upon reaching a number of predefined milestones including among others completion of the ongoing phase 2 trial, phase 3 development milestones and milestones related to upscaling of manufacturing for clinical and commercial production of the vaccine.

All payments are potentially subject to repayment, however only upon successful marketing authorization of the vaccine by the European Commission. Repayment may occur via supply of vaccines and royalty payments from the sale of the vaccine to other customers. Royalty payments are only triggered upon reaching a certain volume in sales. The Danish Ministry of Health could be entitled to an additional, capped royalty payment if the sales reach a certain threshold.

## Summary of the ABNCoV2 technology

We classify ABNCoV2 as a combined protein subunit antigen technology, provided by ExpreS<sup>2</sup>ion, coupled with a capsid Virus Like Particle (cVLP), provided by the AdaptVac platform. The capsid-like particle is coated with 60-80 particles of the recombinant RBD protein fragment. After exposure to the ABN vaccine, mice serum was tested for antibodies to the receptor binding domain of SARS-CoV-2. Researchers have shown in a Nature article that RBD proteins glued to the CLP had a 3-4-fold higher immunogenicity compared to soluble RBD proteins injected without being mounted to the capsid-like particle, a strong rationale for the technology behind the ABNCoV2 cVLP vaccine.

### Schematic figure of cVLP expression and construct



Source: Company presentation

## Potential advantages with ABNCoV2

ABNCoV-2 has the potential to be a very potent COVID-19 vaccine. The readouts from preclinical animal data suggests an equal or stronger activity of neutralizing antibodies after two dosages compared to most other published preclinical animal data, also from



currently approved COVID-19 vaccines, such as Pfizer-BioNTech's and Moderna's.

Preclinical evidence in mice of the potency for ABNCoV2 opens for a possibility of single shot dosing, even if the schedule in the first clinical study makes use of double dosing. It is also speculated that the capsid-based antigen display induces long-lived plasma T-cells, thus potentially conferring immunity for decades, as seen with the HPV vaccines, which are also based on a VLP construct. This would be a differentiating factor to other recombinant proteins, which run the risk of not eliciting long-lasting T-cell response.

An additional advantage with the technology being used by AdaptVac and ExpreS<sup>2</sup>ion is that it would be relatively easy to replace the current vaccine RBD antigen in the event that the SARS-CoV-2 virus should acquire mutations in the RBD domain and thereby reducing the efficacy of an existing vaccine. Another advantage being mentioned by the authors of the Nature article is that the vaccine does not contain any viral material and cannot infect the human cell.

### Summary of potential advantages

- Potent immunogenicity by neutralizing antibodies, also to newer SARS variants of concern,
- No genetic content in the vaccine may confer better safety,
- One single shot administration may be enough in booster indication,
- Long-lasting response with the cVLP adjuvant,
- Stable storage in room temperature, easy to handle

## Vaccine candidate in development

ES2B-C001 is ExpreS<sup>2</sup>ion Biotechnologies in-house proprietary program which is progressing toward a clinical trial in 2024. In May this year ExpreS<sup>2</sup>ion Biotechnologies announced positive preclinical proof-of-concept results for this HER2-breast cancer vaccine candidate from a therapeutic study in HER2-transgenic mice. In the study, all transgenic mice vaccinated with ES2BC001 formulated in an adjuvant were metastasis-free, while all control mice had lung nodules. Furthermore, 73% of mice vaccinated with ES2B-C001 without adjuvant were metastasis-free.

ExpreS<sup>2</sup>ion still has some way to carry this in-house program before entering a clinical phase 1 trial. In 2020 it was expected that the program would be ready for a CTA, Clinical Trial Application, in the first half of 2022. This CTA has for various reasons been pushed into 2024.

In 2020 the program was developed by AdaptVac and called AV001. In the option deal which ExpreS<sup>2</sup>ion struck with AdaptVac in February 2020 described AV001, later to be ES2B-C001, as having shown proof-of-concept in animal testing on mice in an article published 2018 by researchers at the University of Bologna. However, this study was based on a non-proprietary tag catcher method and had to be redone with a proprietary tag catcher system developed by AdaptVac.

These new proof-of-concept studies in animals have been published recently in two separate articles. ES2B-C001 is developed as a therapeutic vaccine for patients with HER2 positive breast cancer, having progressed after initial treatment with the standard anti-HER2 therapy Avastin (trastuzumab). In published research ES2B-C001 has demonstrated a strong tumor-growth inhibiting effect in a mice model and when blood serum from vaccinated mice was applied to cultures of HER2-positive human breast cancer tumors. ES2B-C001 has also shown successful results in HER2-transgenic preventive as well as therapeutic tumor mice models, where ES2B-C001 demonstrated effective inhibition of tumor development compared to control groups.

According to the recently published prospect, two weeks after the inoculation of tumor cells, the first vaccine administrations were given. ES2B-C001 formulated in an adjuvant was found to totally block tumor development, whereas the control group progressively expanded with lung metastases and subcutaneously growing local tumors. Additionally, ES2B-C001 without adjuvant was found to inhibit, but not prevent, tumor development.

### Competitive landscape in HER2+ breast cancer

About 15-20 percent of all breast cancers are HER2+, which makes any new treatment to a potential blockbuster. We note that there are several ongoing vaccine studies on HER2+ breast cancer. Clinicaltrials.gov lists 19 ongoing clinical trials when screening its data base. One of these is a 598-patient phase 3 trial, FLAMINGO-01, sponsored by Texas-based Greenwich Lifesciences, which is not yet recruiting. This competitive landscape needs to be looked into in order to understand the potential advantages of ExpreS<sup>2</sup>ion Biotechnologies lead program ES2B-C001.

We also note that in the second line setting of females with metastatic relapsing breast cancer after failing first line treatment with generic trastuzumab, AstraZeneca/Daiichi scored a recent success with its phase 3 program Enhertu. In the 557-patient study, those taking Enhertu survived for 23.9 months, as compared with 16.8 months for those who received standard chemotherapy. This is considered a very positive result in a difficult to treat patient setting and Enhertu is expected to change the current standard-of-care in second-line HER2+ breast cancer.

### Potential launch of ES2B-C001 in 2029-30

We currently see a potential for ES2B-C001 to reach the market in 2029-30, a delay compared to a previously 2027-28. We have assigned the program a 14 percent chance of reaching the market. We estimate that including the current capital raise of SEK 60 million, management has invested some SEK 100 million in ES2B-C001 and that this is reflected in our current valuation of SEK 185m. This corresponds to SEK 5 / share, if we assume that ExpreS<sup>2</sup>ion will not have to a new shares issue in 2024.

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