UPPDRAGSANALYS

# Promising long-term data

## Signs of superior immunogenic longevity

Bavarian Nordic recently released six-month data on its vaccine candidate ABNCoV2 in a group of 39 individuals taking part in its phase 2 study. Neutralizing antibodies to the SARS-CoV2 Wuhan variant declined less than 50 percent over the period, which may suggest a slower waning and a differentiation to the mRNA vaccines. Even more intriguing were data on the levels of the omicron BA.1 variant, showing no decline after six months.

We interpret the data set as not yet conclusive but still pointing at a potential claim of ABNCoV2 as having a more sustained immunogenic duration than mRNA vaccines.

## Bavarian puts safety first in phase 3

Bavarian Nordic kicked off its governmental-funded phase 3 study with ABNCoV2 in September. A first readout from the study is now expected in early 2023, a major potential trigger for ExpreS²ion Biotechnologies.

The phase 3 study design has had a makeover and will be divided into two separate parts, one of which will aim at proving non-inferiority, or equal efficacy, to the market leader Comirnaty. However, the lion's part of the study, 3 000 subjects, will further substantiate the safety and tolerability of ABNCoV2, which in our view may is conservative and wise disposal of resources.

## Vaccination rates falling abruptly in 2023

The rate of daily COVID vaccinations has fallen dramatically in recent month and appears to be heading further lower in spite of the flu season currently setting off in the norther hemisphere. The database Our World in Data keeps track of daily volumes of Covid-19 vaccinations and is currently at a daily 1.1 million doses, far below the peak at daily 44 million doses in June 2021.

Our best estimate is extrapolating the current level into 2023 which would correspond to a global number of vaccinations of 600-700 million in 2023 compared to close to 8 billion in 2022. Market value will not suffer nearly as much since manufacturers are raising prices substantially.

## Fair value lowered based on new volumes

In light of dwindling vaccination rates and a launch now likely in 2024 we are adjusting our forecast of doses sold in 2024-28 to 130 million (225), corresponding to a 17 percent share in US/EU, a share which may increase if long-term phase 3 data repeat the phase 2 longevity. Our estimate of lower volumes is partly compensated by a higher sales price for ABNCoV2. Fair value of our base scenario for ExpreS²ion is lowered to SEK 25 (30).

# ExpreS²ion Biotech

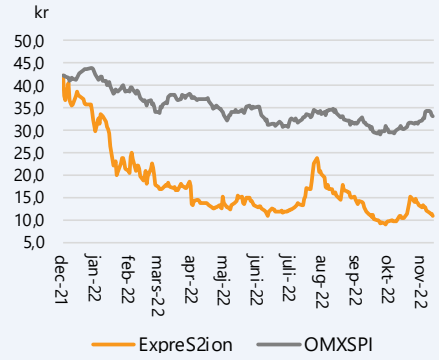
| | |
|---|---|
| Date | 18 november 2022 |
| Analyst | Sten Westerberg |

**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 11 |
| No. of shares, mln. | 37,2 |
| Market cap, SEKm | 410 |
| Cash 2022p, SEKm | 120 |

Web site www.expres2ionbio.com

**Kursutveckling senaste året**




Source: Refinitiv

**Forecasts & Key ratios, SEKm**

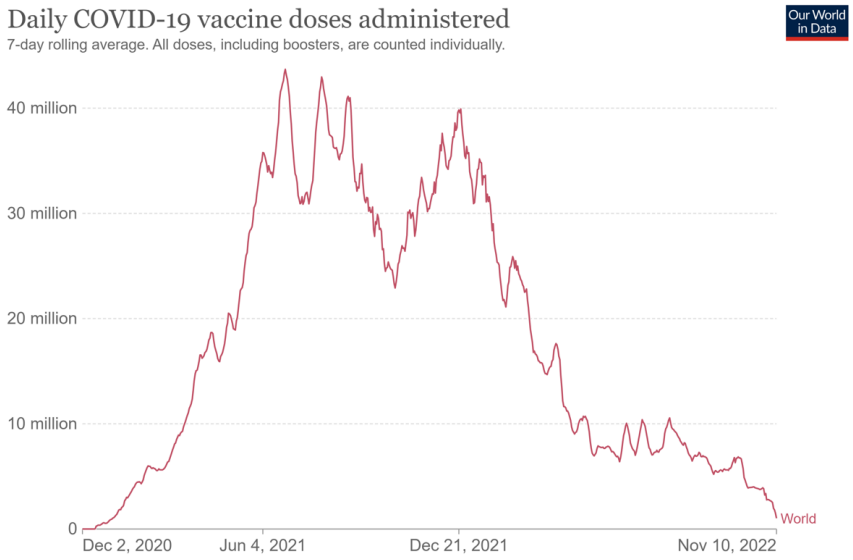
| | 2020 | 2021 | 2022p | 2023p |
|---|---|---|---|---|
| Revenues | 15 | 14 | 6 | 15 |
| EBIT | -29 | -48 | -104 | -106 |
| Net income | -36 | -44 | -108 | -109 |
| Earnings per share | -1,8 kr | -1,5 kr | -2,9 kr | -2,9 kr |
| Dividend | 0 kr | 0 kr | 0 kr | 0 kr |
| Revenue growth | 11% | -10% | -60% | 178% |
| Cash | 107 | 139 | 120 | 61 |
| New share issue | 133 | 83 | 61 | 50 |

Source: Bolaget, Analysguiden

# Covid vaccination rates dwindling

The current use of covid vaccines points to a sharp fall in the year to come. According to data from Our Would in Data, a public internet database, the daily number of global vaccinations has fallen to 1.7 million doses per day from a peak in June last year at 44 million doses per day. If the current vaccination rate is extrapolated into 2023, we should expect total volumes for next year to dwindle down to some 600-700 million doses compared to around 8 billion in 2022.

This volatile scenario can easily be turned over by new major outbreaks and more 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 also are wound down.




Source: Our World in Data, based on official data

At this point in time, we expect Bavarian Nordic to focus on the US and EU markets, which are making up only a part of the possible 700 annual vaccination doses in 2024. A rough estimate would be 200 million doses. Since we now expect ABNCoV2 to be launched in 2024, after regulatory review of 10-12 months, it will be targeting a market over the period 2024-2028 of some 850 million doses. Our base case is that ABNCoV2 will sell 130 million doses during this period, corresponding to a solid market share of 16 percent.

This scenario assumes that ABNCoV2 will be able to partly differentiate itself from the dominating products from Pfizer and Moderna, but also to the current inflow of new booster products, such as vaccines from J&J, Novavax and Sanofi/GSK. We have assumed a EUR 31 per dose selling price for ABNCoV2 (EUR 17 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.

## On the road to differentiation

Bavarian Nordic released its Q3 report last week including more data on its covid booster vaccine candidate ABNCoV2, currently in a 4 000-patient phase 3 program. The design of this program has been under discussion with regulatory agencies for some time and was finally kicked-off in September. In the Q3 report a minor delay was presented for the announcement of first results from the study, now expected to arrive in beginning of 2023.

The program is financed through a DKK 800m grant by the Danish government. Curiously, the study is divided in two different groups, one randomized group including 1 000 Danish and Belgian patients (Part A) and another non-randomized group 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 dominating strain in the initial phase of the pandemic, but at this point in time not very prevalent. All vaccines have so far been tested to this variant and it remains somewhat unclear how this parameter will impact recruitment.

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

### Focus on safety in current phase 3 program

We see this split design as a consequence of the high bar set for safety and tolerability of all SARS-CoV-2 vaccine. Since the AdaptVac VLP-technology is a new and partly unproven technology it may be speculated that regulators have been interested in more safety data than what is established in the phase 2 trial. Devoting three fourths of the phase 3 study population to substantiate safety instead of superiority to Comirnaty in a randomized fashion should be a relevant prioritization.

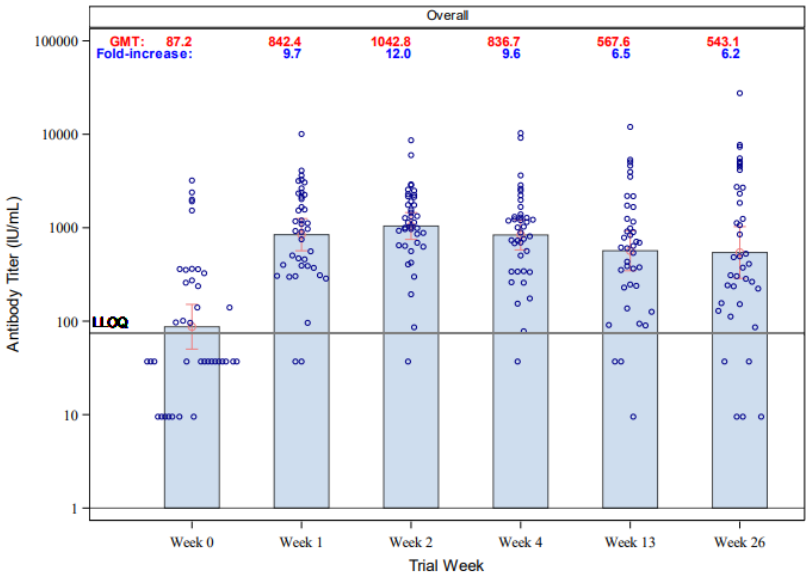
However, even if the smaller part A trial is designed to show statistical non-inferiority to Comirnaty, it cannot be excluded that a 1 000-patient sample will allow immunogenicity, i.e., the level of neutralizing antibodies, to trend towards superiority over Comirnaty. The opposite is off course also possible but seems less likely given the robust responses shown in phase 2.

The phase 3 program will also include long-term follow up of immunogenicity durability of ABNCoV2. Establishing the safety profile of ABNCoV2 is still the obvious priority at this stage, but hopefully the results may also make some therapeutic claims, unless the unique selling point should be pricing and the convenience of storage in room temperature.

# Immunogenicity duration in phase 2

At Bavarian Nordics teleconference, management spent some time discussing the recently 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-moths 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



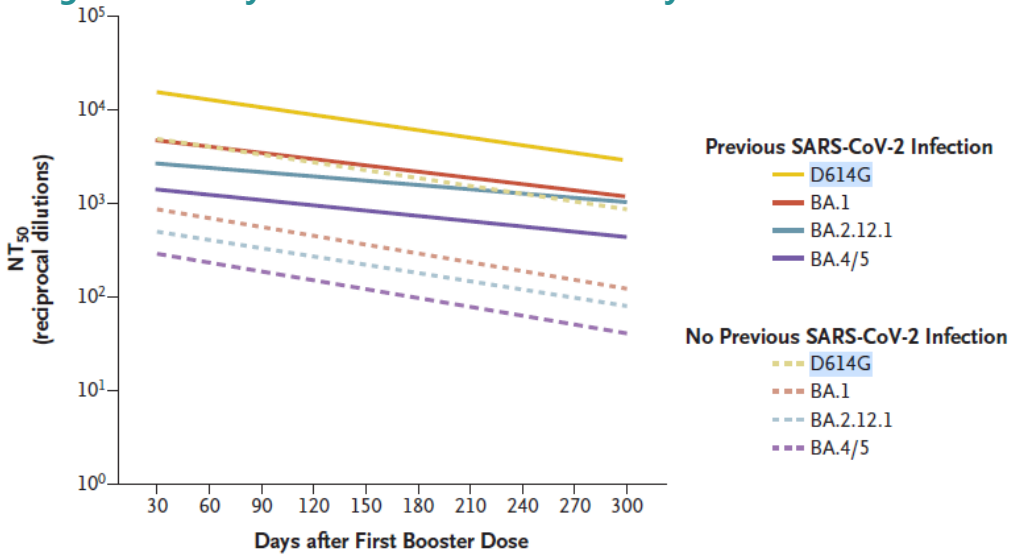

Source: Bavarian Nordic Q3 presentation

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[1].

[1] 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)

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 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.

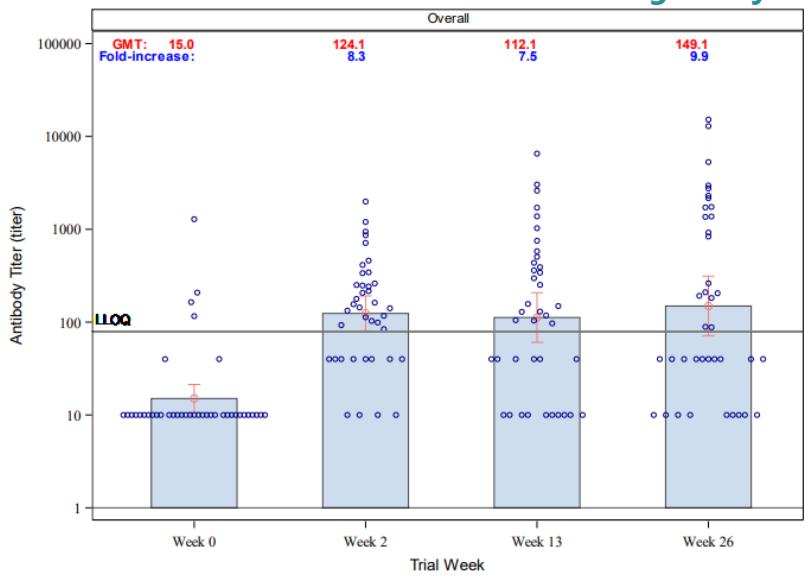
In another reference provided by Bavarian Nordic[2], the decline of neutralizing antibodies to the Wuhan variant in patients with hybrid immunity after a booster with mRNA vaccine was 42 percent during a three-months period, which suggests a faster runaway than in the other reference.

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.

[2] Bellusci et al. Antibody affinity and cross-variant neutralization of SARSCoV-2 Omicron BA.1, BA.2 and BA.3 following third mRNA vaccination

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 lager 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.

## 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.

# Mounting competition

Earlier this year Novavax launched Nuvaxovid, the first protein-based vaccine which bears some similarities with ABNCoV2. Nuvaxovid is expected to sell for USD 2bh in 2023, It differs in respect to that it is making use of an adjuvant, MATRIX M, while ABNCoV2 is unadjuvanted, solely depending on the VLP technology to raise an immune response to the mounted antigen. Nuvaxovid appears crucially dependent on the extrinsic adjuvant, while ABNCoV2 does not, which may prove to be a potential safety benefit.

Another booster vaccine, VidPrevtyn Beta from Sanofi/GSK, was also recently approved by the European Medicines Agency. It said in its statement it concluded from studies based on blood analysis of participants that a booster dose of VidPrevtyn Beta should be at least as effective as Pfizer and BioNTech's first-generation shot at restoring protection against COVID-19.

The Sanofi/GSK vaccine has been substantially delayed in development. Initially it tested a bivalent product - meaning it was based both on original Wuhan strain of the virus and Beta – but later reversed to focus on a monovalent shot based on Beta variant only.

A variant of the Sanofi/GSK vaccine VAT00002 recently showed strong boosting of immune response in an independent phase 3 study, COVIBOOST (VAT013). The proportion of participants with at least a 10-fold increase in neutralizing antibody titers for the original D614 SARS-CoV-2 strain between day 0 and day 15 was:

- 76.1% for the Sanofi-GSK next-generation booster, vs
- 63.2% for the Pfizer BioNTech D614 booster, and
- 55.3% for the Sanofi-GSK D614 (first-generation parent booster candidate).

In spite of the stronger response of the bivalent variant Sanofi-GSK chose to move forward with the monovalent Beta version.

## Market opportunity for Bavarian

We see chances of ABNCoV2 reaching non-inferiority to Comirnaty as high as 80 percent, based on clinical data on the Wuhan strain which has been presented in phase 2. This speaks in favour of a rolling submission to regulatory agencies starting in the first half of next year. However, the regulatory risk that ensues cannot be neglected. In the case of ABNCoV2, regulators may have difficulties reaching a conclusive view on safety based on the 4 000-patient sample. For example, the most comparable vaccine to ABNCoV2, Nuvaxovid, faced a rigorous safety review at the FDA, in spite of already being approved in EU. It also included an FDA Panel discussion, which arrived at a favourable conclusion on June 7.

Nuvaxovid has been tested in more than 50 000 individuals and is likely to be used primarily as a booster vaccine. It is a protein-based vaccine, just as ABNCoV2, and has other structural similarities to ABNCoV2. It differs in respect to that it is making use of an adjuvant, MATRIX M, while ABNCoV2 is unadjuvanted, solely depending on the VLP technology to raise an immune response to the mounted antigen. Nuvaxovid contains 5 µg per dose of the Wuhan spike protein compared to 100 µg of the ABnCoV2. To this Nuvaxovid adds 50 µg per dose of the MATRIX M adjuvant.

Still, we have an 85 percent chance of a positive regulatory review of ABNCoV2 passing FDA and EMA. Our compounded likelihood of approval upon initiation of the phase 3 trial is 68 percent.

# Financial discussion and scenarios

ExpreS²ion Biotechnologies holds an approximately 1 percent stake in future Bavarian sales of ABNCoV2 and more importantly a 34 percent stake in AdaptVac, which holds a +10 percent stake in the Bavarian program. Since Bavarian Nordic has a unique possibility to judge the success of the vaccine candidate it can be speculated that it would launch an offer to acquire ExpreS²ion Biotechnologies as the phase 3 trial approaches a read-out.

It may be speculated that Bavarian Nordic is even more interested to acquire AdaptVac, where Expres²ion holds a 34 percent share of the equity. The control of AdaptVac lies with NextGen Vaccines, holding the remaining 66 percent of AdaptVac. Except the royalty stream AdaptVac may receive up to EUR 136 million in milestone payments.

Given our sales scenario we expect EUR 100 million to be paid in milestone over the period 2023-27. We no longer expect Bavarian Nordic to pay a milestone upon the initiation of the phase 3 trial in September. The distribution of milestone payments which AdaptVac will receive from Bavarian Nordic is a source of uncertainty in the valuation of ExpreS²ion Biotechnologies. ExpreS²ion is a minority holder in AdaptVac and is not in control of future dividend payments. We expect only a minor part of these to be paid as dividend to the shareholders of AdaptVac in the 2023-24. The lion part is likely to stay in operations of AdaptVac, an assumption which may prove to be wrong.

Bavarian Nordic has booked a liability of DKK 596 million, or EUR 75 million, as a net present value of future development and sales milestone to be paid to AdaptVac, a lower number than the total value at EUR 136 million of the milestones presented in the 2020 deal with AdaptVac. We speculate that EUR 75 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 ExpreS²ion to catch 10 percent, i.e., about 1 percent share of sales of ABNCoV2. On top of this ExpreS²ion is entitled to receive EUR 2 mln in commercial milestones from AdaptVac, which we expect to occur in 2024. This may not be enough to be able to take ES2B-C001 into clinical development in 2024 and a new share issue in 2024 cannot be ruled at that point in time.

# Value of the AdaptVac holding

Our NPV calculation of AdaptVac ends up at SEK 1,3bn out of which ExpreS²ion Biotechnologies holds 34 percent after having swapped its initial 50 percent holding for the exclusive license of ES2B-C001 in 2021. In our valuation of the AdaptVac holding we expect 80 (85) percent of the cash pile in AdaptVac on the commercialization of ABNCoV2 to be distributed to its shareholders in 2026-28. This is a rough way of getting to a valuation and it may prove wrong. However, to include a 100 percent at this point in time is not possible in our view, since we expect AdaptVac to make us of some of its cash in other projects.

## Sum-of-The-Parts valuation of ExpreS²ion Biotech

| | Project value (MSEK) | Value / share (SEK) | Peak sales (MEUR) | LOA* | WACC | Share of NPV | Comments |
|---|---|---|---|---|---|---|---|
| ES2B-C001 | 186 | 4,6 | 2 052 | 14% | 14% | 100% | Phase 1 in 2024 |
| Royalty, ABNCoV2 | 232 | 5,7 | 4 334 | 68% | 9% | 100% | 11% of Adaptvac |
| Adaptvac holding | 405 | 9,9 | | 68% | 9% | 34% | of DCF value |
| Platform | 38 | 0,9 | 0,8 | 100% | 7% | 100% | cash flow based |
| Malaria project | 110 | 3,5 | 175 | 21% | 14% | 10% | of consortium |
| Indigo (influenza) | 30 | 0,6 | 952 | 5% | 12% | 8% | of consortium |
| Sum | 1 002 | 25 | *based on the no. of shares by end of 2022, mln* | | | | *37,2* |
| **) Likelihood of approval* | | | *based on the no. of shares by end of 2024, mln* | | | | *40,7* |

Forecasts by Analysguiden

On the other hand, in a future floating of AdaptVac it may prove that the stock market will assign a higher value to the AdaptVac technology. At this point in time, we value ExpreS²ion's holding at 9,9 SEK/share, which is on top of the 5,7 SEK/share coming from the royalty stream. Our sum-of-the-parts valuation of ExpreS²ion Biotechnologies is SEK 25/share, down from SEK 30 in our previous report.

The reduction in fair value is a result of lower expected vaccine volumes, which is partially offset by higher selling prices for the vaccine. We have also added a new number of shares for 2024 based on the belief that the likelihood of a new share issue has increased after the report for the third quarter, which showed a sharp cost increase.

## ExpreS²ion exposure to ABNCoV-2, three scenarios

| | Slow scenario | Main scenario | Strong scenario | Comments |
|---|---|---|---|---|
| Aggregated sales , EURm | 1 000 | 4 334 | 6 500 | 134 mln doses sold in main scen |
| EUR per dosis | 31 | 31 | 31 | Our assumption |
| Adaptvac royalty from Bavarian | 7% | 11% | 13% | Single digit to double digit |
| ExpreS²ions royalty from Adaptvac | 11% | 11% | 11% | Double digit number |
| *royalty of vaccine net sales* | *0,8%* | *1,2%* | *1,4%* | |
| ExpreS²ion revenues, EURm | 8 | 52 | 93 | Over period 2023-2028 |
| *in SEKm* | *85* | *577* | *1 022* | |
| Milestone from Adaptvac, SEKm | 20 | 20 | 20 | EUR 2m on first sales in 2024 |
| ExpreS²ion revenues, SEKm | 105 | 597 | 1 042 | |
| SEK/share | 2,6 | 14,7 | 25,6 | |
| Tax rate | 18% | 18% | 18% | Assuming full taxation |
| Likelihood of Approval (LOA) | 68% | 68% | 68% | 80% phase 3, 85% regul.risk |
| Risk-adjusted after tax, SEK/share | 1,4 | 8,2 | 14,3 | Not discounted, see SoTP |

Forecasts by Analysguiden, price inflation of 1 percent included in main scenario

At the current share price of SEK 12-13 we are under the impression that investors remain cautious about the commercial prospects for ABNCoV2, a view which we believe can start shifting as soon positive topline results from phase 3 are presented in a couple of months. ExpreS²ion has also suffered along with the rest of the biotech sector, which has been underperforming the market since interest yields started climbing beginning of 2022.

## A bull scenario at SEK 50

Our main scenario for ABNCoV2 is based on 17 percent share of projected Covid-19 vaccination doses during 2024-28. In a more bullish scenario, we can see market shares climbing well above that level once long-term safety and immunogenicity data allow Bavarian Nordic to claim a certain superiority over the mRNA vaccines.

A booster market share of 25 percent in EU and US would increase the value of the ABNCoV2 vaccine candidate to SEK 26, adding another SEK 10 per share of the other different parts of the portfolio. If we also raise the likelihood of approval to 75 percent from 68 percent in our base case, we end up a bull scenario value at SEK 45. It is also possible that the selling price of ABNCoV2 in such a scenario will be priced well above EUR 31 per dose, adding at least another SEK 5 to the valuation.

Other potential upsides to the share price are a bid from Bavarian Nordic and a swift regulatory action allowing for a launch in late 2023. At this point in time, we do not see these components in our base scenario. However, all these calculations are based on a total US and EU market of 850 million doses during the period 2024-28.

In a negative scenario, where ABNCoV2 is not able to show non-inferiority to Wuhan protection in the phase 3 trial, the project will be dropped and the share price may fall to level of 5-7 SEK per share, corresponding to our pre-money valuation of ES2B-C001.

## Assumptions in Net Present Valuation of ExpreS²ion Biotech

| SEKm | 2021 | 2022p | 2023p | 2024p | 2025p | 2026p | 2027p |
|---|---|---|---|---|---|---|---|
| Operating income | 14 | 6 | 15 | 90 | 108 | 172 | 70 |
| *ABNCoV-2* | *0* | *0* | *7* | *86* | *101* | *91* | *62* |
| *ES2B-C001* | | | *0* | *-3* | *0* | *73* | *0* |
| *platform/services* | *5* | *6* | *8* | *7* | *7* | *8* | *8* |
| EBIT | -48 | -104 | -106 | -26 | -8 | 2 | 2 |
| Cash | 139 | 120 | 61 | 34 | 25 | | |

| ABNCoV-2 (EURm) | 2021 | 2022p | 2023p | 2024p | 2025p | 2026p | 2027p |
|---|---|---|---|---|---|---|---|
| Net sales | | 0 | 0 | 1 062 | 1 223 | 1 111 | 748 |
| *EUR/dosis* | | *31* | *32* | *32* | *32* | *33* | *33* |
| *No. of doses, mln total of 128* | | *0* | *0* | *33* | *38* | *34* | *23* |
| ExpreS²ion milestones, EURm | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Royalty, MEUR | | 0 | 0 | 8 | 13 | 12 | 8 |
| *Royalty rate* | | | ####### | *0,8%* | *1,1%* | *1,1%* | |
| Expres2ion revenues, SEKm | 0 | 11 | 0 | 90 | 148 | 134 | 91 |
| *Risk-adjusted* | *1,00* | *1,00* | *0,80* | *0,80* | *0,68* | *0,68* | *0,68* |
| Risk adjusted revenues, NPV (SEKm) | | 0,0 | 0,0 | 61,2 | 100,6 | 91,5 | 61,6 |

| | |
|---|---|
| WACC | 9% |
| NPV, royalty (SEKm) | 232 |
| NPV/share, SEK | 5,7 |
| LOA | 68% |

| ES2B-C001 (SEKm) | 2021 | 2022p | *Licens* | 2024p | 2025p | 2026p | 2027p |
|---|---|---|---|---|---|---|---|
| Costs, preclinical / clinical | -36 | -24 | -20 | -14 | 0 | -50 | 0 |
| *incl milestones to Adaptvac* | *-3,5* | *-3,5* | *0* | *-14* | *0* | *-50* | *0* |
| Sales, EURm | | | | | | | 0 |
| Milestones, licensing partner 550 | | | 0 | 0 | 0 | 100 | 0 |
| *Royalty 15%* | | | | | | | *0* |
| Expres2ion revenues, SEKm | | | 0 | -14 | 0 | 970 | 0 |
| *Risk-adjusted* | *0,85* | *0,64* | *0,64* | *0,29* | *0,16* | *0,14* | *0,14* |
| Risk adjusted revenues, NPV (SEKm) | | | 0 | -3 | 0 | 73 | 0 |

| | |
|---|---|
| WACC | 14% |
| Net present value (SEKm) | 186 |
| NPV/share, SEK | 4,6 |
| LOA | 14% |

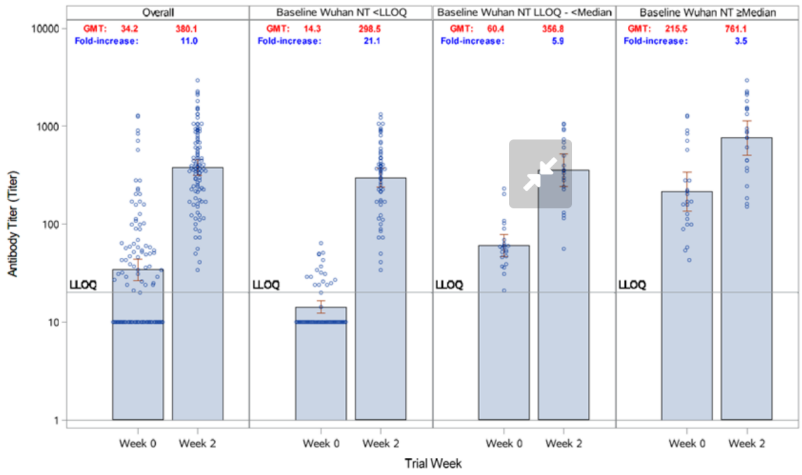
Forecasts by Analysguiden

# Appendices - Outcome of phase 2 study and competing landscape

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.

## ABNoV2 immunization to SARS CoV2 Wuhan variant



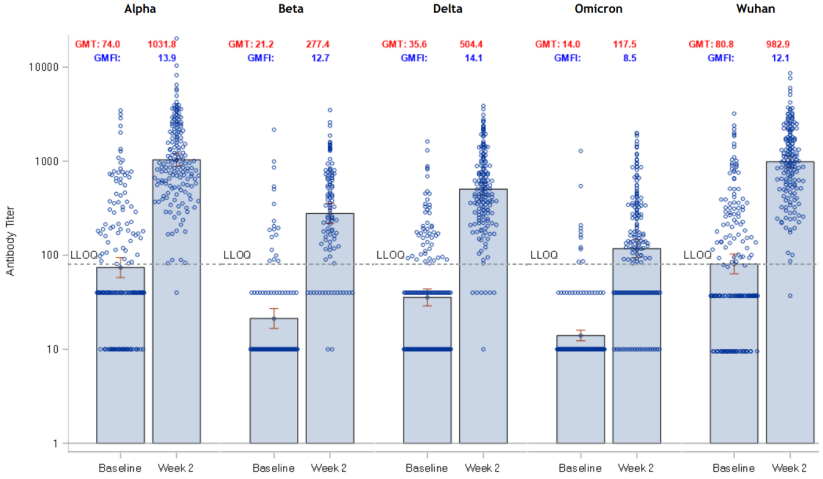

Source: Bavarian Nordic

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

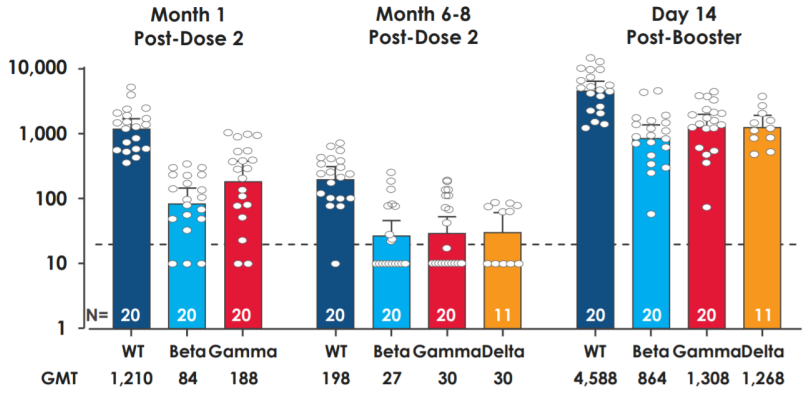
However, when looking at the absolute levels of neutralizing antibodies in subjects infected with the Delta variant, the currently dominating variant, they are trending well below the 1 000-mark (see graph above). This mark believed to correspond to a 96 percent vaccination effect. In Moderna phase 2 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

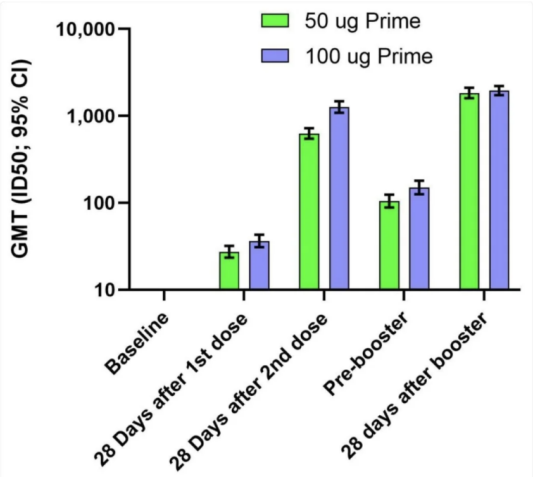
## Moderna shows 23 to-40-fold antibody increase




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.

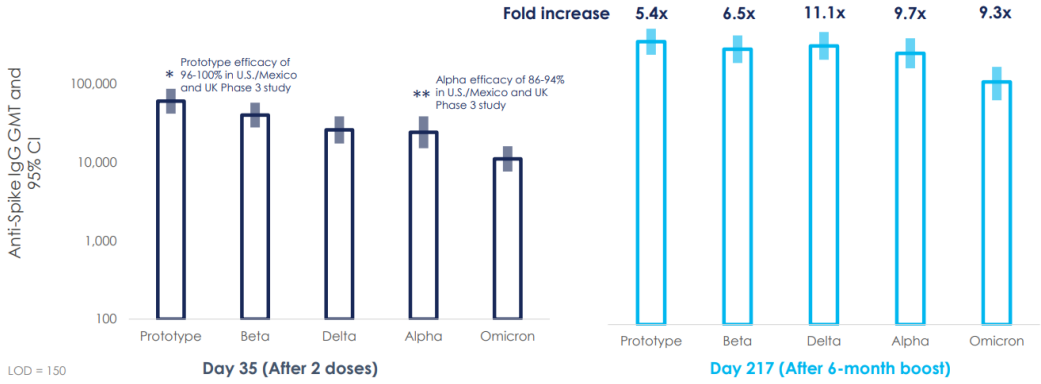
## Strong reneutralization with Moderna 50 µg boost




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

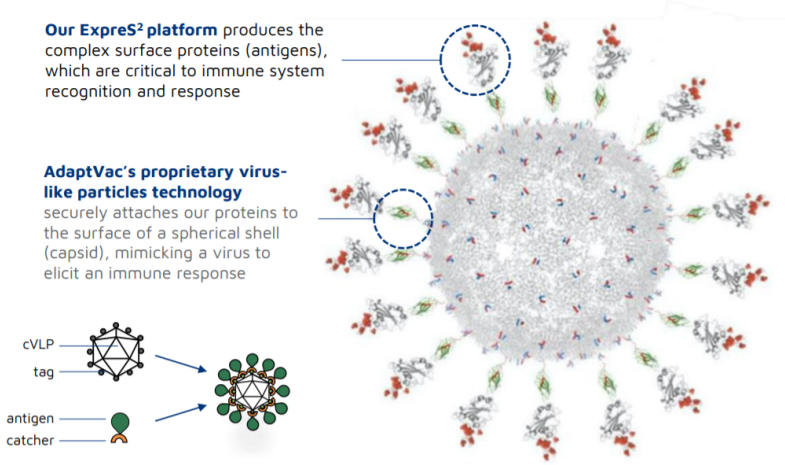
upscaling of manufacturing for clinical and commercial production of the vaccine.

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 ExpreS²ion, 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, Moderna's, and AstraZeneca-Oxford's vaccines.

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 ExpreS²ion 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

# Breast cancer candidate in preclinic

ES2B-C001 is ExpreS²ion Biotechnologies in-house proprietary program which is progressing toward a clinical trial in 2024. In May this year ExpreS²ion 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.

ExpreS²ion 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 ExpreS²ion 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 therapeutical 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. Clinicaltrails.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 ExpreS²ion 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 ExpreS²ion will not have to a new shares issue in 2024.

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