Solid data open for final phase

Bavarian Nordic releases first phase 2 data

In a first readout from Bavarian Nordic's phase 2 study of ABNCoV2, the COVID vaccine candidate licensed from AdaptVac, 103 tested subjects showed a variety of responses to a single-shot booster dose. In one of the groups receiving the 100-microgram dose, antibody levels to the Wuhan virus variant increased by a substantial 40 times (40-fold) two weeks after injection of the vaccine.

In another group receiving the same dose, levels of antibodies only doubled. These different reactions to ABNCoV2 are related to the baseline values, i.e. how antibody levels were on day 0 before receiving and reacting to the shot. As for patients infected with the Delta variant, the currently dominating strain of the virus, the boost to the immune system was less pronounced, but still a solid 21-fold increase in patients with no protection to the virus.

Solid comparison to competitors

After the initial COUGH-1 trial with ABNCoV2, sponsored by a consortium including ExpreS²ion Biotechnologies, a very potent profile was communicated suggesting potential for a superior potency to the currently marketed mRNA vaccines. However, as the program progresses, we are now looking more for a non-inferior profile.

We would speculate that the edge of the ABNCoV2 vaccine candidate is to be found outside short-term efficacy, such as the possibility of long-term immunogenicity and safety. No serious adverse events have been observed in the human trials with ABNCoV2.

Design of phase 3 still pending, fair value unchanged

The latest spreading variant of the SARS CoV2 virus, named omicron, has so far not been tested in a vaccine study. If this variant becomes dominant in 2022, we believe it may impact the design of the upcoming phase 3 study of ABNCoV2, potentially providing the Bavarian candidate with another edge. However, CEO Paul Chaplin also referred to potential difficulties finding an active comparator for the pivotal phase 3 study.

Bavarian Nordic expects starting a phase 3 trial in first half of next year and, assuming everything goes well, submit the product for approval before year-end. This may allow the company to receive pre-orders for 2023, booked in 2022. We still find this scenario a bit stretched and stick to a first order in 2023. Our fair value for ExpreS²ion Biotechnologies remains unchanged at SEK 60.

ExpreS²ion Biotech

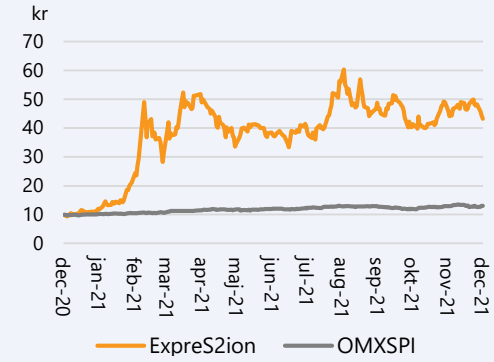
Date	9 december 2021
Analyst	Sten Westerberg

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 44
No. of shares 2021, mln.	31,5
Market cap, SEKm	1 368
Cash 2021e, SEKm	130

Web site www.expres2ionbio.com

Kursutveckling senaste året



Source: Refinitiv

Forecasts & Key ratios, SEKm

	2019	2020	2021p	2022p
Revenues	14	15	13	22
EBIT	-18	-29	-45	-41
Net income	-17	-36	-44	-45
Earnings per share	-0,5 kr	-1,1 kr	-1,4 kr	-1,4 kr
Dividend	0 kr	0 kr	0 kr	0 kr
Revenue growth	55%	7%	-11%	65%
Cash	5	107	130	85
New share issue	8	133	83	0
P/E ratio	neg	neg	neg	neg
Dividend yield	0%	0%	0%	0%

Source: Bolaget, Analysguiden

Investment case

Obvious need for booster vaccines

The need for new vaccines to boost effects of currently approved products continues to spur the development of a large number of candidates in clinical development. So far both the mRNA vaccines, Comirnaty and Spikevax, have gained status as boosters to the prime vaccination, as well as the Johnson & Johnson vaccine.

So far, some 8 billon doses have been administered worldwide with the approved vaccines. What is strikingly clear is that the efficacy rate after prime vaccination is dropping faster than seen in most other viral infections, in many cases falling below preventive levels already at month 6 or earlier.

Main scenario with solid market shares in EU

ExpreS²ion Biotechnologies stands to gain around 1 percent of sales of the COVID-19 vaccine through its partner AdaptVac, in which ExpreS²ion also holds 34 percent of the shares. AdaptVac stands to gain around 10 percent of sales of the vaccine as well as some 130 MEUR remaining of milestones. In 2022 we expect some 20 MEUR to be paid to AdaptVac on the back of positive phase 2 data or initiation of a phase 3 trial.

In our main scenario for the ABNCoV2 vaccine candidate we assume that 450 million doses will be administered during 2023-27. This corresponds to a solid market share in the EU region, but given the prospect of a non-inferiority design in the phase 3 study we are not clear over which role the vaccine will play in regions outside EU. A potential edge would be a more long-lasting T cell response to the virus as well as strong safety profile.

Tough comparison remains for ABNCoV2

Results for the 100-µg arm in the ongoing phase 2 trial are showing a large spread of booster reactions, from a 2 to a 40-fold increase in neutralizing antibodies to the Wuhan virus strain. The booster effect to the dominant Delta virus was less pronounced, a 4 to 20-fold increase. In an apples-to-pears comparison, based on different types of assay technologies and trial designs, we note that Moderna's Spikevax at 50 µg showed a 23 to 44-fold boost of SARS antibody levels in a small phase 2 study. Still, we speculate that ABNCoV2 100 µg will be able to show non-inferiority to an mRNA vaccine, most likely Pfizer's Comirnaty, in the upcoming phase 3 study.

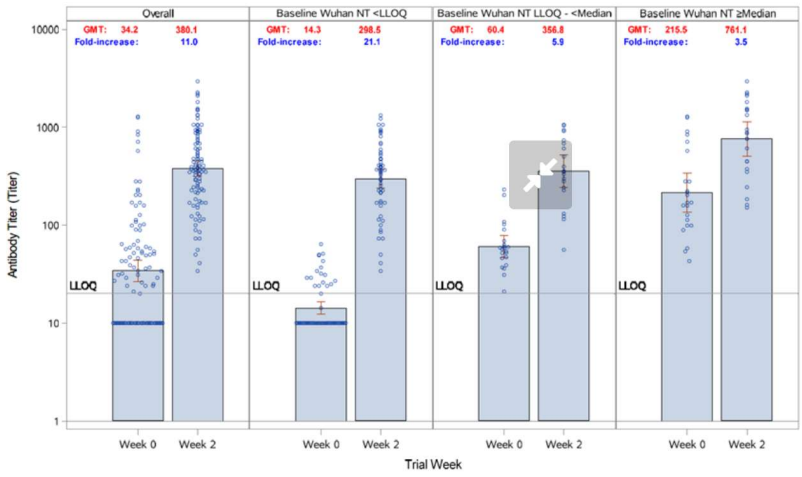
However, the final edge of ABNCoV2 could potentially reside in a more long-term protection to the virus than has been seen with the mRNA platform, which also has provoked some rare serious side effects in the general population. We stick to our scenario for ABNCoV2 with a 60 percent likelihood of approval in 2023. Our fair value for ExpreS²ion Biotechnologies remains at SEK 60.

Entering the booster arena

Bavarian Nordic repeated solid results for its vaccine candidate ABNCoV2 in recently released topline numbers from the phase 2 study arm of the 100-µg dose. This is a non-randomized, non-controlled study, and in contrast to the COUGH-1 study, we no longer find support for a superior effect of ABNCoV2 over the marketed mRNA vaccines Comirnaty and Spikevax. This should not come as a surprise, as we argue below.

Results for the three virus variants Wuhan (the wild type), Alpha and Beta are supporting the strong antibody responses (2- to 40-fold higher levels compared to Wuhan baseline) two weeks after the shot, which also may be necessary in order to show non-inferiority to a marketed vaccine in the phase 3 trial. 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 Delta variant



Source: Bavarian Nordic

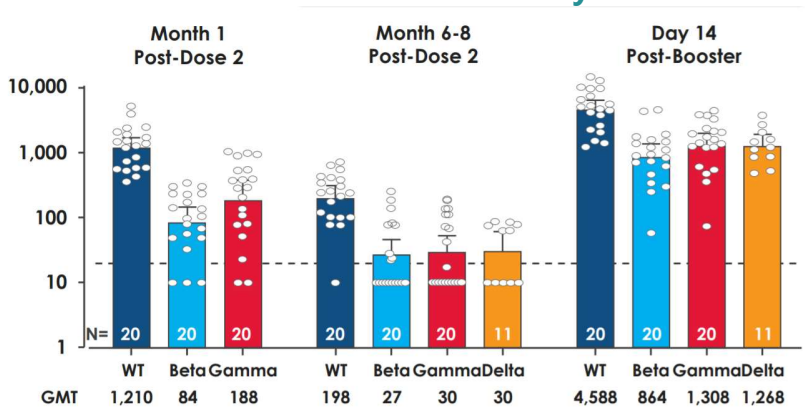
We note that Bavarian Nordic used a different technology, a receptor binding assay, for testing the immunization to the Delta variant, possibly due to a shortage of the standard PRNT50 test. It is not clear to us if and to what extent this different assay has had an impact on the absolute numbers. At least it makes comparisons to other vaccines even more difficult than already is the case in a non-controlled study.

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.

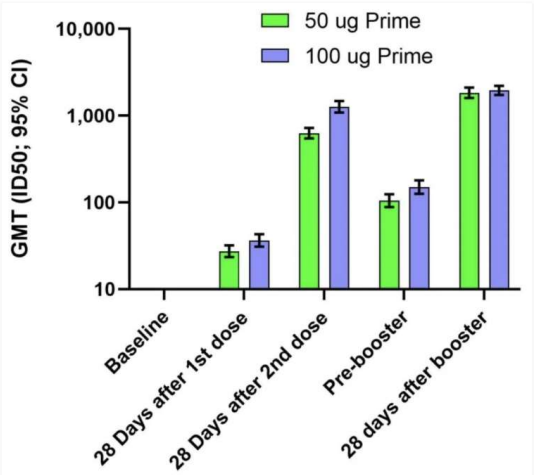
Moderna shows 23 to-40-fold antibody increase



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.

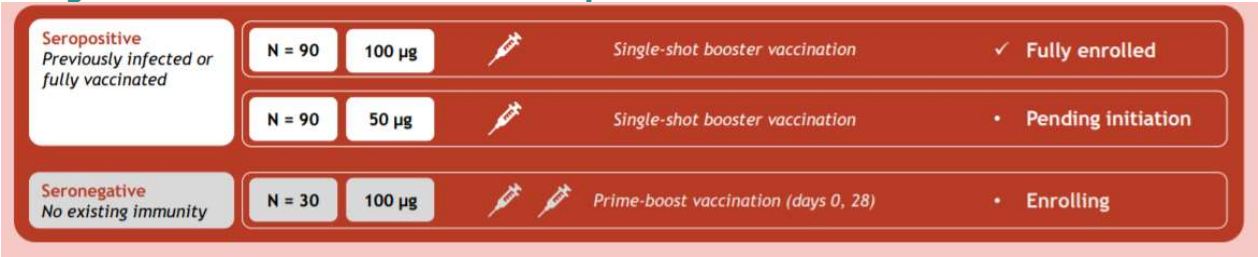
Strong reneutralization with Moderna 50 µg boost



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

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.

Design of Bavarian Nordic's ABNCoV2 phase 2 trial



Source: Bavarian Nordic Q3 presentation

Scope for lowering the dose

According to Bavarian Nordic, the recent findings from the COUGH-1 study may provide rationale for reducing the dose of the vaccine, while maintaining optimal effect, and thus could lead to a reduction of manufacturing costs. Bavarian has decided to add the non-adjuvanted 50 µg dose in its phase 2 program. Were this dose to be approved it would substantially cut manufacturing costs compared to a product based on the 100 µg dose. A lower dose may also confer a better safety profile, even if safety so far has not been an issue with the ABNCoV2 vaccine candidate.

Data from the two enrolling arms, the 50 µg and the 30 seronegative healthy volunteers on 100 µg, will be presented in first quarter of next year. With the full dataset available Bavarian Nordic can pick its final dosing preference and proceed to phase 3.

The phase 3 initiation in 2022

We set a 90 percent likelihood of ABNCoV2 entering a phase 3 trial next year. Bavarian Nordic's management expects to start the trial in first half 2022 after releasing full results from its ongoing phase 2 study. The dosing and design of the phase 3 study are still to be finalized. It is likely to be a two-armed randomized controlled study with a widely marketed mRNA vaccine (Comirnaty or Spikevax) in the comparator arm and ABNCoV2 in the second. It remains for the company decide on the dosing of ABNCoV2 but we would guess that it will pick the 100 µg as long as it shows some superior strength over the 50 µg. However, this superior strength is not yet established judging by the outcome of COUGH-1 study, the first in man trial with ABNCoV2.

In a conference call on Monday CEO Paul Chaplin made some interesting remarks on the availability of a marketed comparator

vaccine to be included in the phase 3 trial. Since the mRNA vaccines are shipped exclusively on contracts with governments around the world there may be difficulties in getting hold to a comparator in the Bavarian Nordic phase 3 trial. It was suggested that this could be circumvented by including ABNCoV2 in an ongoing governmental vaccine program.

CEO Paul Chaplin also made clear that were the Omicron variant, which currently is spreading around the world, to become a dominant variant alongside with the delta, the study will have to include this latest variant. Since no vaccines are yet approved for the Omicron variant this may entangle some delays but on the other hand Bavarian Nordic is hopeful that ABNCoV2 will show strong efficacy to the new Omicron variant, partly based on observations of the Beta variant, which shows some common mutations with the Omicron variant.

First orders possible in 2022

In our main scenario we expect sales of ABNCoV2 to start occurring in 2023 after a full read-out of phase 3 data and a subsequent submission to regulatory bodies around the end of the year. CEO Paul Chaplin made clear that there will be no orders placed for the vaccine before the phase 3 read-out. This could in theory happen before the end of 2022 and then it is up to the company if it will book these orders as income already in 2022, triggering royalty payments to AdaptVac.

This scenario looks tight to us but is supported by the French vaccine developer Valneva, which presented phase 3 topline data for its COVID-19 vaccine VLA2001 in October. As opposed to ABNCoV2, VLA2001 was not documented as a booster vaccine, but as a two shot prime COVID-19 vaccine. The topline results for VAL2001 were awarded an advanced purchase agreement in November from the European Commission, committing itself to buy 60 million doses in 2022-23, of which 27 million in 2022. VAL2001 is based on inactivated viruses and resembles the AstraZeneca product rather than the protein-engineered ABNCoV2 from Adaptvac and ExpreS²ion Biotechnologies.

Financial discussion and scenario

As data are piling up for the vaccine candidate ABNCoV2 we have raised our likelihood of approval (LOA) till 60 percent, including a 90 percent likelihood that the ongoing phase 2 study will be successful, allowing for a phase 3 trial to start half way into next year. Given our scenario for an improving chance of approval for ABNCoV2 we recently raised our fair value to SEK 60, a scenario which we are sticking to in this report.

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	339	10,8	1 171	10%	14%	100%	
Royalty, ABNCoV2	448	14,3	9 452	60%	9%	100%	11% of Adaptvac
Adaptvac holding	871	27,8		60%	9%	34%	of DCF value
Platform	80	2,6	1,8	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	1 878	60	*based on the no. of shares by end of 2021, mln*				*31,3*

**) Likelihood of approval*

Forecasts by Analysguiden

ExpreS²ion exposure to ABNCoV-2, three scenarios

	Slow scenario	Main scenario	Strong scenario	Comments
Aggregated sales , EURm	5 000	9 452	15 000	456 mln doses sold in main scen
EUR per dosis	20	21	21	Our assumption
Adaptvac royalty from Bavarian	7%	10%	13%	Single digit to double digit
ExpreS²ions royalty from Adaptvac	11%	11%	11%	Double digit number
royalty of vaccine net sales	*0,8%*	*1,1%*	*1,4%*	
ExpreS²ion revenues, EURm	39	104	215	Over period 2023-2027
in SEKm	*389*	*1 050*	*2 166*	
Milestone from Adaptvac, SEKm	20	20	20	EUR 2m in 2021-22
ExpreS²ion revenues, SEKm	409	1 070	2 186	
SEK/share	13,1	34,2	69,8	
Tax rate	18%	18%	18%	Assuming full taxation
Likelihood of Approval (LOA)	60%	60%	60%	67% phase 1/2, 65 % phase 3
Risk-adjusted after tax, SEK/share	6,4	16,8	34,3	Not discounted, see SoTP

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

We assume ExpreS²ion to receive 1.1 percent of total vaccine net sales as royalty, which is a product of the two royalty rates we have adopted in the table above. For AdaptVac's part, we believe that the royalty extends between 7-13 percent. AdaptVac's agreement with Bavarian entitles to milestones corresponding to a maximum of EUR 136 million, but only EUR 2 million of these are shipped down to ExpreS²ion in our model.

ExpreS²ion holds 34 percent of ownership in AdaptVac with the Danish academic group NextGen Vaccines ApS holding the remaining majority stake in AdaptVac. NextGen is a spin-out from the University of Copenhagen's Institute of Immunology and Molecular Biology, controlled by a handful of researchers at this institution.

Assumptions in Net Present Valuation of ExpreS²ion Biotech

SEKm	2019	2020	2021p	2022p	2023p	2024p	2025p	2026p	2027p	2030p
Operating income	14	15	13	22	408	281	204	17	18	18
ABNCoV-2		*0*	*5*	*10*	*58*	*268*	*120*	*105*	*53*	*0*
ES2B-C001					*331*	*-2*	*68*	*-2*	*95*	*85*
platform/services	*14*	*11*	*5*	*12*	*19*	*15*	*16*	*17*	*18*	*18*
EBIT	-18	-29	-45	-41	350	237	174	4	5	
Cash	5	107	130	85	432	668	841			

ABNCoV-2 (EURm)	2020	2021p	2022p	2023p	2024p	2025p	2026p	2027p	2030p
Net sales			0	1 236	4 036	1 801	1 575	803	
EUR/dosis			*20*	*20*	*21*	*21*	*21*	*21*	
No. of doses, mln total of 456			*0*	*61*	*196*	*87*	*75*	*38*	
ExpreS²ion milestones, EURm		1	1	0	0	0	0	0	
Royalty, MEUR			0	10	44	20	17	9	
Royalty rate			*#DIV/0!*	*0,8%*	*1,1%*	*1,1%*	*1,1%*		
Expres2ion revenues, SEKm		10	10	96	448	200	175	89	0
Risk-adjusted		*1,00*	*0,90*	*0,60*	*0,60*	*0,60*	*0,60*	*0,60*	
Risk adjusted revenues, NPV (SEKm)			0,0	57,5	268,4	119,8	104,7	53,4	

WACC	9%
NPV, AV001 (SEKm)	448
NPV/share, SEK	14,3
LOA	60%

ES2B-C001 (SEKm)	2020	2021p	2022p	*Licens*	2024p	2025p	2026p	2027p	2030p
Costs, preclinical / clinical	-7	-36	-24	-20	-14	0	-50	0	-75
incl milestones to Adaptvac	*-3,5*	*-3,5*	*-3,5*	*0*	*-14*	*0*	*-50*	*0*	*-75*
Sales, EURm								147	921
Milestones, licensing partner 975 MEUR				75	0	100	0	200	200
Royalty 10%								*15*	*92*
Expres2ion revenues, SEKm				765	-14	1020	-50	998	2904
Risk-adjusted	*1,00*	*0,75*	*0,56*	*0,56*	*0,23*	*0,11*	*0,10*	*0,10*	*0,10*
Risk adjusted revenues, NPV (SEKm)				331	-2	68	-2	95	85

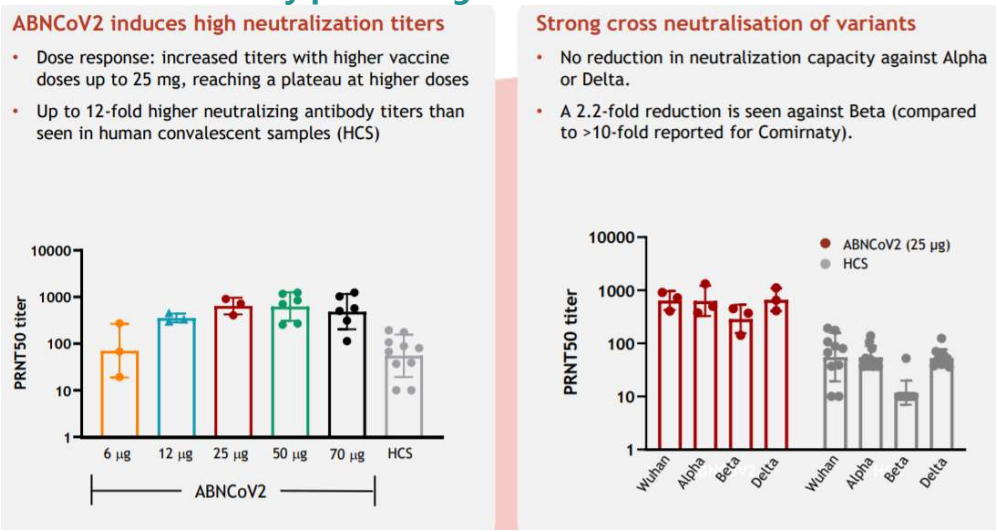
WACC	14%
Net present value (SEKm)	339
NPV/share, SEK	10,8
LOA	10%

Strong efficacy signal in COUGH-1

ExpreS²ion Biotechnologies recently presented the full efficacy data and safety set from the COUGH-1 study, the first human study with the vaccine candidate ABNCoV2. Forty-five healthy volunteers aged up to 65 years were treated at Radboud University Medical Centre in the Netherlands with two doses of six different strengths (6-70 µg) of ABNCoV2. Doses up to 25 µg came with adjuvans while the two highest doses did not include an adjuvant.

Surprisingly, the non-adjuvanted doses, 50 and 70 µg, did not convey any additional clinical benefit over the adjuvanted 25 µg dose. As mentioned, this plateauing of the immune response led Bavarian Nordic to amend its protocol of the ongoing phase 2 study to also include the 50 µg dose, a measure which should have caused some delay to the study. The primary endpoint of the study was to investigate safety, or reactogenicity, of the substance. None of the doses did cause severe side effects (grade 3 or 4) in these patients and it can thus be said that outcome was positive, admitting Bavarian Nordic to move forward with a Phase 2 study.

Vaccination efficacy plateauing



Source: Bavarian Nordic Q3 presentation

The Danish financing agreement

In August Bavarian Nordic entered a funding agreement, valued at up to DKK 800 million, with the Danish Ministry of Health to support the completion of the development of ABNCoV2 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.

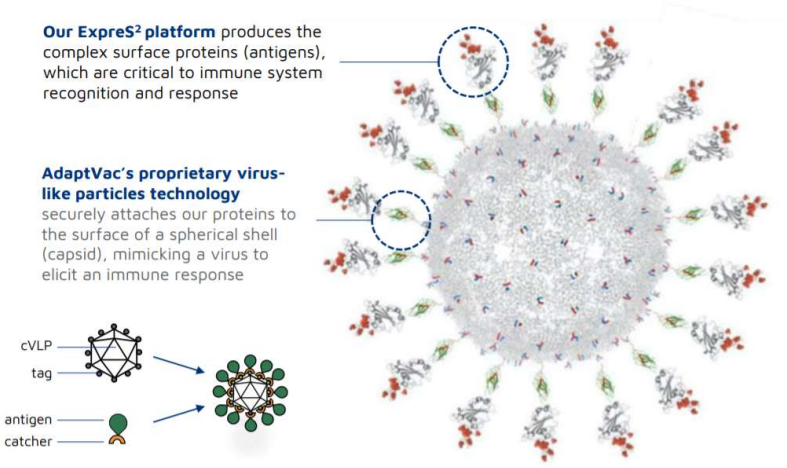
We are surprised by the size of the financing, which in our mind is economical for being a phase 3 financing, which also includes investment in manufacturing capacity. The amount may suggest a phase 3 trial of less of 5 000 patients, which remains to be confirmed by Bavarian Nordic.

So far Bavarian Nordic has paid an upfront payment to AdaptVac of DKK 30 million last summer when the license and collaboration agreement was signed. It has also capitalized development costs of DKK 19 million for running the ongoing phase 2 study.

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 Human Papilloma Virus 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 responses by T-cells.

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 thus cannot infect or replicate in 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

Disclaimer

Aktiespararna, www.aktiespararna.se, publishes reports of companies compiled with the help of sources that have been deemed reliable. However, Aktiespararna cannot guarantee the accuracy of the information. Nothing written in the analysis should be considered a recommendation or encouragement to invest in any financial instrument. Opinions and conclusions expressed in the report are intended for the recipient only. The report is a so-called Assignment Analysis where the analysed Company has signed an agreement with Aktiespararna.

The reports are published regularly during the agreement period and for the usual fixed remuneration. Otherwise Aktiespararna has no financial interest in what is the subject of this report. Aktiespararna has routines for handling conflicts of interest, which ensures objectivity and independence.

The content may be copied, reproduced and distributed. However, Aktiespararna cannot be held liable for either direct or indirect damages caused by decisions made on the basis of information in this report.

Investments in financial instruments offer opportunities for value increases and profits. All such investments are also associated with risks. The risks vary between different types of financial instruments and combinations of these. Historical returns should not be considered as an indication of future returns.

The analyst Sten Westerberg does not own and may not own shares in the analysed company.

Responsible analyst:

Sten Westerberg