UPPDRAGSANALYS

A moving target

Bavarian Nordic close to start of final study

Bavarian Nordic expects shortly to start a registrational phase 3 trial for its Covid-19 vaccine candidate ABNCoV2 as booster regime following primary vaccination with other products. Development of the vaccine is funded by the Danish state.

The trial is expected to start enrolling before end of June and will include some 4 000 subjects. We assume a 71 percent likelihood of an approval of ABNCoV2 by late 2023. ABNCoV2 was licensed in 2020 from the Danish vaccine developer AdaptVac, in which ExpreS²ion Biotechnologies holds 34 percent of the shares.

Milestone payments coming closer

So far Bavarian Nordic has paid an EUR 4m upfront payment to AdaptVac. Total development and commercial milestones may reach EUR 136m, primarily depending on the commercial success. However, we expect AdaptVac to receive additional milestone payments also this year, possible upon initiation of the phase 3 study in Q2, and certainly after submission for approval to regulators in Q4 this year. In total we speculate that these payments may amount to EUR 15m.

A rapidly shifting commercial landscape

Bavarian Nordic's annual report states that ABNCoV2 is not expected to play a major role in the prevention of the current pandemic, but rather in a later endemic stage for protection of elderly and vulnerable persons. It describes the annual Covid-19 booster market as "a multi-billion USD market". We revise our estimate to EUR 10bn (24), corresponding to 500 million annual doses.

New assumptions render lower fair value

We note that the darlings of the stock market in 2020, the Covid-19 vaccine producers, have lost some 50-65 percent of peak market capitalizations during the last six months, partly reflecting a new market outlook. Our changes in forecast of market size and of the ABNCoV2 price per dose lead us to a fair value for ExpreS²ion Biotechnologies of SEK 39 compared to a previous estimate at SEK 60. In a more optimistic scenario, including an edge of the longevity of the protection compared to mRNA vaccines, the fair value may be at least SEK 80.

In our view a major attraction of the investment case lies in the possibility of ExpreS²ion Biotechnologies receiving dividends and royalties from AdaptVac, funding its development of the breast cancer vaccine candidate ES2B-C001, currently being studied in animals.

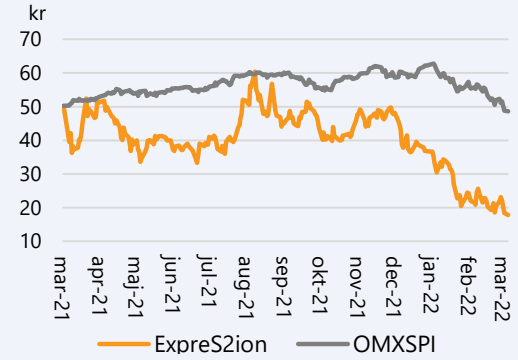
ExpreS²ion Biotech

Date	8 mars 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 18
No. of shares 2021, mln.	31,5
Market cap, SEKm	567
Cash 2021, SEKm	139
Web site	www.expres2ionbio.com

Kursutveckling senaste året



Source: Refinitiv

Forecasts & Key ratios, SEKm

	2020	2021	2022p	2023p
Revenues	15	14	30	84
EBIT	-29	-48	-37	-13
Net income	-36	-44	-41	-16
Earnings per share	-1,8 kr	-1,5 kr	-1,3 kr	-0,5 kr
Dividend	0 kr	0 kr	0 kr	0 kr
Revenue growth	11%	-10%	115%	180%
Cash	107	139	98	83
New share issue	133	83	0	0

Source: Bolaget, Analysguiden

Investment case

The continued need of booster vaccines

By March 2022, more than ten COVID-19 vaccines have been approved across the globe, and more are still in development. In spite of this, we believe there is a continued need for new and more effective booster vaccines for those at-risk of complications from the infection. Also, while more than 10 billion doses have been deployed globally, only around 12% of the population in low-income countries have been vaccinated, leaving a substantial obligation for the society to solve.

We estimate that the annual market for booster vaccines in the coming years will be some 500 million doses, adding up to a EUR 10bn market. This is a substantial change from the EUR 51bn market we saw at the peak of the infection in 2021, but still leaves plenty of commercial scope for Bavarian Nordic's candidate ABNCoV2.

Main scenario with solid market shares in EU

We speculate that ExpreS²ion Biotechnologies stands to gain 1 percent of ABNCoV2 sales as revenue in its books. On top of this ExpreS²ion also holds 34 percent of shares in AdaptVac, which over time may end up with a SEK 5bn cash pile from receiving around 10 percent of sales of ABNCoV2. AdaptVac will also receive up to 136 MEUR in milestones on development and sales achievements.

Our main scenario for the ABNCoV2 vaccine candidate is sales of 260 million doses administered during 2023-27, corresponding to a 10-12 percent global market share. We expect a solid market share in the EU region, but given the current prospect of a non-inferiority design in the phase 3 study we are not clear over how the vaccine will differentiate itself. A potential edge lies in a more long-lasting T cell response to the virus as well as strong safety profile, data which remains to be shown.

Self-funding business model

In 2022 we expect Bavarian Nordic to pay a total of 15 MEUR in milestones to AdaptVac, possibly at the initiation of the phase 3 trial in Q2, as well upon submission for approval by the end of the year. In total we believe that AdaptVac stands to gain EUR 100-130m in future milestones from Bavarian Nordic depending on commercial success. This means that ExpreS²ion Biotechnology may receive dividend and royalty payments from AdaptVac, which together with the current cash pile at SEK 139m will fund development of its breast cancer vaccine ES2B-C001 into a proof-of-concept study 2024-25.

Given our new scenario for ABNCoV2 we arrive at a fair value for ExpreS²ion Biotechnologies of SEK 39, down from a previous scenario at SEK 60. The uncertainty of the future Covid-19 market should continue to spark volatility and in more optimistic scenario, depending on the rollout of phase 3 and 4 clinical data, we arrive at a fair value at SEK 80.

Entering the final phase

As expected, Bavarian Nordic is continuing its preparations for a phase 3 trial with vaccine candidate ABNCoV2. The aim is to start enrolment of around 4 000 subjects before end of June, allowing the trial to report topline data before the end of 2022. Upon successful results, which we assign a 75 percent chance, ABNCoV2 will be submitted for regulatory approval before year-end. We assign a 95 percent chance of a successful regulatory review, which would make an approval possible sometime in October-November next year. At this point in time, we do not believe that an Emergency Use Pathway will be accepted for new Covid-19 vaccine candidates.

The phase 3 trial will be designed to show non-inferiority to the approved mRNA vaccines, based on the vaccine's ability to raise an antibody response to the different strains of the corona virus, including the dominant omicron variant. All participants will have had a previous primary vaccination with two doses and the dose of ABNCoV2 will be 100 µg, a dose which showed a tendency of superior immunogenicity over the 50-µg dose in the phase 2 study.

No details have been released on the trial design, but an overall agreement has been made with regulatory authorities. The manufacturing of vaccine bulk for the trial has been completed but pending filling procedures at the manufacturing line in the near future. The trial is funded by the Danish government and Bavarian Nordic is capitalizing all development costs, referring to a lower development risk than what usually is the case in vaccine development.

Aiming at a moving target

The ABNCoV2 vaccine candidate will not be tailored to respond to the omicron virus variant. In a rapidly shifting landscape this may not be a major drawback. When ABNCoV2 is approved, possibly by the end of 2023, there may be other variants dominating the infection. The exact wording of a potential approval for ABNCoV2 is difficult to predict since the virus behind infection is shifting in shape. The original Wuhan variant, which all current vaccines have been designed to fight, is no longer present in most populations. The current dominating strain of the virus, omicron, is being treated with vaccines designed for the Wuhan variant.

Both Moderna and Pfizer are developing omicron-tailored vaccines and it remains to be seen if these will reach the market before the omicron variant is dealt with by existing immune defenses. This could potentially put ABNCoV2 at a temporarily disadvantage. However, Bavarian Nordic's management does not expect ABNCoV2 to play a role in current fight against the pandemic but rather enter in a later seasonal endemic phase, protecting high-risk groups. This reminds of the current flu vaccination practice which are carried out in elderly and high-risk populations every year before the flu season starts.

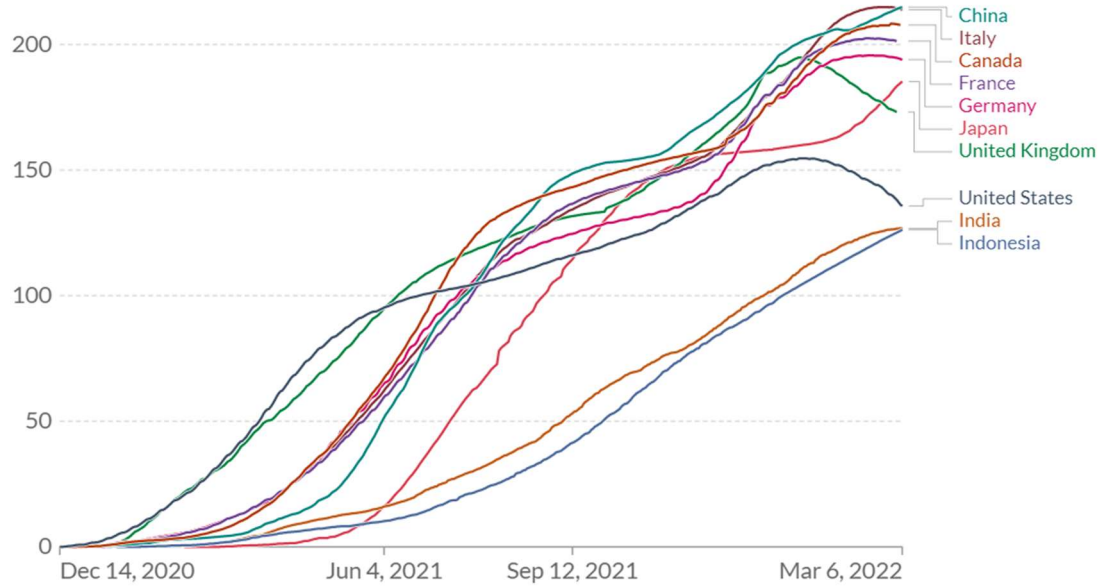
Initial marketing efforts for ABNCoV2 would target government programs, but over time moving towards a more traditional market for private vaccinations. ABNCoV2 would be sold to private clinics to provide prevention of breakthrough infections (reinfections after primary doses) in high-risk groups.

Value proposition with long-term protection

It is not clear to us how ABNCoV2 will be able to differentiate itself to other currently marketed vaccines. Overtime it is speculated that ABNCoV2 will be able to show a more long-lasting protection to the virus by means of CD4 lymphocytes, a specialized group of white blood cell carrying the memory of the pathogen DNA. This defense mechanism is substantially more long-acting than the antibodies which are currently looked at in the different phase 3 studies. However, these data are not likely to be ready for publication by the time of a first regulatory submission in late 2022.

If ABNCoV2 would be able to show a sustained protection thorough CD4 T cells, we believe it can be sold at a premium price to the current level of EUR 19-20, where Pfizer's Comirnaty and Novavax' Nuvaxovid are priced. Pending these data, we assume a price for ABNCoV2 at EUR 17 a dose.

No of doses/100 inhabitants, rolling12 month basis



Source: Our World In Data, based on official data

Financials discussion and scenarios

In our model we have assumed that Adaptvac, where ExpreS²ion Biotechnologies holds 34 percent, will return 50 percent of milestone it stands to gain in 2022-24 from Bavarian Nordic as a dividend to its two shareholders. However, this is merely a speculation from our side and it did not materialize after the EUR 4m upfront payment to AdaptVac from Bavarian Nordic in 2020. A non-specified one-time dividend was paid to AdaptVac shareholders in 2021.

Beyond 2024 we have assumed that the cash pile in AdaptVac will be reflected in the valuation of this entity, implying the possibility of a full cash distribution to its shareholders. Assuming all turns out in a positive way and our main scenario materializes, then AdaptVac will sit on a cash pile of SEK 5.0bn by end of 2027, corresponding to a NPV of SEK 3,8bn (WACC 9,0 percent). After tax and remaining risks this corresponds to 17 SEK per share in ExpreS²ion Biotechnologies, or 44 percent of our fair value (see table below).

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	267	8,5	1 333	14%	14%	100%	
Royalty, ABNCoV2	228	7,3	4 591	71%	9%	100%	11% of Adaptvac
Adaptvac holding	534	17,0		71%	9%	34%	of DCF value
Platform	67	2,1	1,5	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	1 236	39	*based on the no. of shares by end of 2021, mln*				*31,3*

**) Likelihood of approval*

Forecasts by Analysguiden

On top of this we have assumed that ExpreS²ion receives 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. This milestone is described as commercial milestones in the annual report.

ExpreS²ion exposure to ABNCoV-2, three scenarios

	Slow scenario	Main scenario	Strong scenario	Comments
Aggregated sales , EURm	2 500	4 591	10 000	259 mln doses sold in main scen
EUR per dosis	17	17	17	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	19	50	143	Over period 2023-2027
in SEKm	*202*	*530*	*1 502*	
Milestone from Adaptvac, SEKm	20	20	20	EUR 2m in 2021-22
ExpreS²ion revenues, SEKm	222	550	1 522	
SEK/share	7,1	17,6	48,6	
Tax rate	18%	18%	18%	Assuming full taxation
Likelihood of Approval (LOA)	71%	71%	71%	67% phase 1/2, 65 % phase 3
Risk-adjusted after tax, SEK/share	4,1	10,3	28,4	Not discounted, see SoTP

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

The other shareholder in AdaptVac is the Danish academic group NextGen Vaccines ApS, controlling 66 percent of AdaptVac, and thus in control over the AdaptVac cash flow. 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.

In a more positive scenario with data showing long-lasting protection to the virus we see the fair value of ExpreS²ion Biotechnologies at least doubling to SEK 80. We expect this data to start being published by the end of 2023 giving a boost to sales in 2024. The aggregated sales of ABNCoV2 would then surge to some EUR 10bn, more than double of our main scenario at EUR 4.6bn.

In a clearly negative scenario, where ABNCoV2 is not able to show non-inferiority to omicron protection in the phase 3 trial, the project will be dropped and the share price should fall below a level at 8 SEK per share, corresponding to our undiluted valuation of the preclinical ES2B-C001 breast cancer vaccine candidate.

Assumptions in Net Present Valuation of ExpreS²ion Biotech

SEKm	2020	2021	2022p	2023p	2024p	2025p	2026p	2027p	2030p
Operating income	15	14	30	84	159	199	14	15	15
ABNCoV-2	*0*	*0*	*20*	*65*	*51*	*90*	*92*	*94*	*0*
ES2B-C001				*0*	*96*	*95*	*-4*	*67*	*144*
platform/services	*11*	*5*	*10*	*19*	*12*	*13*	*14*	*15*	*15*
EBIT	-29	-48	-37	-13	94	147	3	4	
Cash	107	139	98	83	175	321			

ABNCoV-2 (EURm)	2020	2021	2022p	2023p	2024p	2025p	2026p	2027p	2030p
Net sales			0	350	893	1 094	1 116	1 138	
EUR/dosis			*17*	*17*	*18*	*18*	*18*	*18*	
No. of doses, mln total of 259			*0*	*20*	*51*	*62*	*62*	*63*	
ExpreS²ion milestones, EURm		0	1	0	0	0	0	0	
Royalty, MEUR			0	2	7	12	12	13	
Royalty rate				*0,6%*	*0,8%*	*1,1%*	*1,1%*		
Expres2ion revenues, SEKm		0	11	20	72	126	129	131	
Risk-adjusted		*1,00*	*1,00*	*0,75*	*0,71*	*0,71*	*0,71*	*0,71*	
Risk adjusted revenues, NPV (SEKm)			0,0	14,4	51,5	90,0	91,8	93,6	

WACC	9%
NPV, royalty (SEKm)	228
NPV/share, SEK	7,3
LOA	71%

ES2B-C001 (SEKm)	2020	2021	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								0	1234
Milestones, licensing partner 600 MEUR				0	50	100	0	100	200
Royalty 10%								*0*	*123*
Expres2ion revenues, SEKm				0	496	1020	-50	475	3224
Risk-adjusted	*1,00*	*0,90*	*0,63*	*0,63*	*0,28*	*0,16*	*0,14*	*0,14*	*0,14*
Risk adjusted revenues, NPV (SEKm)				0	96	95	-4	67	144

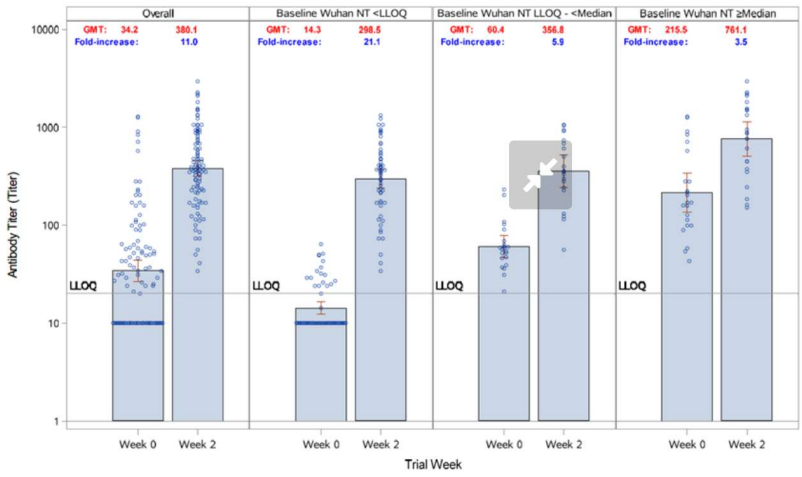
WACC	14%
Net present value (SEKm)	267
NPV/share, SEK	8,5
LOA	14%

Solid phase 2 data pave the way

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

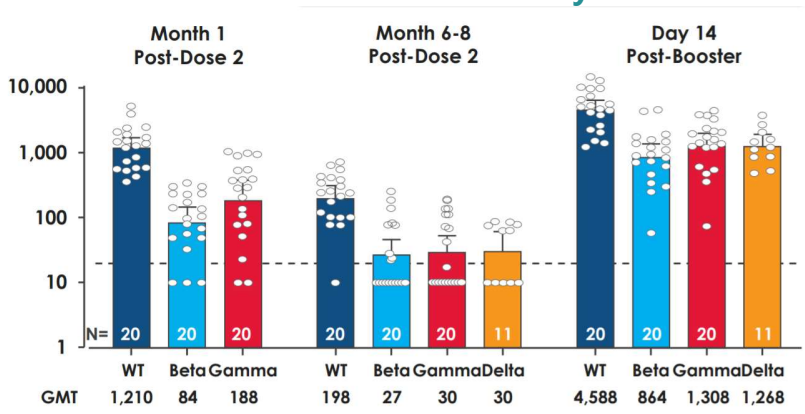
We note that Bavarian Nordic used a different technology, a receptor binding assay, for testing the immunization to the Delta variant, possibly due to a shortage of the standard PRNT50 test. It is not clear to us if and to what extent this different assay has had an impact on the absolute numbers. At 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.

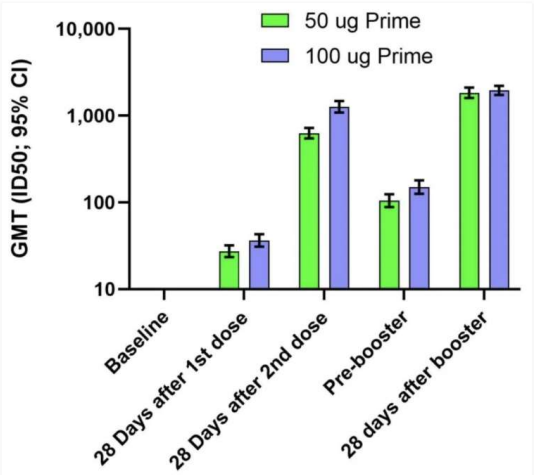
Moderna shows 23 to-40-fold antibody increase



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.

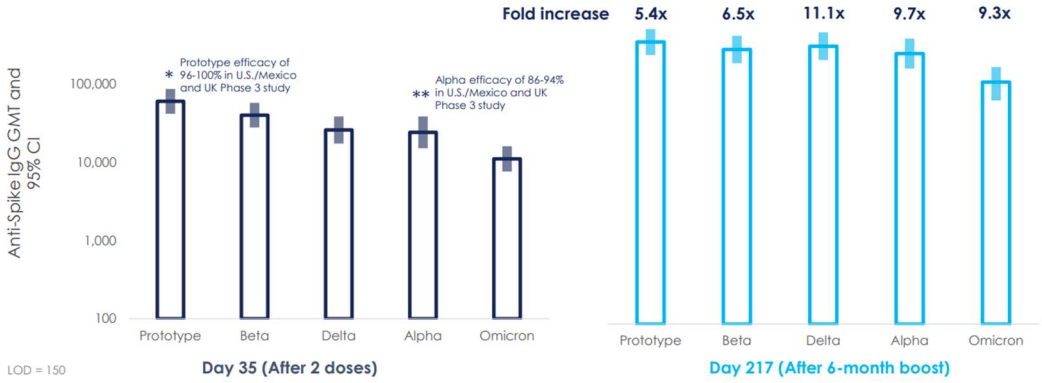
Strong reneutralization with Moderna 50 µg boost



Source: Chu, L.(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)



Källa: Novavax investor presentation

The Danish financing agreement

In August last year 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.

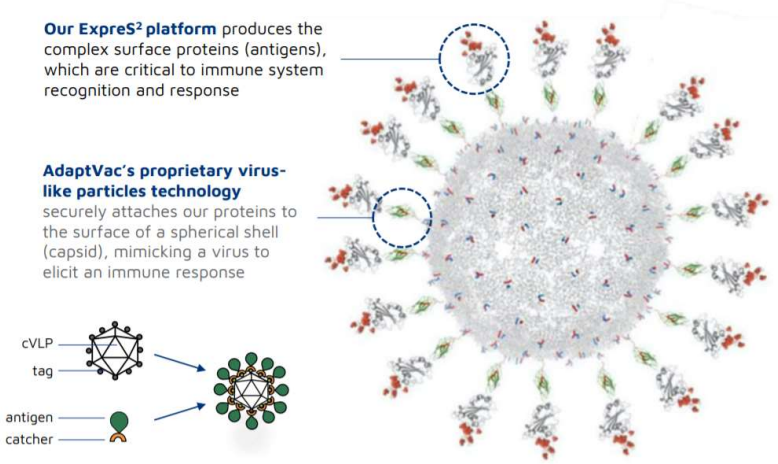
All payments are potentially subject to repayment, however only upon successful marketing authorization of the vaccine by the European Commission. Repayment may occur via supply of vaccines and royalty payments from the sale of the vaccine to other customers. Royalty payments are only triggered upon 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.

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.

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

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