
26th October 2022
Proteins
for Life
ExpreS2ion Biotech Holding AB
Økonomisk Ugebrev / Investor Pitch
Bent U. Frandsen, CEO
ØU Økonomisk Ugebrev
EXPRES2ION
BIOTECHNOLOGIES

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Investment Highlights

Key player in advanced protein sciences, with deep pipeline of novel vaccines addressing high-value markets

- High-potential pipeline of key focus within infections diseases and oncology, backed up by strong intellectual property rights
- Vaccine development platform with track record and partner validation. Now clinical Phase III-stage. +500 proteins produced while posting +90% success rate
- Global vaccine market rapidly growing, from USD 33bn (2019) to USD 187bn (2021), corresponding to 460% growth
- ExpreS^{2}ion is advancing towards key catalysts during 2022-23, further de-risking the company's pipeline. COVID-19 vaccine clinical Phase III initiation in Q3 2022

Management Team

>200 years of professional skills and experience from the *life sciences* industry

Management

- **Bent U. Frandsen**, Chief Executive Officer
- **Keith Alexander**, Chief Financial Officer
- **Dr. Max Soegaard**, VP R&D and Technology
- **Dr. Mette Thorn**, VP Preclinical Development
- **Dr. Mattis F. Ranthe**, Chief Medical Officer

Board of Directors

- **Dr. Martin R. Jensen**, Chairman & Co-founder
- **Jakob Knudsen**, Member of the Board
- **Dr. Karin Garre**, Member of the Board
- **Sara Sande**, Member of the Board

Technology Platforms

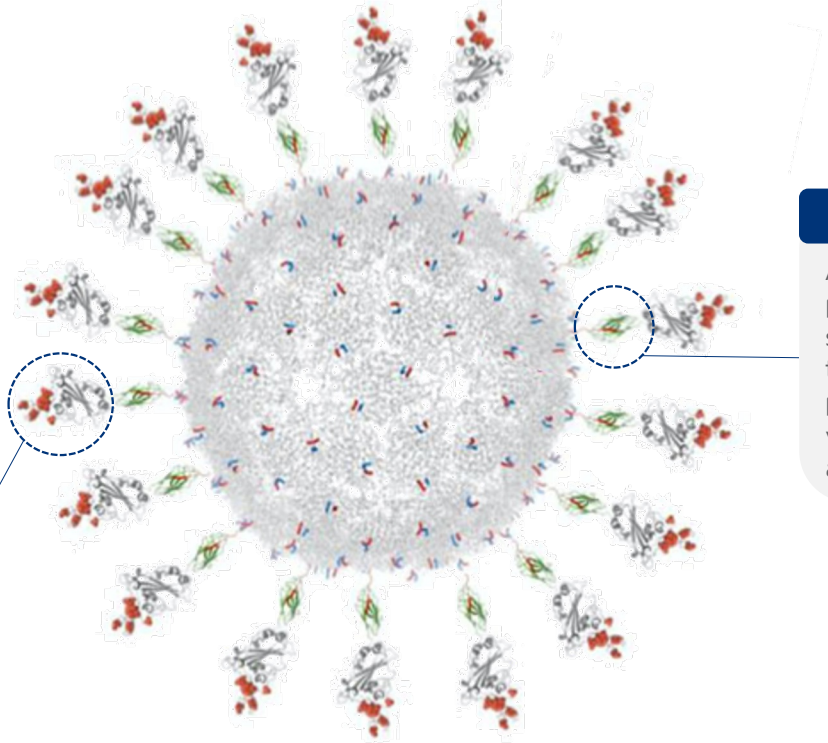
ExpreS²ion's ExpreS² and AdaptVac's cVLP platform

Cell line derived from *Drosophila melanogaster* (fruit fly) S2 cells[1]

ExpreS² platform

Combines S2 cells with patented expression vectors (add a specific gene into a target cell and command the cell to produce the gene encoded protein), adapted culture agents and reagents (stimulating cell growth)

100% ownership



ExpreS² protein (antigen) combined with AdaptVac's cVLP containing no viral genetic material causing an immune reaction

Particle (VLP) technology

AdaptVac's proprietary virus-like particles (VLP) technology securely attaches our proteins to the surface of a capsid (outer protein protective shell of a virus), mimicking a virus to elicit an immune response

34% ownership

[1] Schneider I (1972). "Cell Lines Derived from Late Embryonic Stages of *Drosophila melanogaster*". *J. Embryol. Exp. Morphol.* 27: 363–365.
Note: ExpreS²ion Biotech founders invented an Improved Vector System derived from S2 cells; granted patent until 2032 (US); glyco-engineered S2 cells pending patents until 2040.

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BIOTECHNOLOGIES

2022 Publications Support the Platform

biomedicines

MDPI

Article

Prevention and Therapy of Metastatic HER-2⁺ Mammary Carcinoma with a Human Candidate HER-2 Virus-like Particle Vaccine

Francesca Ruzzi [1,†], Arianna Palladini [1,2,†], Stine Clemmensen [3], Anette Strøbæk [3], Nicolaas Buijs [3], Tanja Domeyer [3], Jerzy Dorosz [3], Vladislav Soroka [3], Dagmara Grzadziela [3], Christina Jo Rasmussen [3], Ida Busch Nielsen [3], Max Soegaard [3], Maria Sofia Semprini [1], Laura Scalambra [1], Stefania Angelicola [1], Lorena Landuzzi [4], Pier-Luigi Lollini [1,*,‡] and Mette Thorn [3,‡]

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† These authors contributed equally to this work.
‡ Pier-Luigi Lollini and Mette Thorn jointly supervised this work.

Abstract: Vaccines are a promising therapeutic alternative to monoclonal antibodies against HER-2⁺ breast cancer. We present the preclinical activity of an ES2B-C001, a VLP-based vaccine being developed for human breast cancer therapy. FVB mice challenged with HER-2⁺ mammary carcinoma cells QD developed progressive tumors, whereas all mice vaccinated with ES2B-C001+Montanide ISA 51, and 70% of mice vaccinated without adjuvant, remained tumor-free. ES2B-C001 completely inhibited lung metastases in mice challenged intravenously. HER-2 transgenic Delta16 mice developed mammary carcinomas by 4–8 months of age; two administrations of ES2B-C001+Montanide prevented tumor onset for >1 year. Young Delta16 mice challenged intravenously with QD cells developed a mean of 68 lung nodules in 13 weeks, whereas all mice vaccinated with ES2B-C001+Montanide, and 73% of mice vaccinated without adjuvant, remained metastasis-free. ES2B-C001 in adjuvant elicited strong anti-HER-2 antibody responses comprising all Ig isotypes; titers ranging from 1–10 mg/mL persisted for many months. Antibodies inhibited the 3D growth of human HER-2⁺ trastuzumab-sensitive and -resistant breast cancer cells. Vaccination did not induce cytokine storms; however, it increased the ELISpot frequency of IFN-γ secreting HER-2-specific splenocytes. ES2B-C001 is a promising candidate vaccine for the therapy of tumors expressing HER-2. Preclinical results warrant further development towards human clinical studies.

Keywords: breast cancer; vaccine; virus-like particles (cVLP); HER-2; tyrosine kinase receptor; target therapies; cancer immunotherapy; metastasis

Citation: Ruzzi, F.; Palladini, A.; Clemmensen, S.; Strøbæk, A.; Buijs, N.; Domeyer, T.; Dorosz, J.; Soroka, V.; Grzadziela, D.; Rasmussen, C.J.; et al. Prevention and Therapy of Metastatic Her-2⁺ Mammary Carcinoma with a Human Candidate Her-2 Virus-like Particle Vaccine. *Biomedicines* **2022**, *10*, 2654. https://doi.org/10.3390/biomedicines10102654

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Moderate-Throughput
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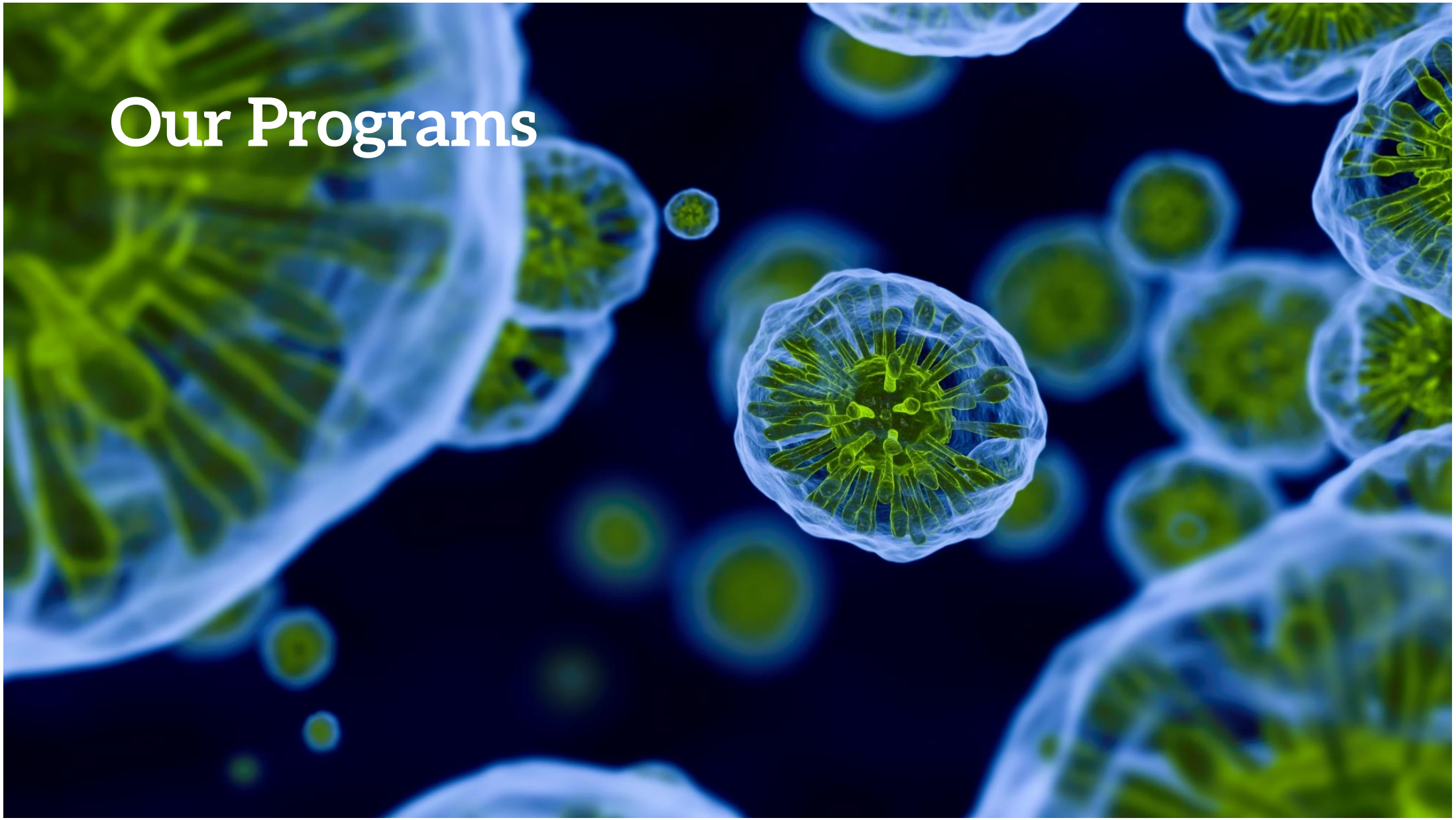
Our Programs



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Deep Pipeline for Value Creation

Market Potential	DISEASE	Project/Target	Development Progress: Discovery / Pre-clinical Pharmacology / cGMP / Tox / Phase I / Phase II / Phase III	Partner/Funding
>€30 billion[1]	Coronavirus	ABNCoV2/SARS-CoV-2 cVLP	Ph. III initiated	adaptVAC, BAVARIAN NORDIC, PREVENT-nCoV
>€10 billion[2]	Breast Cancer	ES2B-C001/HER2 cVLP	Progressed into cGMP/Tox	100% ExpreS²ion
>€4 billion[3]	Influenza	Hemagglutinin		INDIGO
>€0.4 billion[3]	Malaria:			
	1: Blood-Stage	RH5		MultiViVax, THE JENNER INSTITUTE, OXFORD
	2: Blood-Stage	RH5-VLP		wellcome trust, THE JENNER INSTITUTE, OXFORD
	3: Transmission	Pfs 48/45		OptimalVax, THE JENNER INSTITUTE, OXFORD
	4: Placenta-Borne	VAR2CSA		UNIVERSITY OF COPENHAGEN, UNIVERSITÄT TÜBINGEN
	5: Blood-Stage	CYRPA complex		Walter+Eliza Hall Institute of Medical Research, DISCOVERIES FOR HUMANITY

Note: AdaptVac is a joint venture between ExpreS²ion (34% owned) and NextGen Vaccines (66% owned)

[1] 2024 estimate from Evaluate Pharma for top 10 products and other, as of 9 June 2022
[2] Global Data, 2022, for HER2+ breast cancer
[3] Company estimate

Significant events in 2022

BREAST CANCER

EXPRES²ION BIOTECHNOLOGIES

The Most Common Cancer

1 in 8

women will be diagnosed with invasive breast cancer in her lifetime

~25%

have overexpression of HER2 receptors, associated with more aggressive tumors and reduced survival[2]

685,000

deaths worldwide in 2020 due to breast cancer[1]

1. Breast Cancer Research Foundation (https://www.bcrf.org/breast-cancer-statistics-and-resources. 2. Mitri Z et al. The HER2 Receptor in Breast Cancer: Pathophysiology, Clinical Use, and New Advances in Therapy. Chemother Res Pract. 2012; 2012: 743193)

Breast Cancer Overview

The ES2B-C001 vaccine can offer significant benefits compared to current treatment options

Monoclonal antibodies are the cornerstone of treatment for HER2+ breast cancer (>USD 11bn sales)[1]

- Target the HER2 receptor on tumor cells to reduce proliferation and induce tumor cell destruction

Herceptin® trastuzumab

PERJETA® pertuzumab

Serious drawbacks exist with these therapies[2]

- **Resistance** to monoclonal antibodies may develop
- **Potential for cardiac toxicity**
- **Repeated administration required**: 28-day half-life requires administration every 3rd week until remission or resistance develops, costs USD 30-50k

ExpreS²ion's vaccine-like approach offers potential to overcome drawbacks through *internal antibody production*

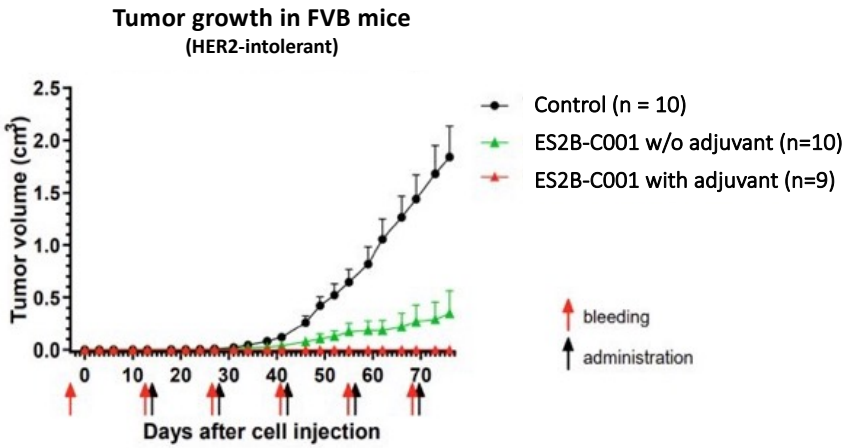
[1] GlobalData, 2022
[2] Pallerla et al. 2021. Cancer Vaccines, Treatment of the Future: With Emphasis onHER2-Positive Breast Cancer, International Journal of Molecular Sciences.; Krasniqi et al. 2019. Immunotherapy in HER2-positive breastcancer: state of the art and futureperspectives, Journal of Hematology & Oncology.

BREAST CANCER

ES2B-C001 Preclinical Proof-of-Concept (I)

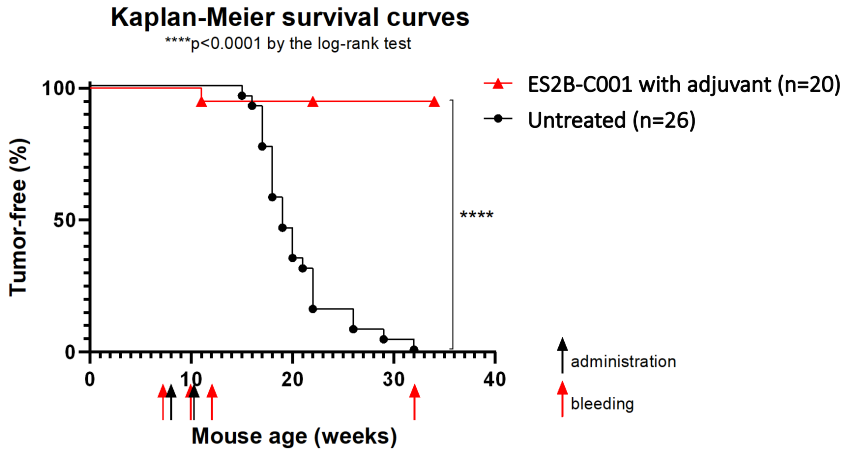
ES2B-C001 has demonstrated *in vivo* proof-of-concept

Effectively inhibited tumor development



- Two weeks after the inoculation of tumor cells, the first vaccine administration was given. Repeated every 2nd week during the study
- **ES2B-C001 formulated in an adjuvant totally blocks tumor development. ES2B-C001 without adjuvant partly blocks tumor development** and if tumors develop, growth is significantly inhibited

Prevented tumor development with 95% efficiency



- At mouse age 6-8 weeks, 2 vaccinations with 2 weeks interval were administered to Delta16 mice
- **Two vaccinations prevented tumor development with 95% efficiency** as compared to a control group, where all mice spontaneously developed tumors

Note: FVB mice are mice being challenged with tumors, while Delta16 mice spontaneously develop tumors and have been inoculated with tumor cells to accelerate tumor development

BREAST CANCER

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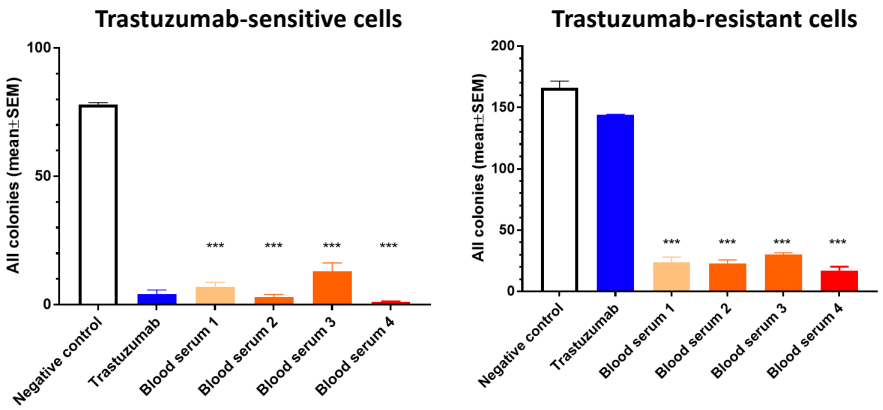
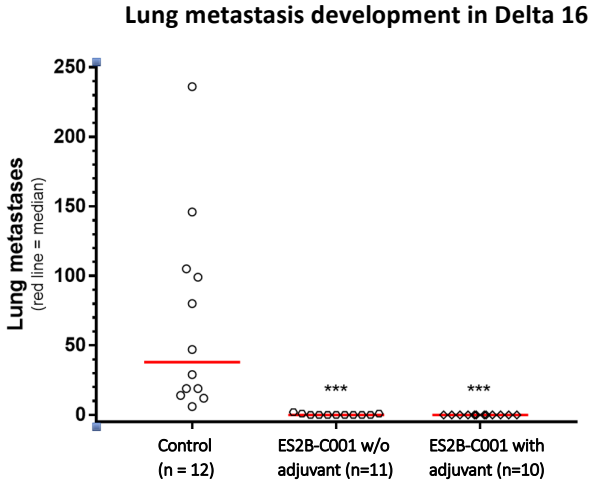
ES2B-C001 Preclinical Proof-of-Concept (II)

ES2B-C001 has demonstrated further preclinial proof-of-concept

Overcomes trastuzumab-resistance of tumors *in vitro*

Inhibited tumor development in delta16 HER2 tg mice





- *In vitro* PoC data in a growth inhibition assay: Blood serum from ES2B-C001-vaccinated mice **significantly inhibited the growth of HER2+ trastuzumab-sensitive as well as trastuzumab-resistant human tumor breast cancer cells**

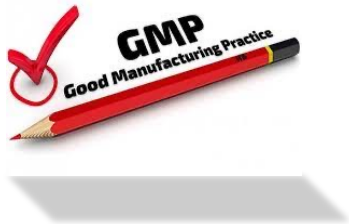
- One week after the intravenous (i.v.) injection of HER2+ tumor cells, the first vaccine administration was given. Repeated every 2nd week during the study
- **All mice vaccinated with E2SB-C001 with adjuvant were tumor-free**
- 73% of mice (8/11) vaccinated with ES2B-C001 without adjuvant were tumor-free, the remaining had 1-2 tumor lung nodules

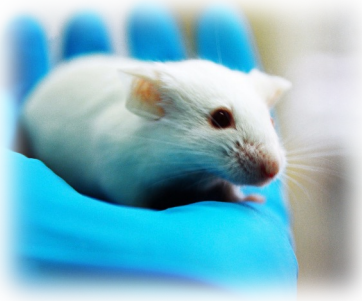
*** statistical significance (*in vitro* assay: p<0.001 vs negative control, Tukey's test; metastastic outgrowth *in vivo* model: p<0.0001 vs control, Dunn's non parametric, multiple comparisons test)

Progression as Planned

Important steps as ES2B-C001 is moving closer to the planned clinical Phase I trial in 2024

- GMP Manufacturing
  - GMP (Good Manufacturing Practice) Manufacturers selected and Work Order Statements executed
  - ExpreS^{2}ion's processes for manufacturing of material for HER2 antigen and VLP are transferred to the contract manufacturers
  - Development of GMP manufacturing processes are progressing as planned
- Preclinical Safety
  - GLP (Good Laboratory Practice) CRO (Contract Research Organisation) selected and Master Service Agreement executed
  - In accordance with feedback from DKMA (Danish Medicines Agency) preclinical safety studies have been planned in two species (1-month short-term testing in a rodent and non-rodent model) as well as long-term general GLP study in NHP (non-human primates)
  - The *in vivo* part of the short-term rodent safety study has been carried out, and the final report of the study is expected towards the end of 2022





CORONAVIRUS

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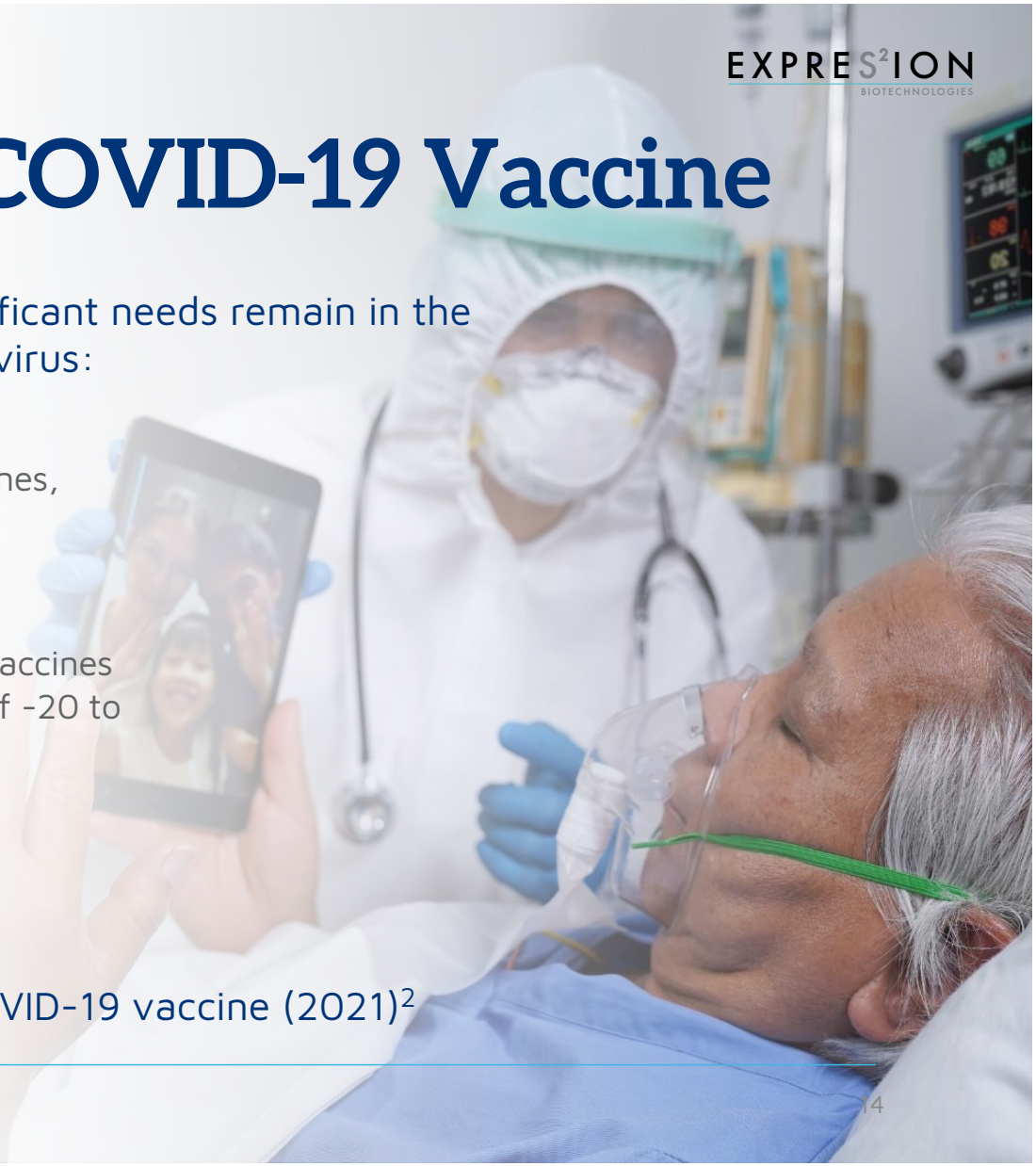
The 2nd Generation COVID-19 Vaccine

With **over 6.5 million deaths worldwide**[1], significant needs remain in the global long-term fight against the SARS-CoV-2 virus:

- Uncertain duration of effect with current vaccines, expected to need repeated boosters
- Storage and handling requirements for many vaccines create logistical constraints (requires storage of -20 to -80 degrees Celsius)
- Potential mutated variants may require rapid development of new vaccines



Global market size of **USD 137 billion** for the COVID-19 vaccine (2021)[2]

[1] WHO Coronavirus (Covid-19) Dashboard
[2] Meticulous Market Research, 2021

CORONAVIRUS

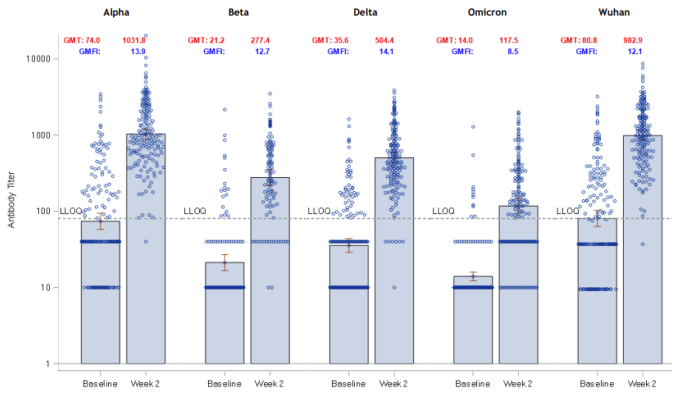
ABNCoV2 COVID-19 Vaccine

Bavarian Nordic completed the Phase II study, and initiated the Phase III study

Phase II results confirms ABNCoV2 as universal booster

- Evaluation as a booster vaccine in individuals with existing immunity. Study also assessed neutralizing immune responses against circulating variants and durability.
- **Strong boosting effect across all variants of concern**
- **Level of neutralizing antibodies at levels reported to be associated with high level of protection (>90%)[1]**
- **Level of neutralizing antibodies lowest for beta and omicron**
- **Potentially greater durability across variants of concern than mRNA vaccines**

Announced 17 October 2022



Phase III study initiated in USA and Europe

- 4,000 previously vaccinated subjects who will receive a booster vaccination with ABNCoV2 or an mRNA-based vaccine, aiming to demonstrate non-inferiority of ABNCoV2 to the licensed mRNA vaccine
- Manufacturing of vaccine bulk for the trial has been completed, filling now ongoing at BN's own manufacturing line

Trial initiated 2nd September 2022 and with anticipated headline results towards end 2022

Bavarian Nordic plans a rolling submission and potential launch in 2023

1) P. B. Gilbert et al., Science 10.1126/science.abm3425 (2021)

CORONAVIRUS

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Partnership with Bavarian Nordic

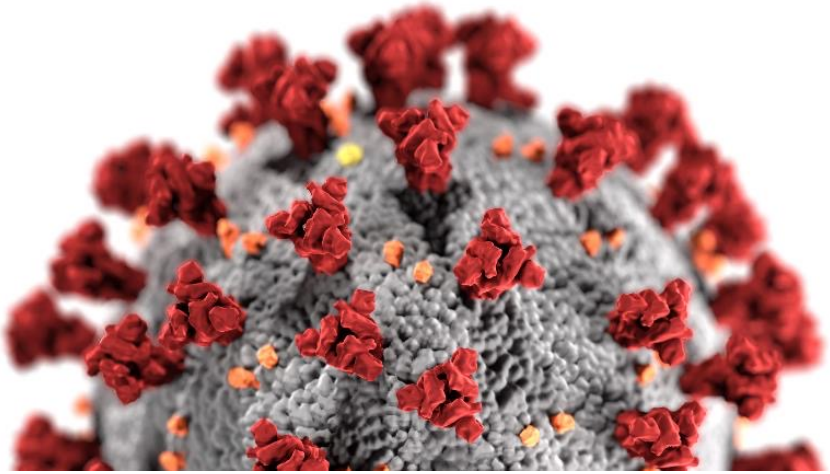
ABNCoV2 is already out-licensed with near-term revenue streams supporting ExpreS²ion

AdaptVac receive from Bavarian Nordic

- EUR 4 million upfront (paid in July 2020)
- Up to EUR 136 million in development and sales milestones
- Single- to double-digit-% royalties of Bavarian revenues

ExpreS²ion receive from AdaptVac

- 34% ownership of AdaptVac
- Up to EUR 2 million in commercial milestone payments
- Lower double-digit percentage of AdaptVac royalties




Financials and Outlook

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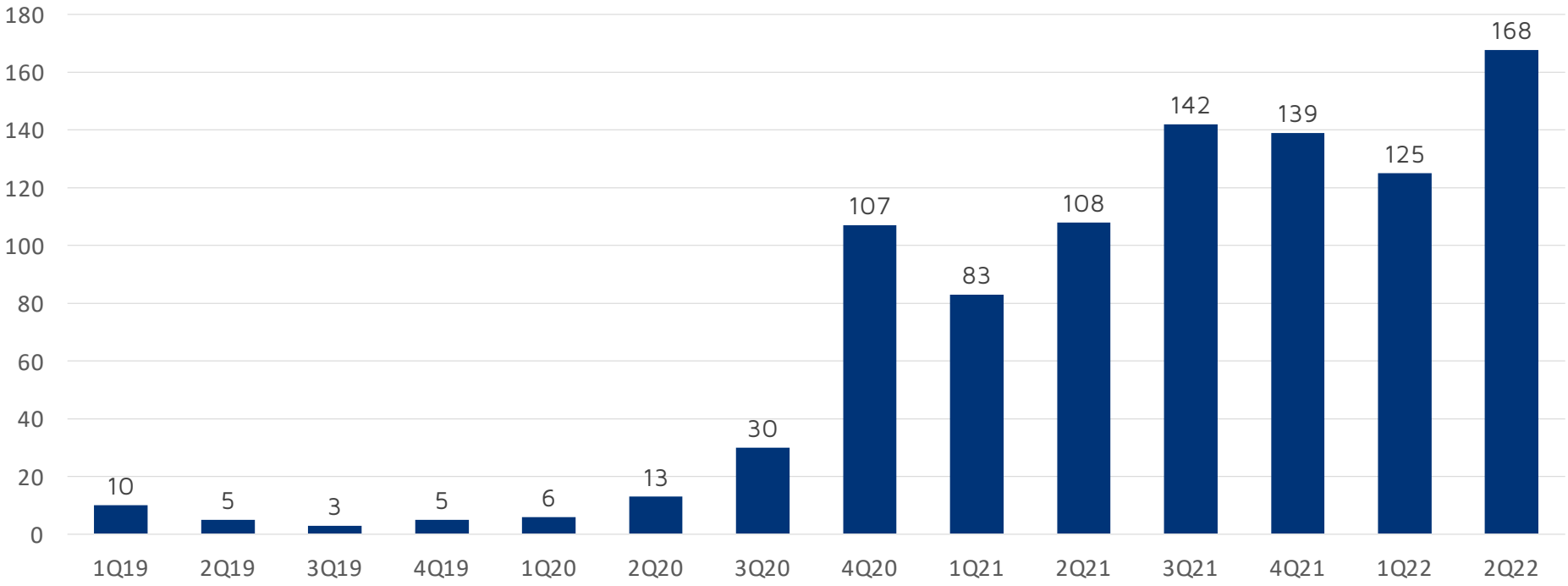
Cash Balance[1], 2019-2022 Quarterly

SEK millions



[1] For Q4 2021 and Q1 2022, the cash balance combines funds on the Company's SKAT account (interest-free tax asset with Denmark's tax authorities), and cash and bank. See page 16 of the 2Q 2022 report for more information.

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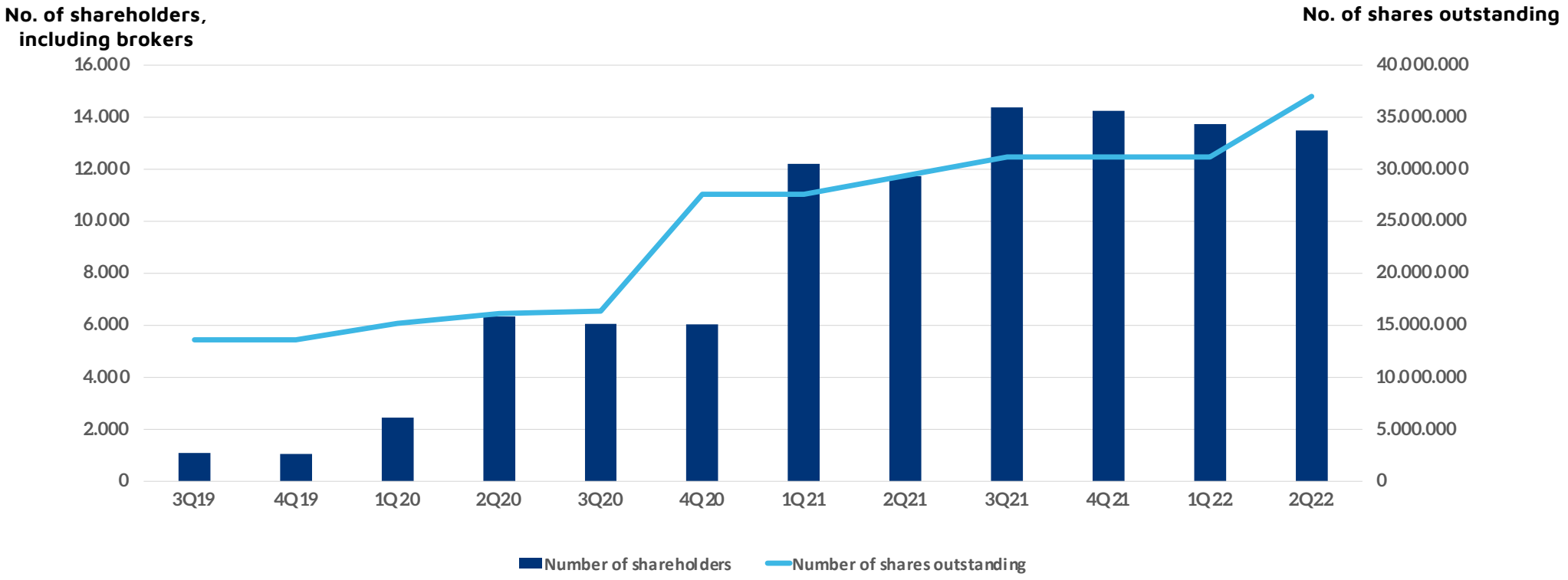
Shareholder Composition

No. of shareholders has increased to ~14,000, now holding ~37.6 million shares



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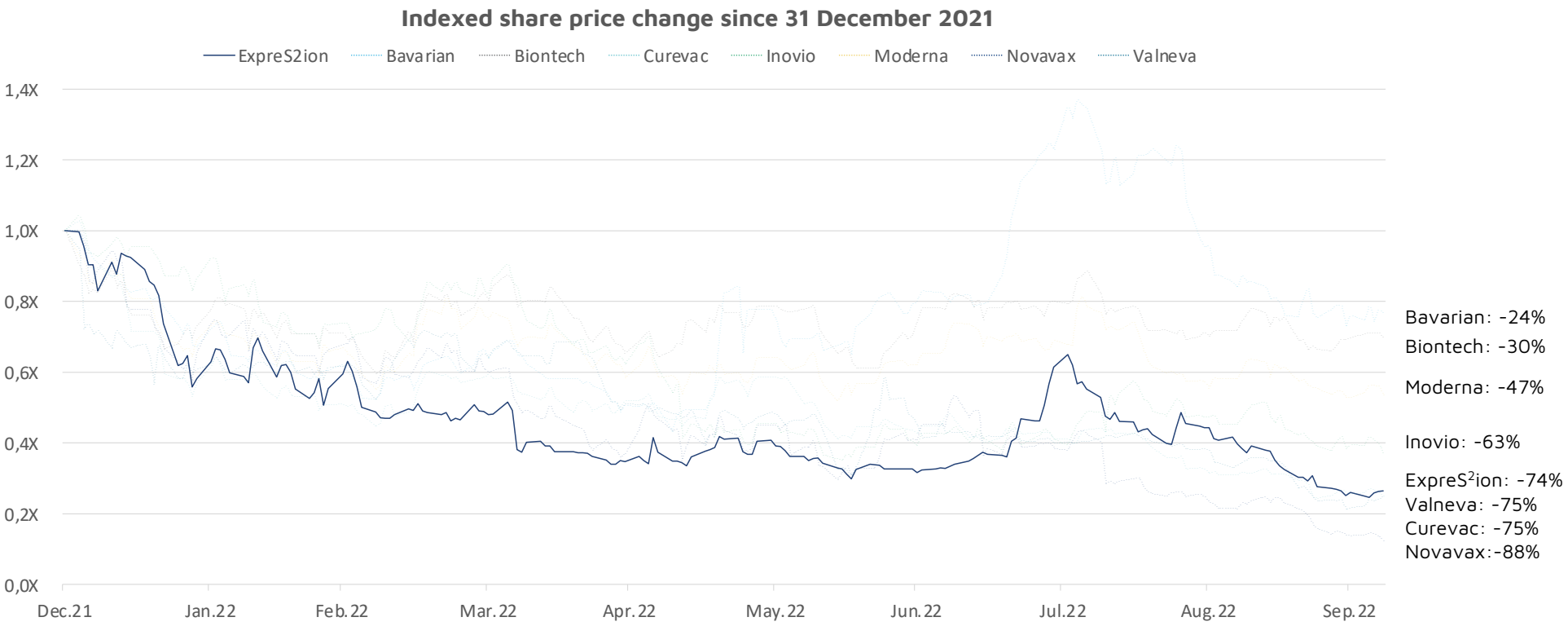
Peer Comparison Market Valuations

Lower sales estimates and systematic risk taking reducing COVID-19 vaccine valuations



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Advancing Towards Key Catalysts

	2022	2023	2024
 **CORONAVIRUS (ABNCoV2)**	✓BN Phase II study initiation Q3 21 · ✓BN Phase II study readout H1 2022 · ✓BN Phase III study initiation Q3 2022 · **BN Phase III initial trial results towards end of 2022**	**BN initiating rolling submission in H1 2023** · **BN ready for market launch** (subject to regulatory approval)	
 **BREAST CANCER (ES2B-C001)**	✓Executed in-licensing (Feb 2021) · ✓Preclinical animal studies initiated (Q2) · ✓Preclinical animal proof-of-concept results H1 2022 · GMP manufacturing processing	Preclinical safety studies readout · Filing of clinical study application H2 2023	**Initiation of first human clinical study 2024** · **Outlicensing window opens pending human data**
 **INFLUENZA**	✓Advance/support further development of one or more candidates in 2022	cGMP/Preclinical safety studies initiation (subject to new grant funding)	
 **MALARIA**	✓Phase IIa results from the Rh5 vaccine published in 2021 · ✓RH5 Additional phase I study in a malaria endemic region in Africa launched during 2021, with alternative adjuvant · **Pfs 48/45 phase I study initiation 2022**	**RH5-VLP phase I initiation 2023** · **RH5 phase I study readout H2 2023**	

Note: Timeline for ABNCoV2 is based on Bavarian Nordic's communicated timeline, and is subject to potential revision


Thank you!
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