14th December 2022

Proteins for Life

ExpreS²ion Biotech Holding AB – a clinical Phase III development stage biotech company

Virtual Nordic Growth Days organised by H. C. Andersen Capital / Inderes

Bent U. Frandsen, CEO

EXPRES²ION BIOTECHNOLOGIES

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Investment Highlights

We turn complex proteins into tomorrow's vaccines

High-potential **pipeline** of key focus within infections diseases and oncology, backed up by strong intellectual property rights

Vaccine development platform with strong track record and partner validation and regulatory approved for late-stage clinical development. +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

ExpreS²ion is **advancing towards key catalysts** during 2023, further de-risking the company's pipeline. COVID-19 vaccine clinical Phase III initiation in Q3 2022. Moving towards commercial launch in 2023-24.

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]	COVID-19	ABNCoV2/SARS-CoV-2 cVLP					Ph. III initiated		BAVARIAN NORDIC, adaptVAC
>€10 billion[2]	Breast Cancer	ES2B-C001/HER2-cVLP			Progressed into cGMP/Tox				100% ExpreS²ion
>€4 billion[3]	Influenza	INDIGO/Hemagglutinin							INDIGO
>€0.5 billion[3]	CMV	ES2B-I002	New research programme						50% / 50% ExpreS²ion / Evaxion
>€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, EBERHARD KARLS 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

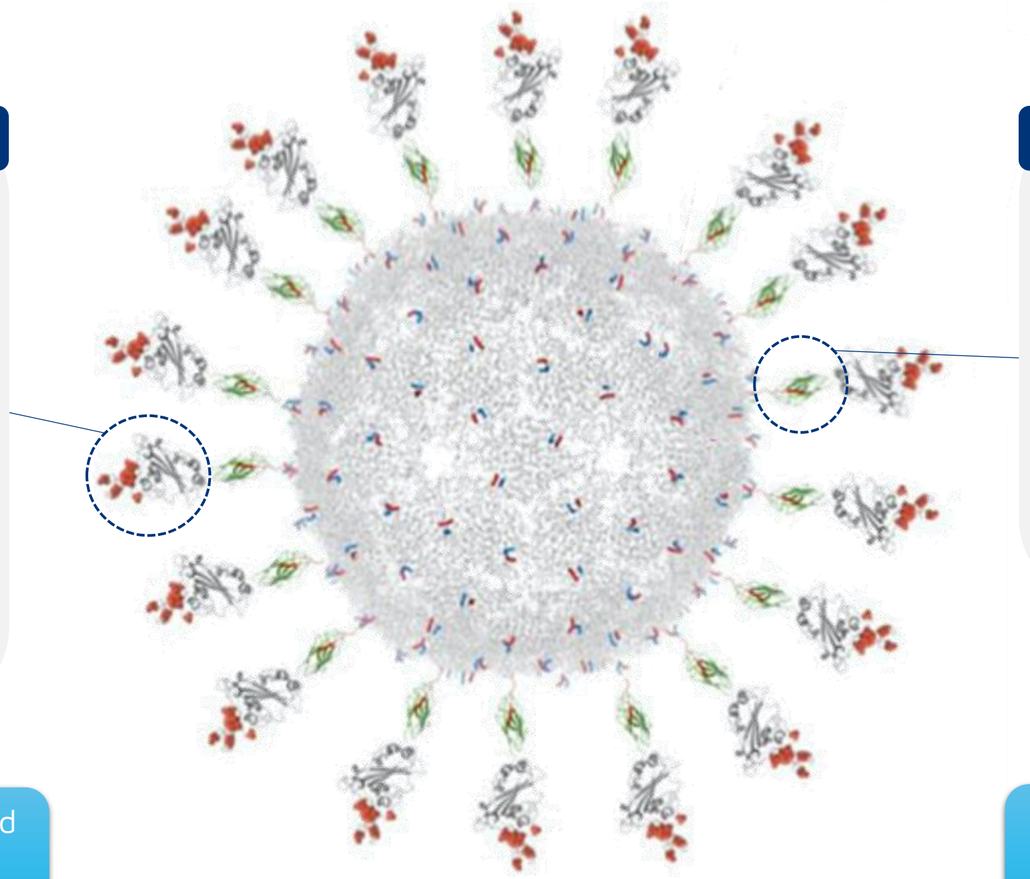
Unique Technology Platform(s)

Making highly immunogenic antigens and coupling with unique presentation technology

ExpreS2™ platform

- Combines S2 insect 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)
- Produces the complex surface proteins (antigens), that are critical to immune system recognition and response

100% ownership



Particle (VLP) technology

- AdaptVac's proprietary virus-like particles (VLP) technology via a unique tag-catcher isopeptide bonding method (superglue) 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

ExpreS2™ technology platform applied in all pipeline assets, including influenza, CMV, and malaria

Same technology platforms applied for the HER2 vaccine ES2B-C001 and COVID-19 vaccine ABN-CoV2

[1] Schneider I (1972). "Cell Lines Derived from Late Embryonic Stages of *Drosophila melanogaster*". *J. Embryol. Exp. Morphol.* 27: 363–365. *Drosophila melanogaster* is also known as the fruit fly.

Notes: ExpreS^{2}ion Biotech founders invented an Improved Vector System derived from S2 cells; granted patent until 2032 (US); glyco-engineered S2 cells pending patents until 2040.

The ExpreS2™ platform is 100% owned by ExpreS^{2}ion. The VLP technology applied in ES2B-C001 and ABNCoV2 is 100% owned by AdaptVac, which ExpreS^{2}ion owns 34% of.

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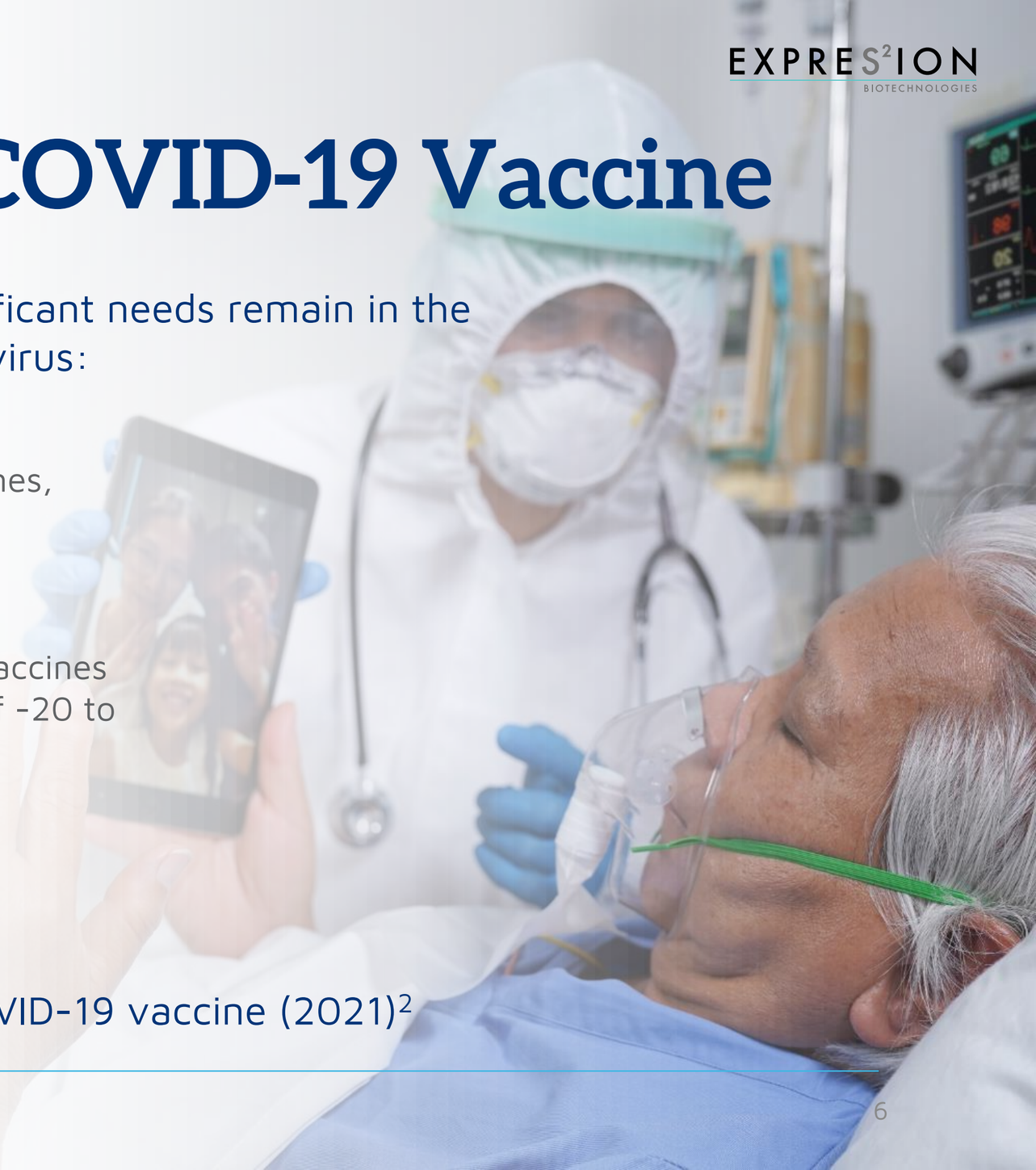
The 2nd Generation COVID-19 Vaccine

With **over 6.6 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

COVID-19

ABNCoV2 COVID-19 Vaccine

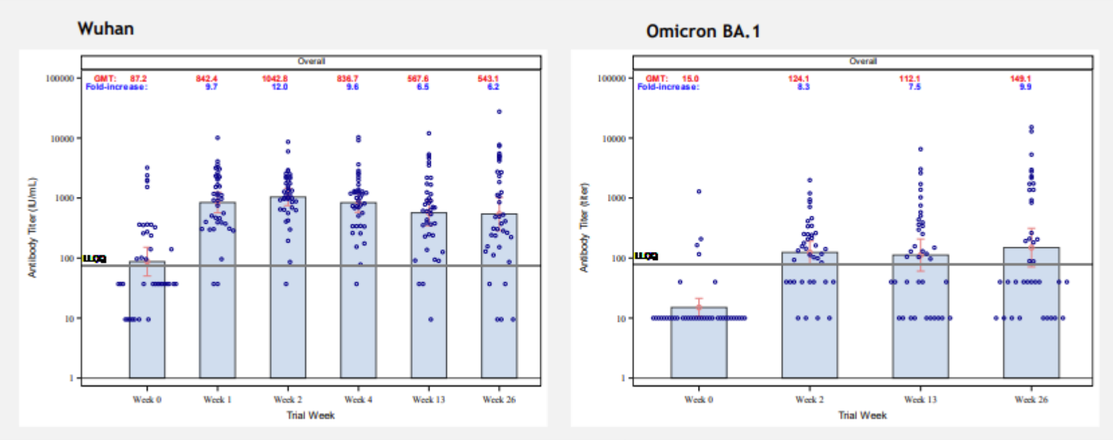
Bavarian Nordic completed the Phase II study, and initiated the Phase III study

Phase II results confirms ABNCoV2 as universal booster

- Evaluation as a booster vaccine in ~100 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

Announced 17 October 2022

- **Phase II six-month follow up data in 41 out of 103 subjects demonstrated durable antibody levels across variants of concern**



Bavarian Nordic data published 9th November 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 Bavarian Nordic's own manufacturing line

Trial initiated 2nd September 2022 with initial data read-out expected early 2023

Bavarian Nordic plans a rolling submission in 2023 and subject to approval, launch

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

COVID-19

Partnership with Bavarian Nordic

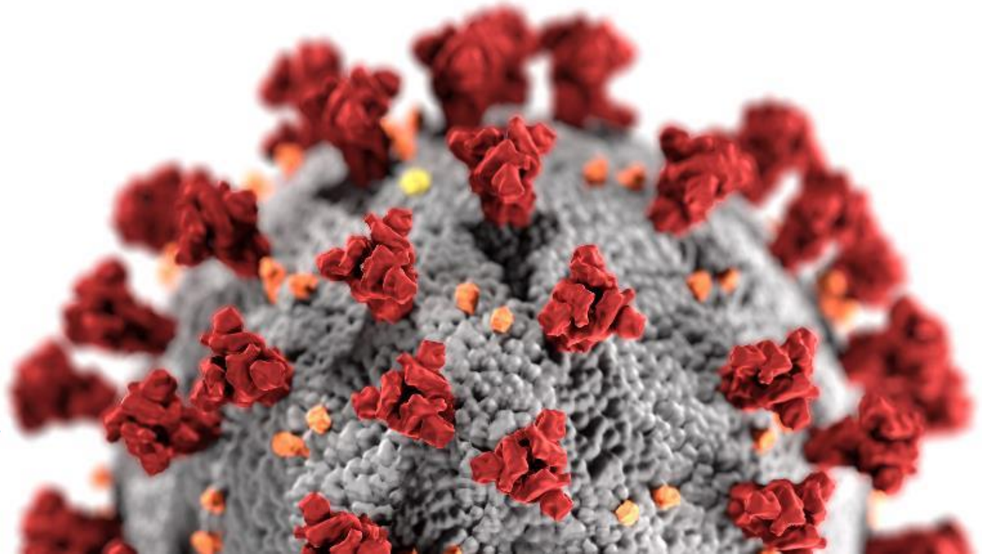
ABNCoV2 is already out-licensed with near-term revenue streams supporting ExpreS²ion

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



BREAST CANCER

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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)

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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 HER2-targeted vaccine approach offers potential to overcome some of the drawbacks through *internal polyclonal 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 future perspectives, Journal of Hematology & Oncology.

BREAST CANCER

EXPRES²ION BIOTECHNOLOGIES

New Publication Supports ES2B-C001

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,‡]

[1] Alma Mater Institute on Healthy Planet and Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, 40126 Bologna, Italy
[2] Department of Molecular Medicine, University of Pavia, 27100 Pavia, Italy
[3] ExpreS2ion Biotechnologies, SCION-DTU Science Park, 2970 Hørsholm, Denmark
[4] Experimental Oncology Laboratory, IRCCS Istituto Ortopedico Rizzoli, 40136 Bologna, Italy
* Correspondence: pierluigi.lollini@unibo.it; Tel.: +39-051-2094786
† 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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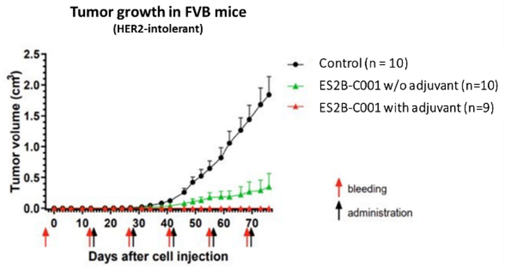
Published: 20 October 2022

Accepted 17 October 2022

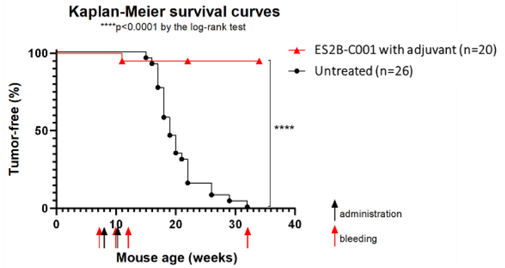
Preclinical Proof-of-Concept

Effectively inhibited tumor development



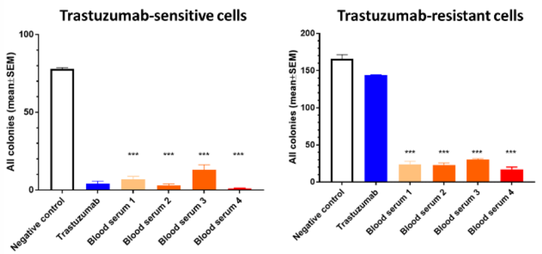
- Two weeks after the inoculation of tumor cells, the first vaccine administration was given. Repeated every 2nd week during the study
- **ES2B-C001 formulated in an adjuvant totally blocks tumor development. ES2B-C001 without adjuvant partly blocks tumor development** and if tumors develop, growth is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

Prevented tumor development with 95% efficiency



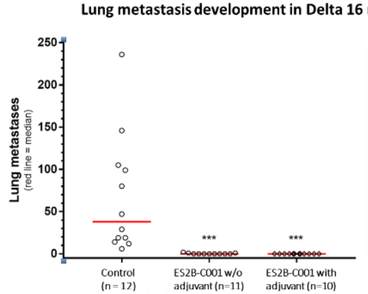
- At mouse age 6-8 weeks, 2 vaccinations with 2 weeks interval were administered to Delta16 mice
- **Two vaccinations prevented tumor development with 95% efficiency** as compared to a control group, where all mice spontaneously developed tumors

Overcomes trastuzumab-resistance of tumors *in vitro*



- *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**

Inhibited tumor development in delta16 HER2 tg mice



- 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

Reference: F. Ruzzi *et al* (2022): "Prevention and Therapy of Metastatic HER-2+ Mammary Carcinoma with a Human Candidate HER-2 Virus-like Particle Vaccine", **Biomedicines**. https://www.mdpi.com/2227-9059/10/10/2654

CYTOMEGALO-
VIRUS
(CMV)

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A Very Common Infection

1 in 3

children is already infected with CMV by age 5

>50%

of US adults are infected with the virus by age 40[1]

1 in 5

organ transplants (kidney, liver, heart) are at risk of CMV infection[2]

1 in 200

born with congenital CMV infection (CCMI). ~20% newborns with CCMI have long-term health problems

1. Centers for Disease Control & Prevention (https://www.cdc.gov/cmv/index.html).
2. Cytomegalovirus infection in transplant recipients, Luiz Sergio Azevedo (Clinics, 2015)

Uniting Forces in CMV Vaccine Research

ExpreS²ion and Evaxion Biotech new vaccine research partnership since December 2022

Announced 6 December 2022

- **Vaccine Discovery Collaboration Agreement**
- Research partnership with focus on discovery and development of a **novel CMV Vaccine / ES2B-I002**
- Joint research efforts in discovery phase for ~2 years
  - EVX: AI Platform[1], including RAVEN™
  - ES2B: ExpreS2™ platform and know how in vaccine production and development
  - EVX: Early establishment of Immunogenicity in preclinical models
- 50:50 cost sharing during discovery phase
- **Selection of vaccine candidate**, expected in 2025
  - ES2B first option to in-license CMV vaccine asset
  - ES2B sponsors development onwards thereafter

AI = Artificial Intelligence - Using AI, Evaxion (EVX) simulates the human immune system and generate predictive models to identify and develop next-generation medicines

Advancing Towards Key Catalysts

	2022	2023	2024	2025
COVID-19 (ABNCoV2)	✓ BN Phase II study readout H1 2022 ✓ BN Phase III study initiation Q3 2022	BN Phase III initial readout BN initiating rolling submission BN ready for market launch (subject to regulatory approval)	Royalties from sales?	
BREAST CANCER (ES2B-C001)	✓ Preclinical animal proof-of-concept results H1 2022 ✓ Preliminary preclinical safety studies initiated GMP manufacturing processing	Preclinical safety studies readout Filing of clinical study application H2 2023	Initiation of first human clinical study 2024	Out-licensing window opens pending human data
INFLUENZA (INDIGO)	✓ Advance/support further development of one or more candidates in 2022	cGMP/Preclinical safety studies initiation (subject to new grant funding)		
CYTOMEGALOVIRUS (ES2B-I002)	✓ Establish 50:50 discovery partnership on CMV vaccine with Evaxion	Early research on CMV vaccine target, applying AI	Preclinical testing of immunogenicity of CMV vaccine target	Selection of lead CMV vaccine candidate
MALARIA	✓ 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 2023 (pending University of Oxford) RH5-VLP phase I initiation 2023 (pending University of Oxford) 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!

Contact:
info@expreS2ionbio.com

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for Life

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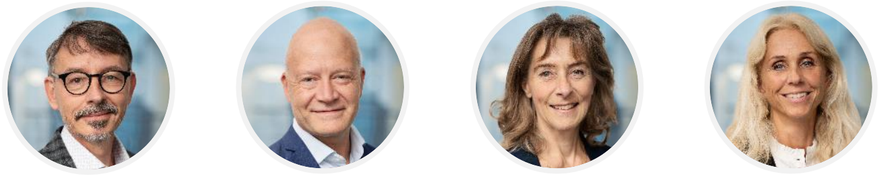
Management Team

>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

New Scientific Advisory Board

Key Opinion Leaders (KOLs) providing clinical advise on our oncology development programme

Dr. Giuseppe Curigliano, MD, PhD
Associate Professor of Medical Oncology at the University of Milano and the Head of the Division of Early Drug Development at the European Institute of Oncology, Italy (IRCCS). Dr. Curigliano is recognized among the leading experts in the world within the field of HER2 expressing breast cancer and has authored or co-authored more than 650 peer-reviewed scientific papers.

Dr. Daniel Lenihan, MD, FACC, FESC, FIC-OS
Dr. Lenihan has been active in cardio-oncology, for over 25 years. He has previously held positions at MD Anderson Cancer Center in Houston, Texas, Vanderbilt University in Nashville, Tennessee, and Washington University in St Louis, Missouri. His current research projects include early phase clinical trials in cardio-oncology, heart failure and amyloidosis. Dr. Lenihan serves as editor on several scientific journals and has authored or co-authored more than 210 peer-reviewed scientific papers.

Dr. Javier Cortes, MD, PhD
Doctor in Medical Oncology, and Head of the International Breast Cancer Centre (IBCC) in Barcelona. Dr. Cortes He is an active member of the Spanish, European, and American Societies of Medical Oncology (SEOM, ESMO, ASCO), and is a member of expert panels that develop the treatment guidelines for metastatic breast cancer. He is the author of more than 380 publications.

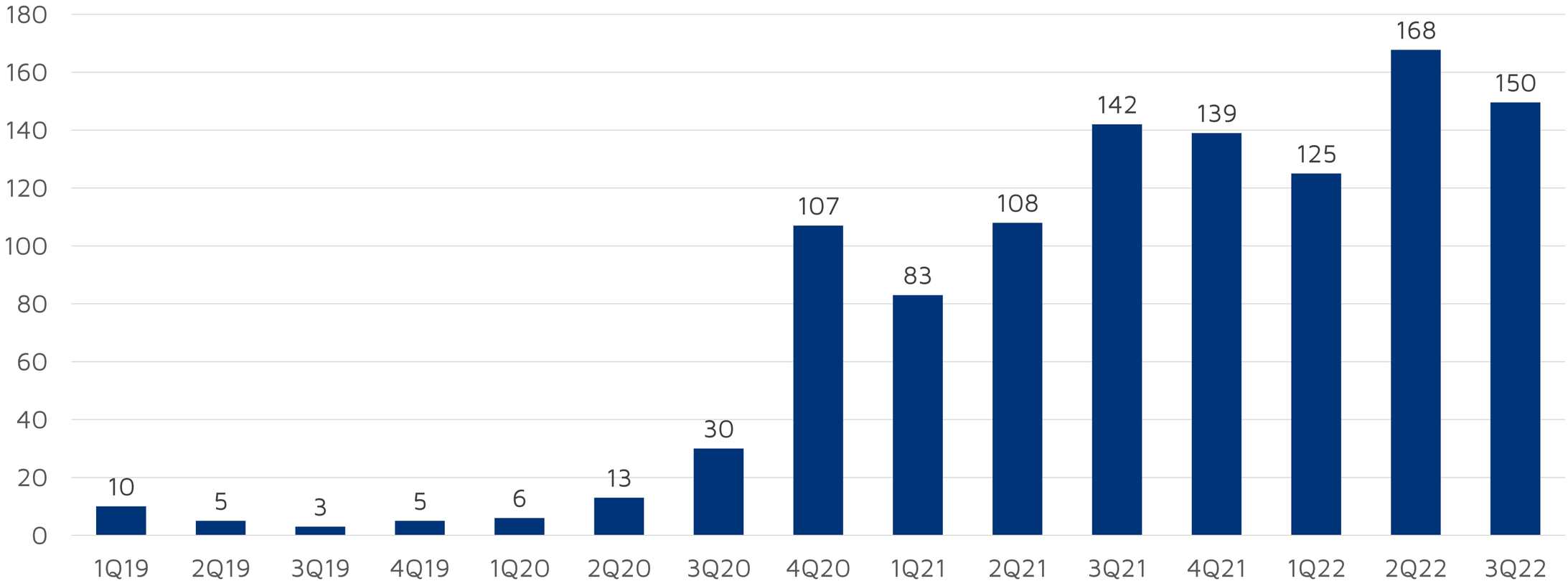
Dr. Ulrik Lassen, MD, PhD
Professor at University of Copenhagen, Department of Clinical Medicine. In 2017, he was appointed Head of the Department of Oncology at Copenhagen University Hospital, Rigshospitalet, Denmark. As a Clinical Oncologist he has been working with Phase 1 Oncology trials since 2005 and is ESMO board certified in Medical Oncology. Dr. Lassen has (co-)authored ~300 peer reviewed publications.

Dr. Michael Andersson, MD, DMSci
Dr. Andersson is a Clinical Oncologist working as consultant at the Breast Oncology Unit in the Copenhagen University Hospital, Rigshospitalet, Denmark since 1998. He has special interest in HER2-positive breast cancer and has published on and been Principal Investigator in several national and international studies of HER2-positive early and metastatic breast cancer. Dr. Andersson has authored or co-authored more than 140 peer reviewed publications.

Dr. Rupert Bartsch, MD
Associate Professor of medicine at the Medical University of Vienna in Austria and serves as the director of the Breast Cancer Programme at the Department of Oncology. Dr. Bartsch has a longstanding clinical and scientific focus on breast cancer and brain metastases. Together with his colleagues, he has published over 150 articles in peer-reviewed journals.

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.