

30th November 2022

Proteins for Life

Expres²ion Biotech Holding AB
BioStock Life Science Summit
Lund, Sweden

Bent U. Frandsen, CEO

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




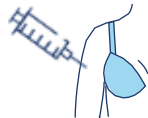












Global vaccine market rapidly growing, from USD 33bn (2019) to USD 187bn (2021), corresponding to 460% growth

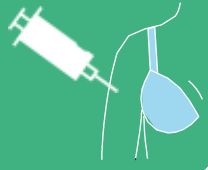


ExpreS²ion is advancing towards key catalysts during 2022-23, further de-risking the company's pipeline. COVID-19 vaccine clinical Phase III initiation in Q3 2022. Moving towards commercial launch in 2023-24.

Deep Pipeline for Value Creation

Market Potential	DISEASE	Project/Target	Development Progress						Partner/Funding
			Discovery	Pre-clinical Pharmacology	cGMP / Tox	Phase I	Phase II	Phase III	
>€30 billion ¹	Coronavirus		ABNCoV2/SARS-CoV-2 cVLP						  BAVARIAN NORDIC PREVENT-nCoV
>€10 billion ²	Breast Cancer		ES2B-C001/HER2 cVLP						100% ExpreS ² ion
>€4 billion ³	Influenza		Hemagglutinin						 INDIGO
>€0.4 billion ³	Malaria:								
	1: Blood-Stage		RH5						 MultiViVax
	2: Blood-Stage		RH5-VLP						 
	3: Transmission		Pfs 48/45						 OptimalVax
	4: Placenta-Borne		VAR2CSA						  UNIVERSITÄT TUBINGEN
	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)



The Most Common Cancer

1 in 8

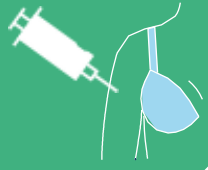
women will be diagnosed with
invasive breast cancer in her
lifetime

~25%

have overexpression of HER2
receptors, associated with
more aggressive tumors and
reduced survival²

685,000

deaths worldwide in 2020
due to breast cancer¹



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

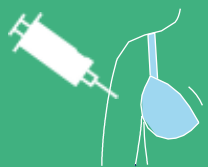
- Target the HER2 receptor on tumor cells to reduce proliferation and induce tumor cell destruction



Serious drawbacks exist with these therapies²

- **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*



Same technology platforms applied
for the COVID-19 vaccine ABN-CoV2

Unique Technology Platforms

Our HER2 vaccine ES2B-C001 combines a highly immunogenic antigen with unique presentation technology

ExpreS² platform

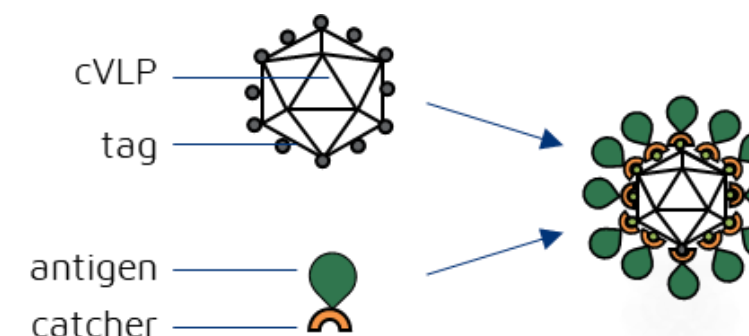
- Combines S2 cells with patented expression vectors (add a specific gene into a target cell and command the cell to produce the gene encoded protein), adapted culture agents and reagents (stimulating cell growth)
- Produces the complex surface proteins (antigens), like HER2, which are critical to immune system recognition and response

100% ownership

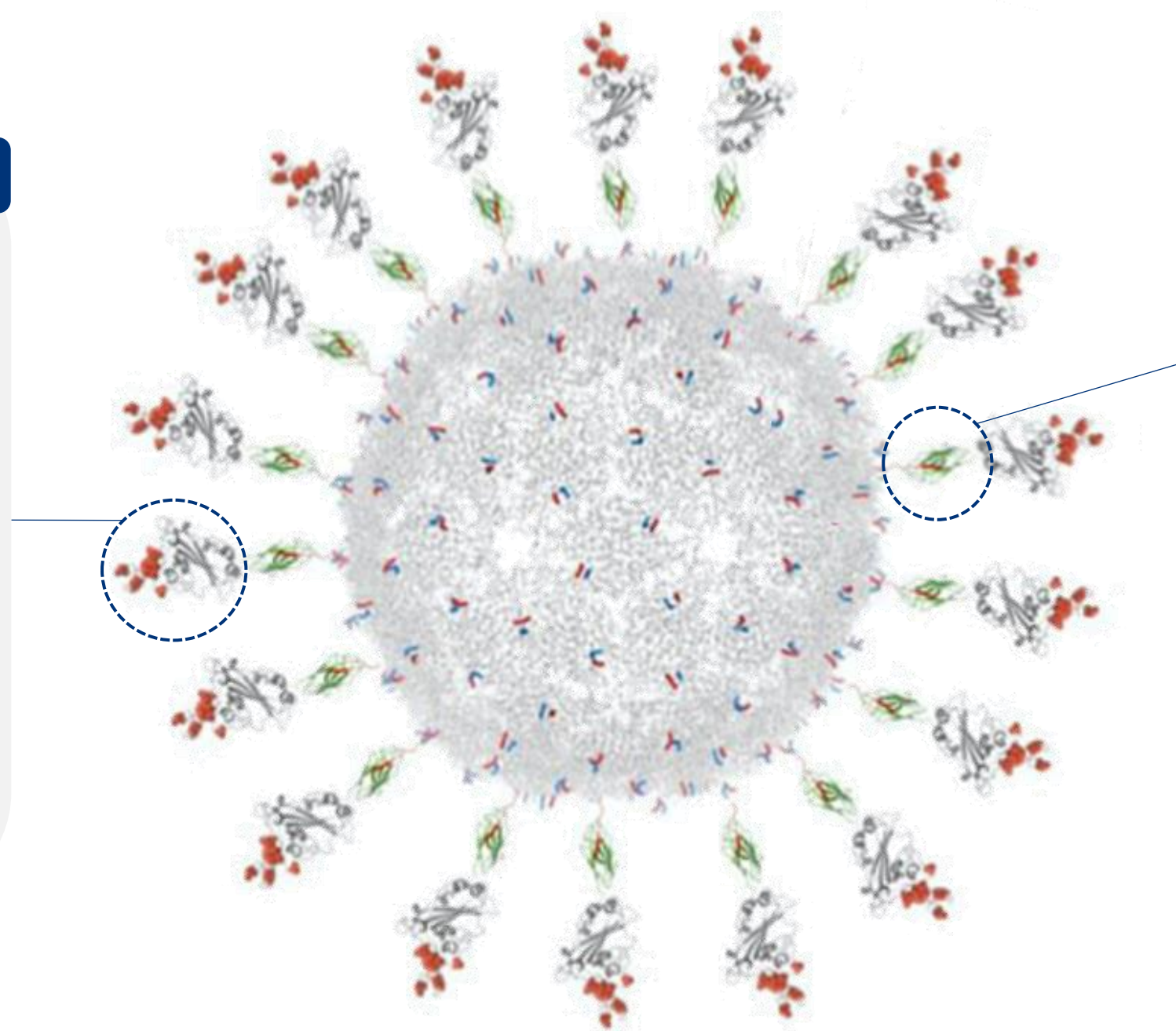
Particle (VLP) technology

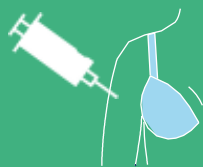
- AdaptVac's proprietary virus-like particles (VLP) technology securely attaches our proteins to the surface of a capsid (outer protein protective shell of a virus), mimicking a virus to elicit an immune response

34% ownership



cVLP: Capsid Virus Like Particle





New Publication Supports ES2B-C001



Article

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

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 - ² Department of Molecular Medicine, University of Pavia, 27100 Pavia, Italy
 - ³ ExpreS2ion Biotechnologies, SCION-DTU Science Park, 2970 Hørsholm, Denmark
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- * 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.; Dömeier, 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>

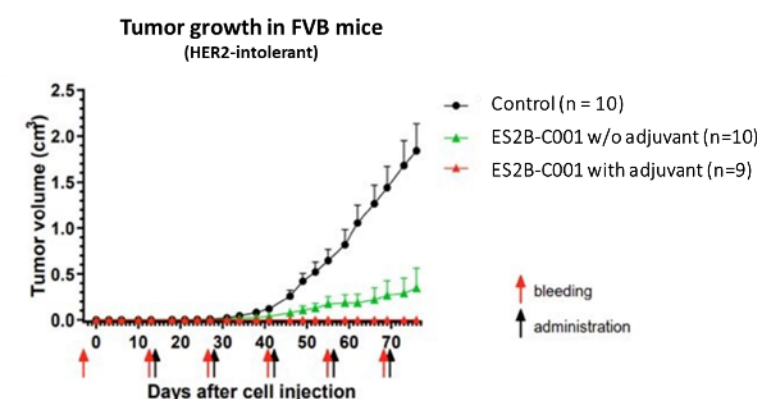
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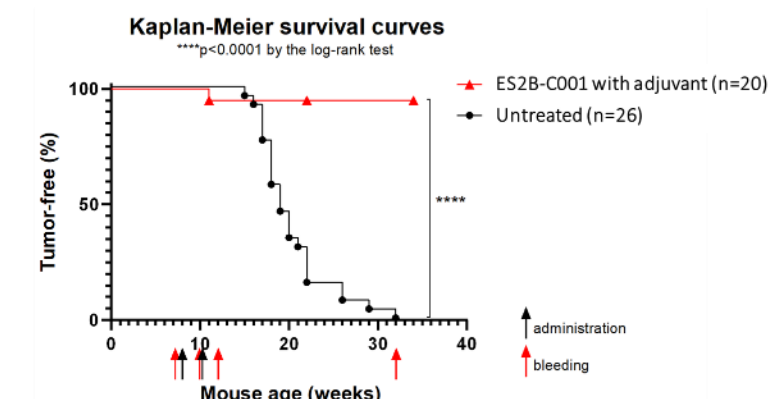
Preclinical Proof-of-Concept

Effectively inhibited tumor development



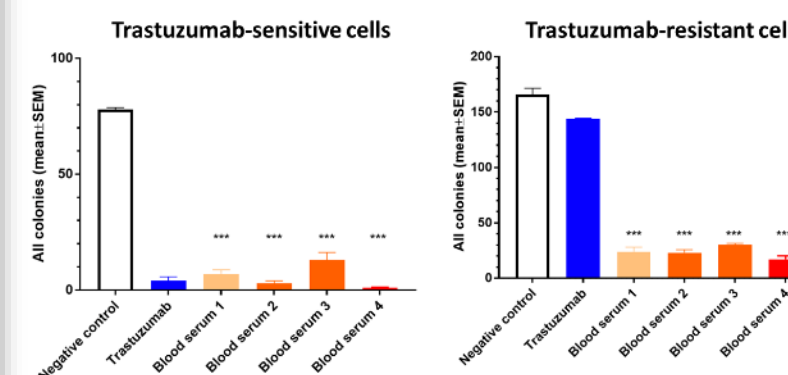
- Two weeks after the inoculation of tumor cells, the first vaccine administration was given. Repeated every 2nd week during the study
- ES2B-C001 formulated in an adjuvant totally blocks tumor development. ES2B-C001 without adjuvant partly blocks tumor development** and if tumors develop, growth is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

Prevented tumor development with 95% efficiency



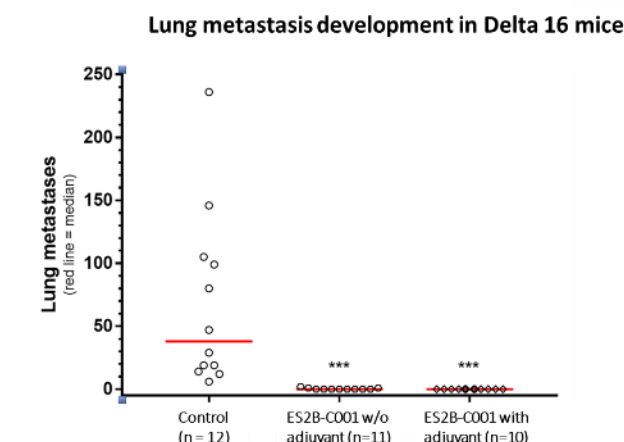
- At mouse age 6–8 weeks, 2 vaccinations with 2 weeks interval were administered to Delta16 mice
- Two vaccinations prevented tumor development with 95% efficiency** as compared to a control group, where all mice spontaneously developed tumors

Overcomes trastuzumab-resistance of tumors *in vitro*



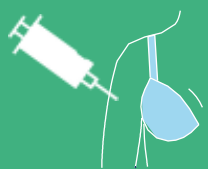
- In vitro* PoC data in a growth inhibition assay: Blood serum from ES2B-C001-vaccinated mice **significantly inhibited the growth of HER2⁺ trastuzumab-sensitive as well as trastuzumab-resistant human tumor breast cancer cells**

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 ES2B-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

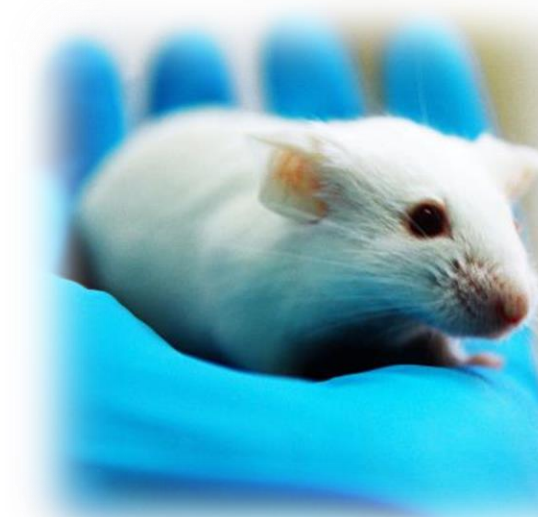
Reference: F. Ruzzi *et al.* (2022): "Prevention and Therapy of Metastatic HER-2⁺ Mammary Carcinoma with a Human Candidate HER-2 Virus-like Particle Vaccine", *Biomedicines*. <https://www.mdpi.com/2227-9059/10/10/2654>



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
 - ✓ ExpreS²ion'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 in the beginning of 2023
 - GLP study in NHP in 2023 with data expected mid-year
- Clinical trial application planned for submission end 2023





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



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

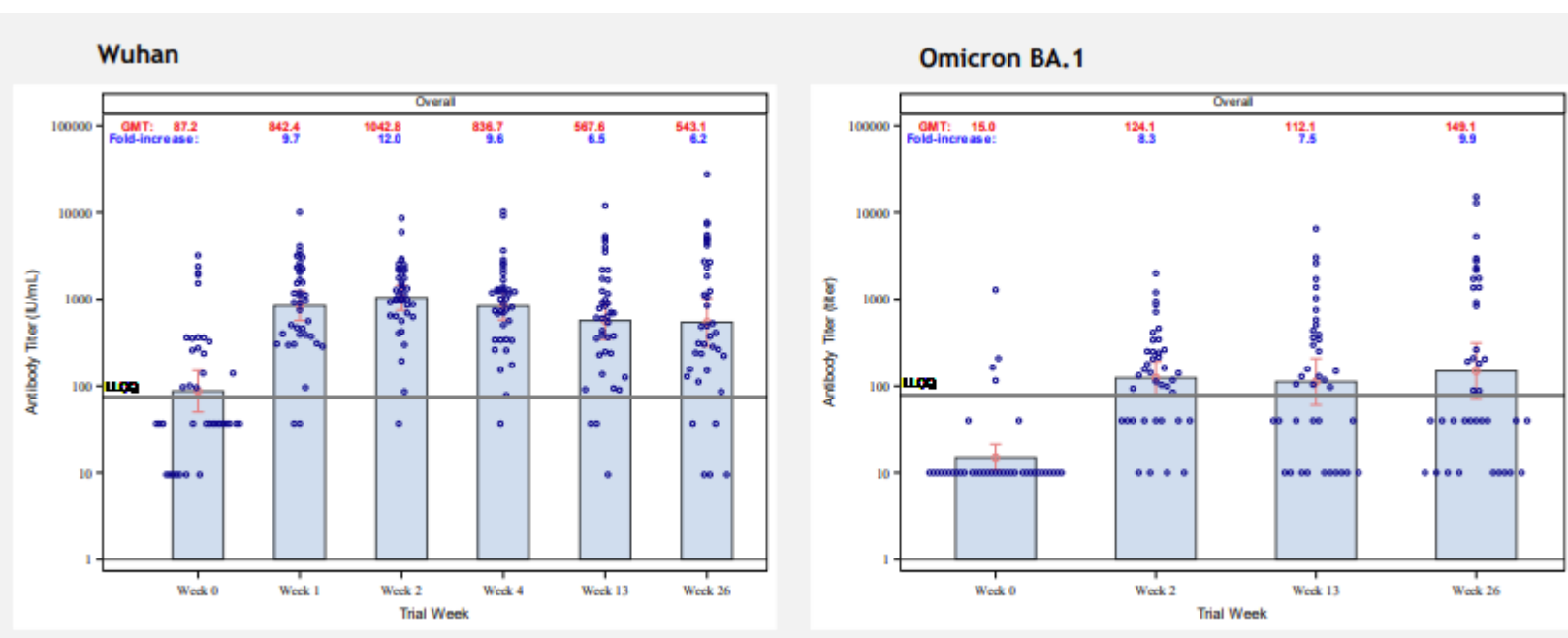
Phase III study initiated in USA and Europe

- 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 with initial data read-out expected early 2023

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



Bavarian Nordic data published 9th November 2022

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



Partnership with Bavarian Nordic

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

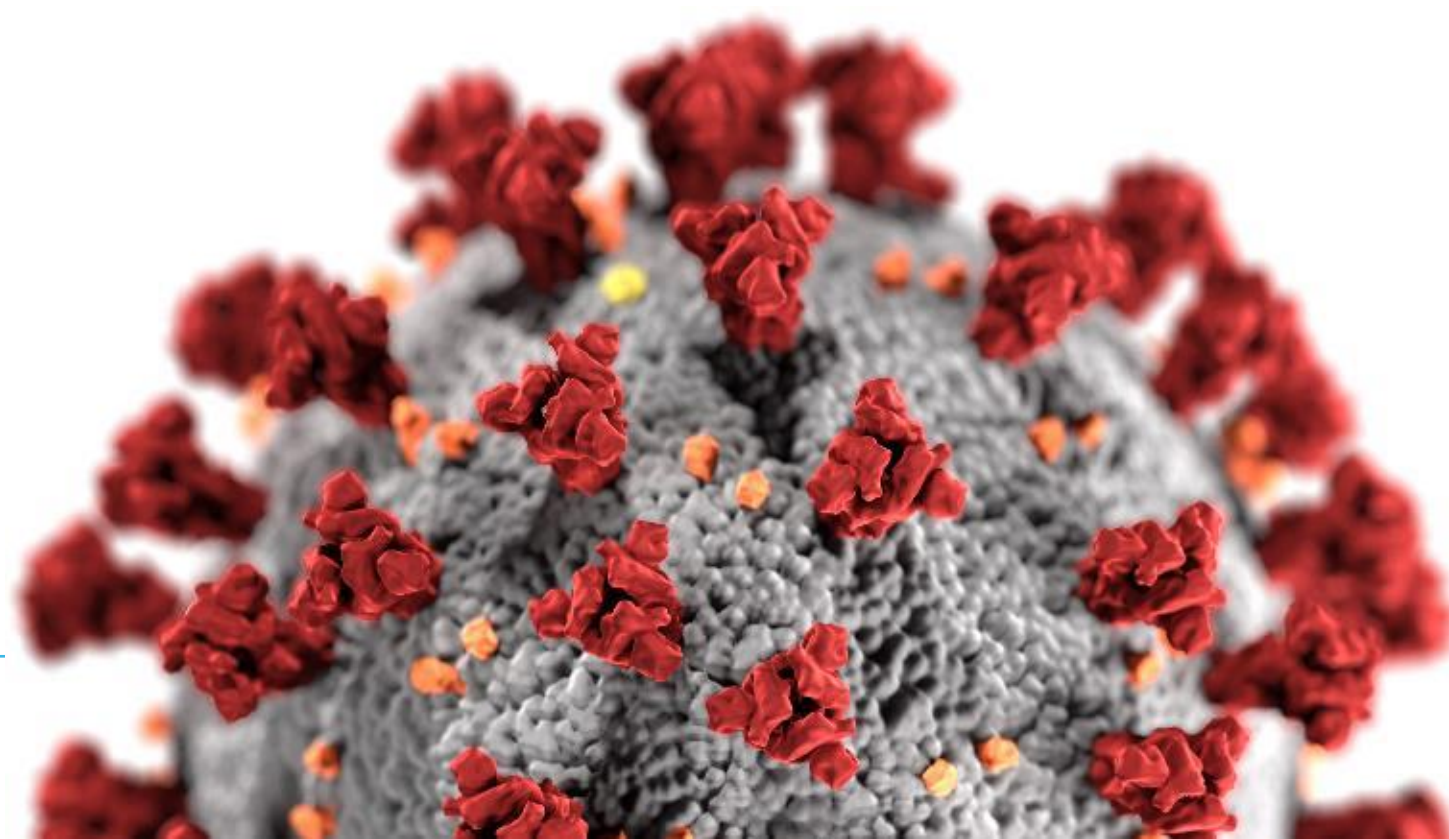
AdaptVac receive from Bavarian Nordic

- 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



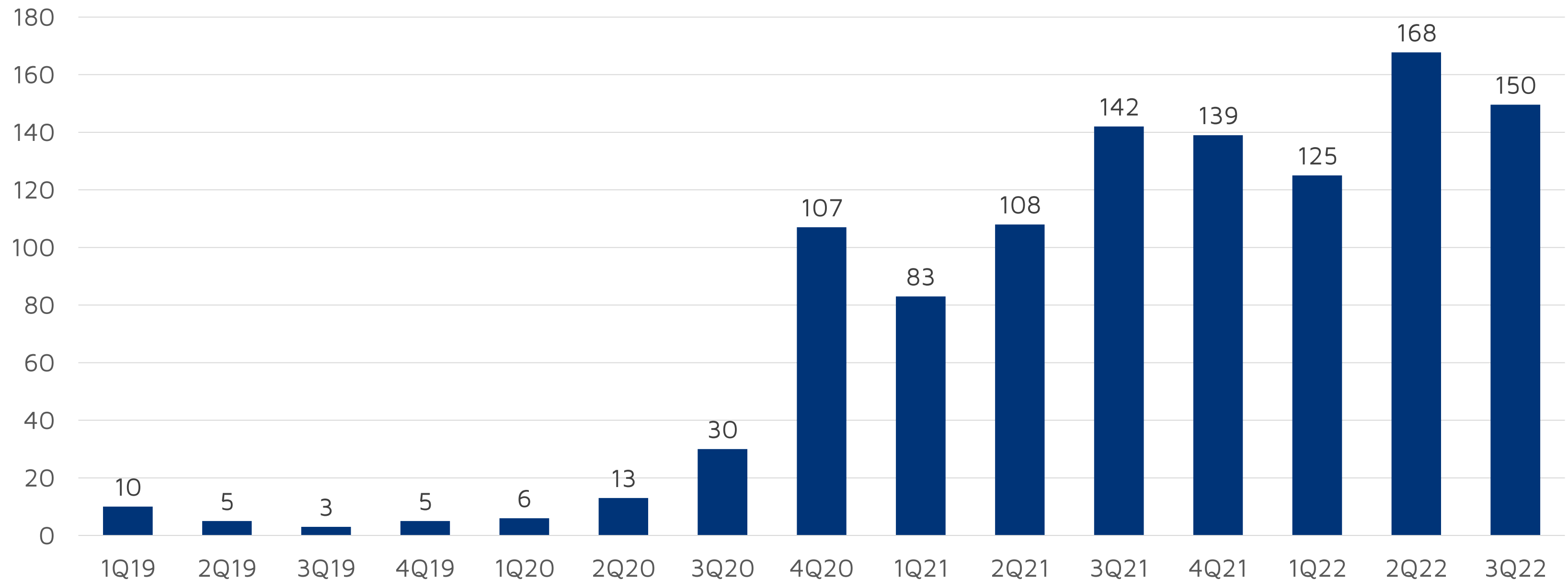
ExpreS²ion receive from AdaptVac

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



Cash Balance¹, 2019-2022 Quarterly

SEK millions



Advancing Towards Key Catalysts

	2022	2023	2024
 CORONAVIRUS (ABNCoV2) <ul style="list-style-type: none"> ✓ 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 readout in early 2023 BN initiating rolling submission BN ready for market launch (subject to regulatory approval)		
 BREAST CANCER (ES2B-C001) <ul style="list-style-type: none"> ✓ 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 <div>Out-licensing window opens pending human data</div>		
 INFLUENZA <ul style="list-style-type: none"> ✓ Advance/support further development of one or more candidates in 2022 	cGMP/Preclinical safety studies initiation (subject to new grant funding)		
 MALARIA <ul style="list-style-type: none"> ✓ 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 (pending University of Oxford) 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

A person is shown from the side, holding a piece of paper and drawing three virus-like particles with blue markers. The particles are spherical with a textured surface and several spikes or protrusions. The background is a wooden desk.

Thank you!

Contact:
info@expres2ionbio.com

Proteins
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EXPRES²ION
BIOTECHNOLOGIES

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



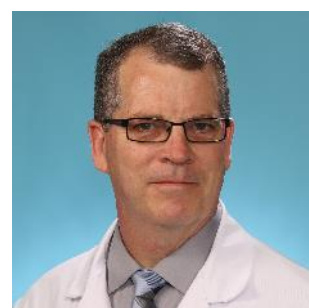
Dr. Giuseppe Curigliano, MD, PhD

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. 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. 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. 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. 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. 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.