

# **ANNUAL REPORT**

**2017**



BAVARIAN NORDIC

# FORWARD-LOOKING STATEMENTS

*This presentation includes forward-looking statements that involve risks, uncertainties and other factors, many of which are outside of our control that could cause actual results to differ materially from the results discussed in the forward-looking statements. Forward-looking statements include statements regarding our short-term objectives and opportunities, financial expectations for the full year and financial preparedness as of year end, as well as statements concerning our plans, objectives, goals, future events, performance and/or other information that is not historical information. All such forward-looking statements are expressly qualified by these cautionary statements and any other cautionary statements which may accompany the forward-looking statements. We undertake no obligation to publicly update or revise forward-looking statements to reflect subsequent events or circumstances after the date made, except as required by law.*

The background is a solid teal color. It features several large, semi-transparent circles of varying sizes. One large circle is in the top right corner, another is in the center, and a third is in the bottom right. There are also several smaller circles scattered in the middle right area.

# FINANCIALS

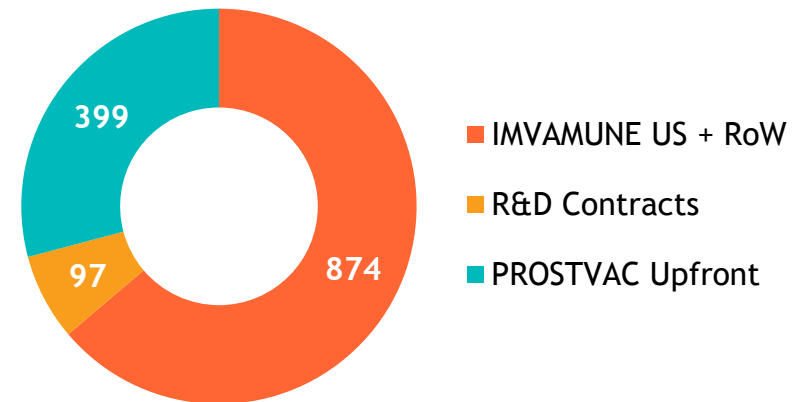
OLE LARSEN, CFO

# FINANCIAL RESULTS 2017

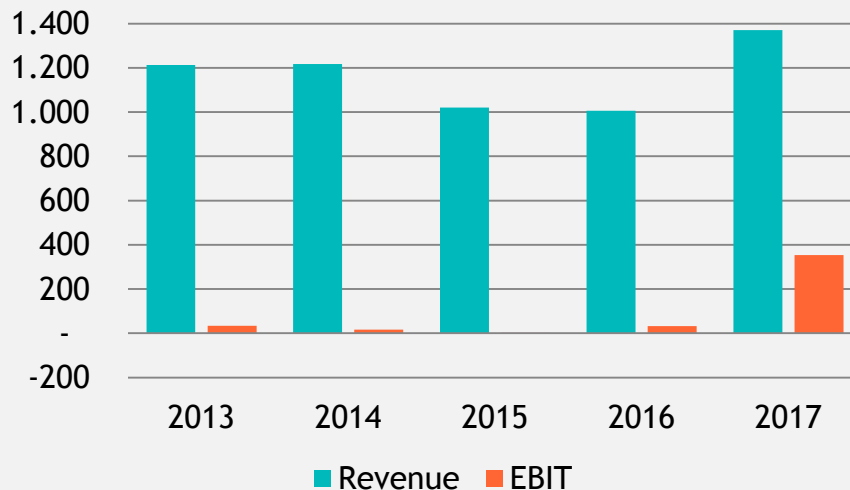
- Revenues and results were in line with our guidance
- PROSTVAC upfront payment was recognized as income
- Cash preparedness was further strengthened

## Revenue 2017

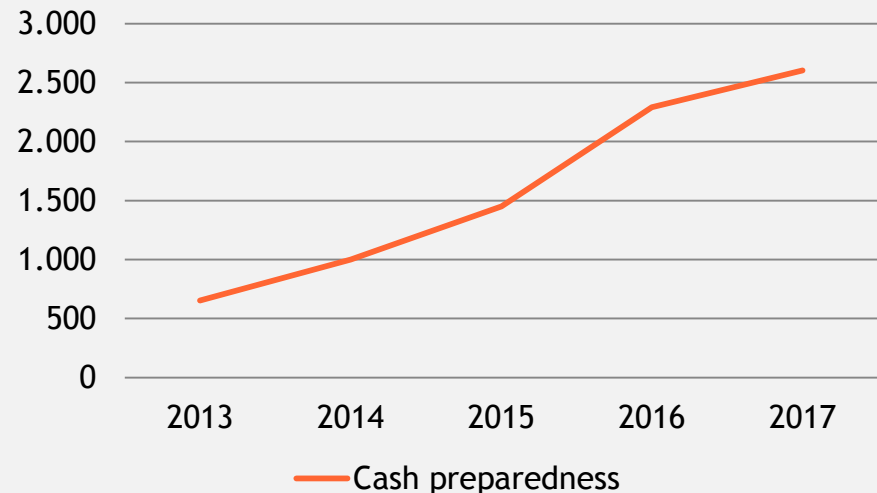
mDKK



mDKK



mDKK



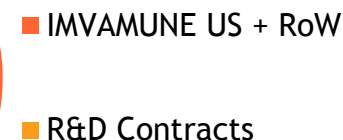
# FINANCIAL STATEMENTS



|  | mDKK         |              | mUSD       |            |
|--|--------------|--------------|------------|------------|
|  | FY 2017      | FY 2016      | FY 2017    | FY 2016    |
| Revenue  | 1,370        | 1,007        | 221        | 162        |
| Production costs                               | 291          | 298          | 47         | 48         |
| <b>Gross profit</b>                            | <b>1,080</b> | <b>709</b>   | <b>174</b> | <b>114</b> |
| Research and development costs                 | 518          | 463          | 83         | 75         |
| Distribution and administrative costs          | 208          | 213          | 33         | 34         |
| <b>Total operating costs</b>                   | <b>726</b>   | <b>676</b>   | <b>117</b> | <b>109</b> |
| <b>Income before interest and taxes (EBIT)</b> | <b>353</b>   | <b>33</b>    | <b>57</b>  | <b>5</b>   |
| Financial income/loss                          | (51)         | 7            | (8)        | 1          |
| <b>Income before company tax</b>               | <b>302</b>   | <b>40</b>    | <b>49</b>  | <b>6</b>   |
| Tax  | 121          | 9            | 19         | 1          |
| <b>Net profit for the period</b>               | <b>181</b>   | <b>31</b>    | <b>29</b>  | <b>5</b>   |
|  |              |              |            |            |
| <b>Cash preparedness (end of period)</b>       | <b>2,604</b> | <b>2,292</b> | <b>419</b> | <b>369</b> |

USD / DKK = 6.21

- mDKK

 $USD/DKK = 6.21$ 

BAVARIAN NORDIC



# A SOLID FOUNDATION

PAUL CHAPLIN, CEO AND PRESIDENT

# A SOLID FOUNDATION FOR GROWTH

PROSTVAC Phase 3 failure was a setback, but we have positioned ourselves for growth through:

- Expansion of industry and public partnerships
- Diversification of pipeline
- Strong cash preparedness allows for significant investments in R&D
- Investment in fill-finish facility to secure future supply of IMVAMUNE and other vaccines

## Key pipeline assets

IMVAMUNE

CV301

MVA-BN RSV

Brachyury

## Industry partnerships



Bristol-Myers Squibb

# OUR STRATEGY IN ACTION

1

**Maintain the global leadership of our smallpox vaccine franchise**



- Awarded freeze-dried contract from BARDA
- Strong efficacy data read out from Phase III
- Investing in fill/finish line securing future manufacturing requirements

2

**Rapidly advance our pipeline of infectious disease programs**



- Completed Phase 2 and outlined development strategy for RSV
- Expanded collaboration with Janssen on HIV & HBV

3

**Establishing a broad and deep cancer immunotherapy franchise**



- Industry and sponsor collaborations for combination studies of CV301 in multiple indications
- Advancing BN-Brachyury into Phase 2









**Strong financial position enables executing on strategy going forward**

# PIPELINE

## AMBITIOUS AND WELL-BALANCED PORTFOLIO

Infectious diseases

Oncology

| PRODUCT                              | INDICATION                   | PHASE 1      | PHASE 2      | PHASE 3      | PARTNER  |
|--------------------------------------|------------------------------|--------------|--------------|--------------|--|
| IMVAMUNE liquid-frozen <sup>1)</sup> | <i>Smallpox</i>              |              |              | File H2 2018 |  |
| IMVAMUNE freeze-dried                | <i>Smallpox</i>              |              |              |              |  |
| MVA-BN RSV                           | <i>RSV</i>                   |              |              |              |  |
| CV301 + pembrolizumab                | <i>Lung cancer (NSCLC)</i>   |              |              |              |  |
| CV301 + atezolizumab                 | <i>Bladder cancer</i>        |              | Planned 2018 |              |  |
| CV301 + durvalumab                   | <i>Colorectal cancer</i>     |              | Planned 2018 |              |  |
| CV301 + nivolumab                    | <i>Colorectal cancer</i>     |              | Planned 2018 |              |  |
| BN-Brachyury                         | <i>Chordoma</i>              |              | Planned 2018 |              |  |
| PROSTVAC combinations                | <i>Prostate cancer</i>       |              |              |              |  Bristol-Myers Squibb |
| MVA-BN Filo + AdVac                  | <i>Ebola</i>                 |              |              |              |                      |
| MVA-BN Filo + AdVac                  | <i>Ebola/Marburg</i>         |              |              |              |                     |
| MVA-BN HPV + AdVac                   | <i>Chronic HPV infection</i> | Planned 2018 |              |              |                     |
| MVA-BN HIV + AdVac                   | <i>HIV1 Infected</i>         | Planned 2018 |              |              |                     |
| MVA-BN HBV + AdVac                   | <i>Hepatitis B infected</i>  |              |              |              |                     |

<sup>1)</sup> Approved in Canada and the European Union (marketed as IMVANEX® in the EU). Phase 3 completed in the U.S.

# SUCCESSFUL PARTNERSHIP WITH THE U.S. GOVERNMENT

## Liquid-frozen

Phase 3 completed

BLA submission  
H2, 2018

FDA approval and  
award of a Priority  
Review Voucher

## INVAMUNE®

28M doses supplied to SNS  
to date

US strategic long-term  
stockpiling goal:

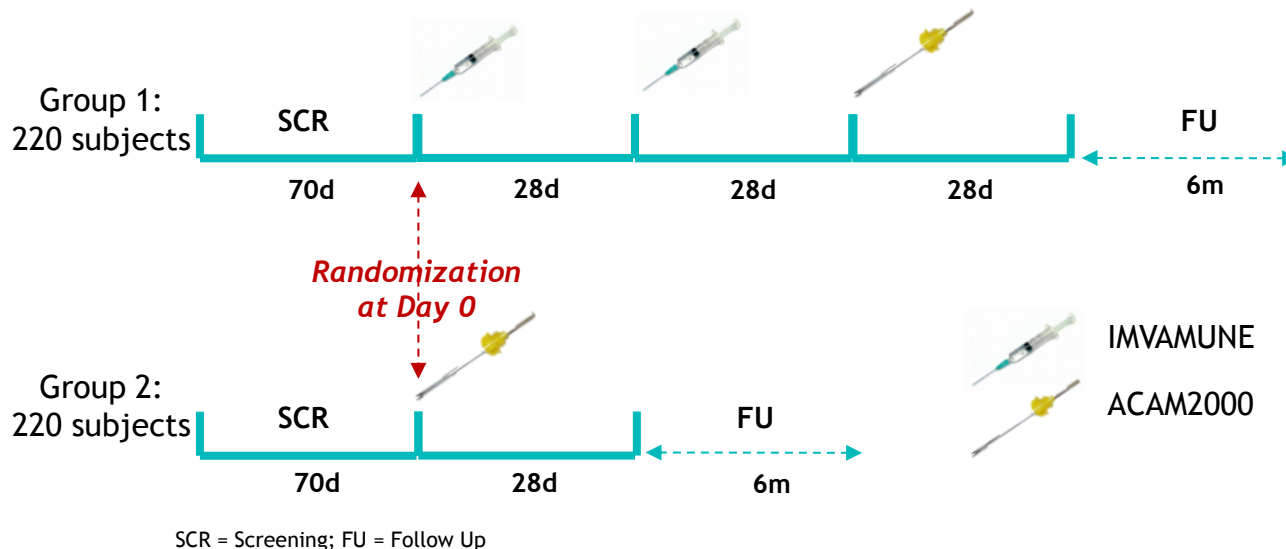
**To protect 66 million  
citizens with a safer  
smallpox vaccine**

BARDA Broad Agency Announcement

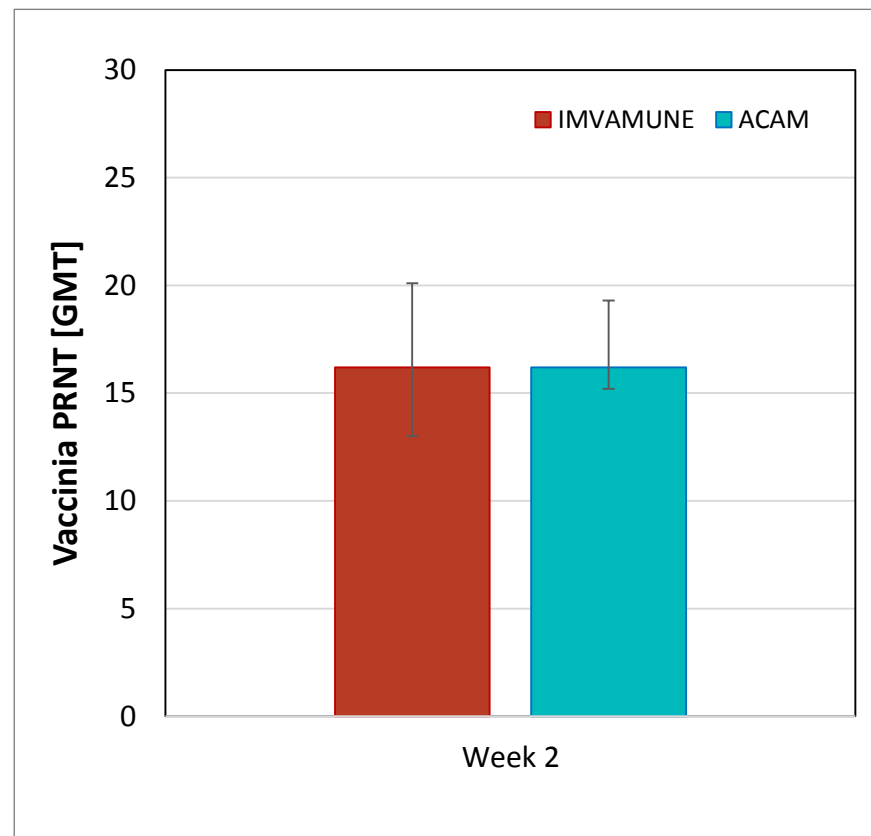
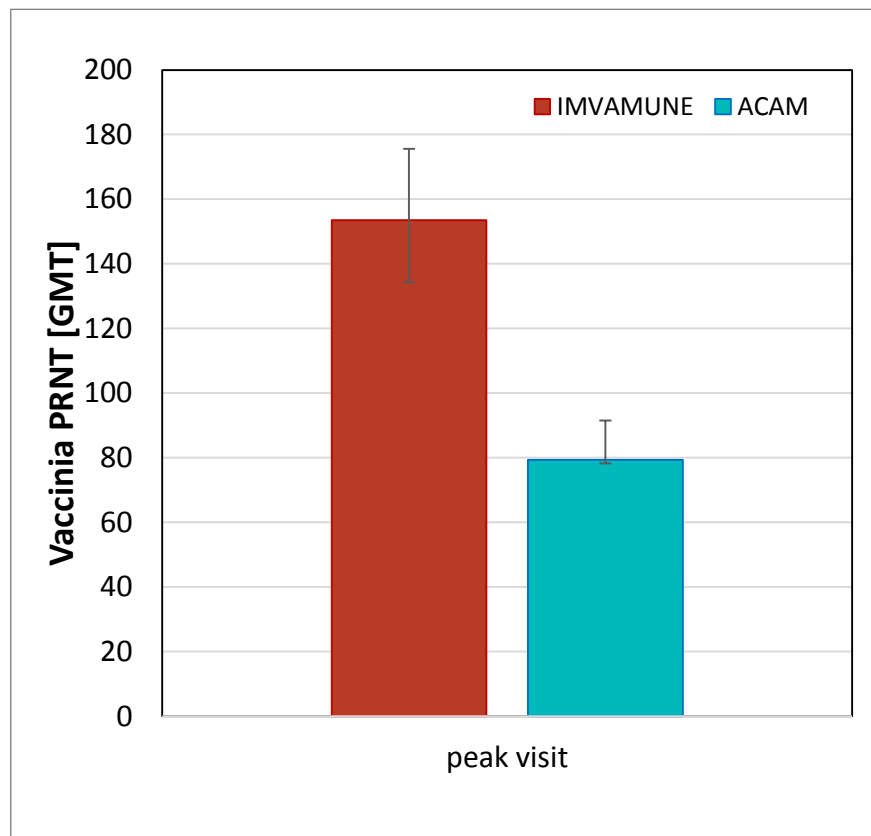
**132 million doses**

# PHASE III (POX-MVA-006) TRIAL DESIGN

- Randomized Phase III pivotal trial performed at military sites in South Korea
- Total 440 (2 groups of 220) healthy, vaccinia-naïve subjects
- Co-primary Objectives to demonstrate
  - Non-inferiority of the neutralizing antibody responses induced by IMVAMUNE and ACAM2000 at Peak Visits (immunogenicity)
  - Attenuation of the ACAM2000 vaccine “take” following IMVAMUNE vaccination (efficacy)



# IMMUNE RESPONSE DATA - PRIMARY ENDPOINT



Requirement to demonstrate non-inferiority of IMVAMUNE to ACAM in PRNT (peak visit):  
the lower (two-sided) 95% CI limit of the GMT ratio (IMVAMUNE/ACAM) is above 0.5 (predefined non-inferiority margin).

Vaccinations: IMVAMUNE (week 0, week 4), ACAM (week 0)

# EFFICACY DATA - CO-PRIMARY ENDPOINT

- The absence or attenuation of a vaccine take following re-vaccination with a traditional (replicating) smallpox vaccine was a historical measure that the vaccinee was protected against smallpox



A Full vaccine take<sup>1</sup> following vaccination with ACAM2000. A 93% Full & 4% partial<sup>2</sup> vaccine take rate was observed in the subjects vaccinated with ACAM2000



No take was observed in the majority of the subjects that had been previously vaccinated with IMVAMUNE



The ACAM2000 take was attenuated in 23% of the subjects previously vaccinated with IMVAMUNE

<sup>1</sup> Full vaccine take : a maximum central lesion diameter  $\geq 5\text{mm}$  at the 6 to 8 day visit after scarification

<sup>2</sup> Partial take : a maximum central lesion diameter  $< 5\text{mm}$  at the 6 to 8 day visit after scarification

# IMVAMUNE PHASE 3 SUCCESSFULLY COMPLETED

- Study met both primary endpoints, thus demonstrating non-inferiority to ACAM2000, the current U.S. licensed smallpox vaccine
  - Peak neutralizing antibodies induced by IMVAMUNE were shown to be 2-fold higher than those stimulated by ACAM2000
  - Primary vaccination with IMVAMUNE resulted in a highly attenuated take (reduction in lesion size), and in fact prevented the vaccine take in the majority of subjects re-vaccinated with ACAM2000
- BLA filing expected in second half of 2018

## IMVAMUNE (liquid-frozen) Phase 3 program

### Lot-consistency study, n=4,000

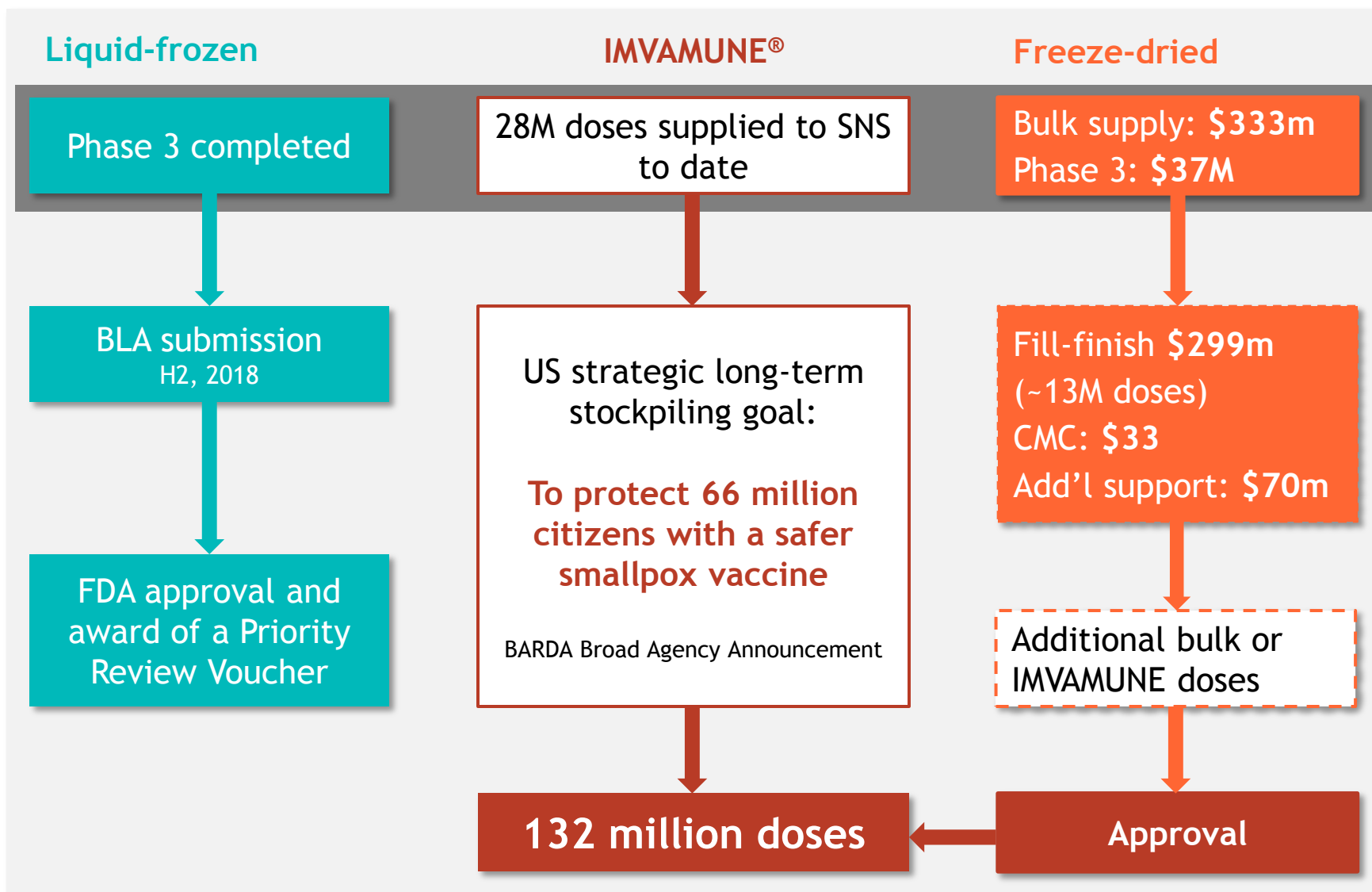
Antibody responses and safety of three consecutive manufacturing lots vs. placebo

### Non-inferiority study, n=440

Comparison of efficacy endpoints between IMVAMUNE and ACAM2000

# SUCCESSFUL PARTNERSHIP WITH THE U.S. GOVERNMENT

\$1.8 BILLION IN R&D AND SUPPLY CONTRACTS TO-DATE



# ESTABLISHMENT OF FILL-FINISH CAPACITY

## Taking full control of value chain in manufacturing

- BN will invest approx. USD 75 million in a fill-finish line at its existing facility in Denmark
- Contract options of USD 33 million for process transfer and validation of the new manufacturing line
- Secures deliverables for future supply orders and pipeline assets
- Capacity for handling both liquid-frozen and freeze-dried products



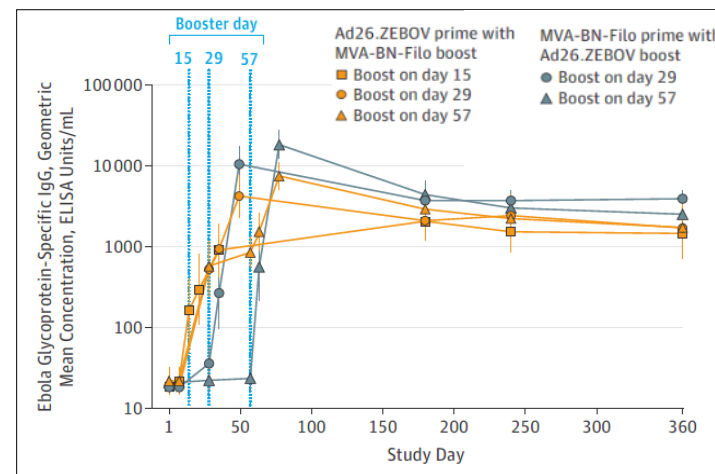
# OUR COLLABORATION WITH JANSSEN

## A LONG-TERM VALUE DRIVER



### Prime-boost vaccine regimen with sustained response

- Combinations of Janssen's AdVac + MVA-BN have demonstrated prolonged protection in clinical studies with activity seen out to one year.
- This data has been key to extending our collaboration into three additional indications:



MVA-BN Filo (Ebola)

Phase 3 ongoing

MVA-BN HPV

Phase 1 in 2018

MVA-BN HIV

Phase 1 in 2018

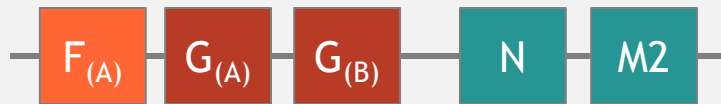
MVA-BN HBV

Potential milestone payments of  
~\$1BN + royalties

# AT THE FOREFRONT OF RSV VACCINE DEVELOPMENT

## Balanced vaccine construct

Encodes 5 distinct targets of RSV to provide protection against multiple antigens providing a balanced T-cell and antibody response

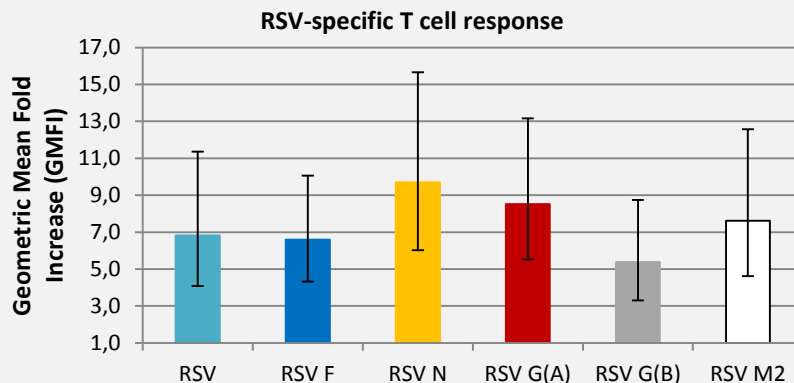


## Competitive advantages

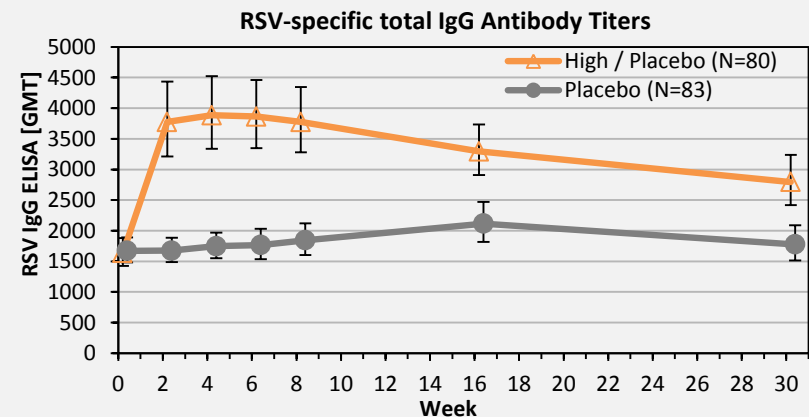
Designed to mimic natural RSV infection:

- Induction of T-cells and antibodies against RSV
- Induction of mucosal immunity
- Durable immune response lasting an RSV season

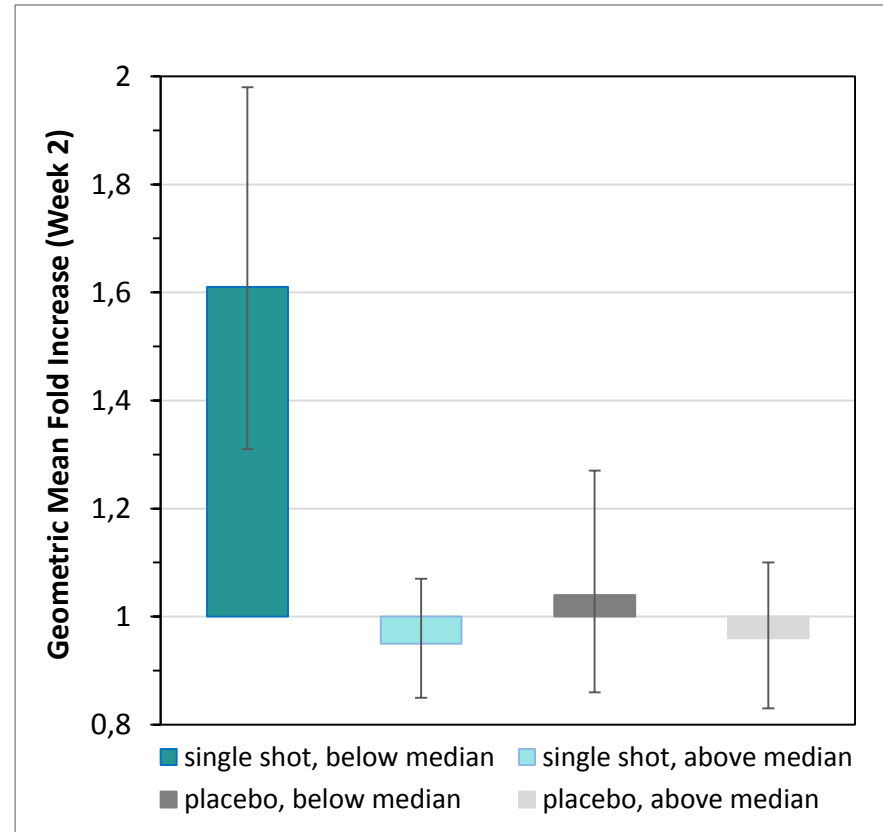
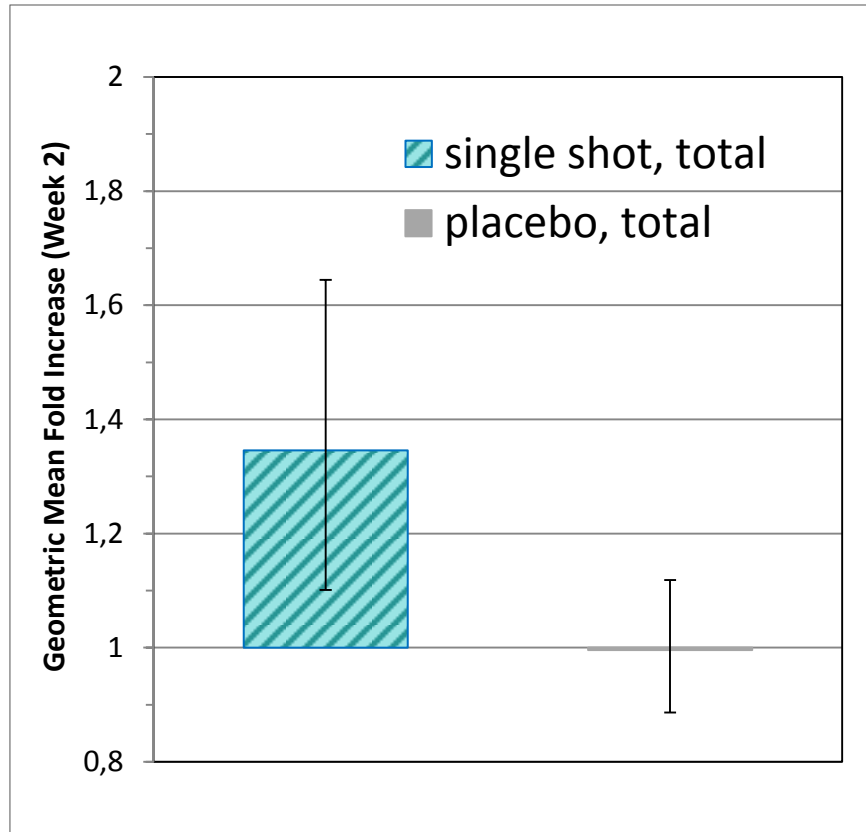
## Robust T-cell responses demonstrated in Phase 1 and 2 studies



## Strong antibody responses demonstrated over a full RSV season (Phase 2)



# VACCINATION WITH MVA-BN RSV INDUCES MUCOSAL IGA RESPONSES AGAINST RSV

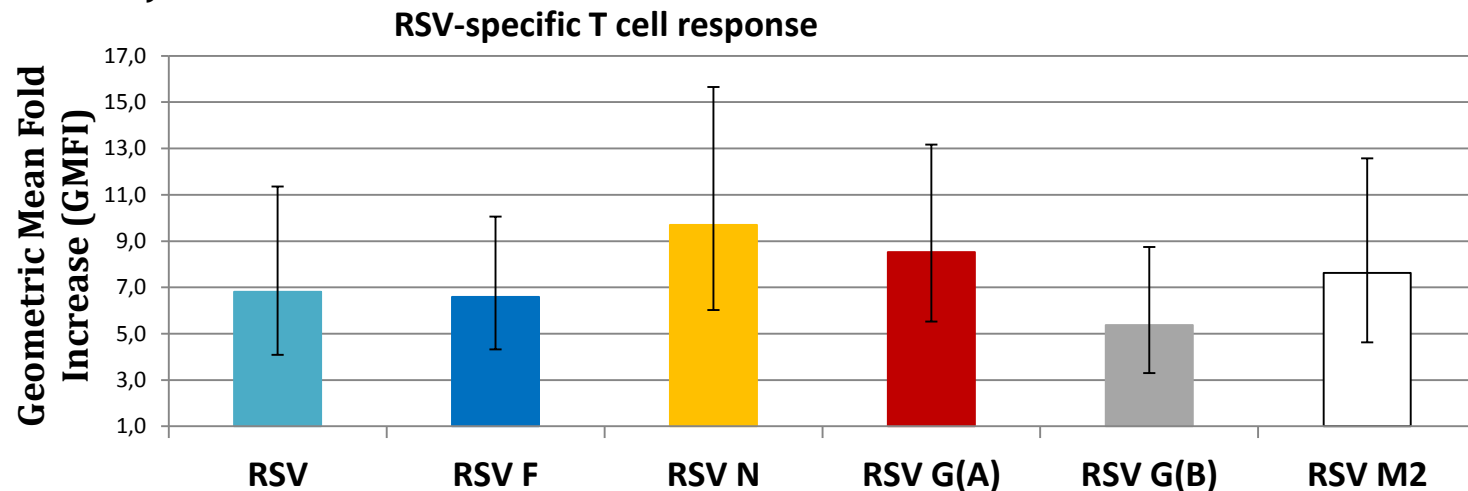


Boosting effects were more pronounced in individuals with a lower baseline mucosal IgA at the time of vaccination, suggesting that the vaccine has the desired effect of boosting memory responses against RSV in patients with a poor underlying immunity.

# PREVENTION AND CLEARANCE OF RSV

## BOTH ARE KEY TO A SUCCESSFUL VACCINE

- Published data indicate two of the strongest correlates of protection in RSV infections are:
  - Presence of pre-infection nasal IgA correlates strongly with protection against infection in challenge studies <sup>1</sup>
  - Virus-specific CD8<sup>+</sup> T-cells emerging in peripheral blood and lung tissue correlated with declining viral titres once infected <sup>2</sup>
  - A deficient RSV F-specific T cell responses contribute to susceptibility to severe RSV disease in the elderly <sup>3</sup>



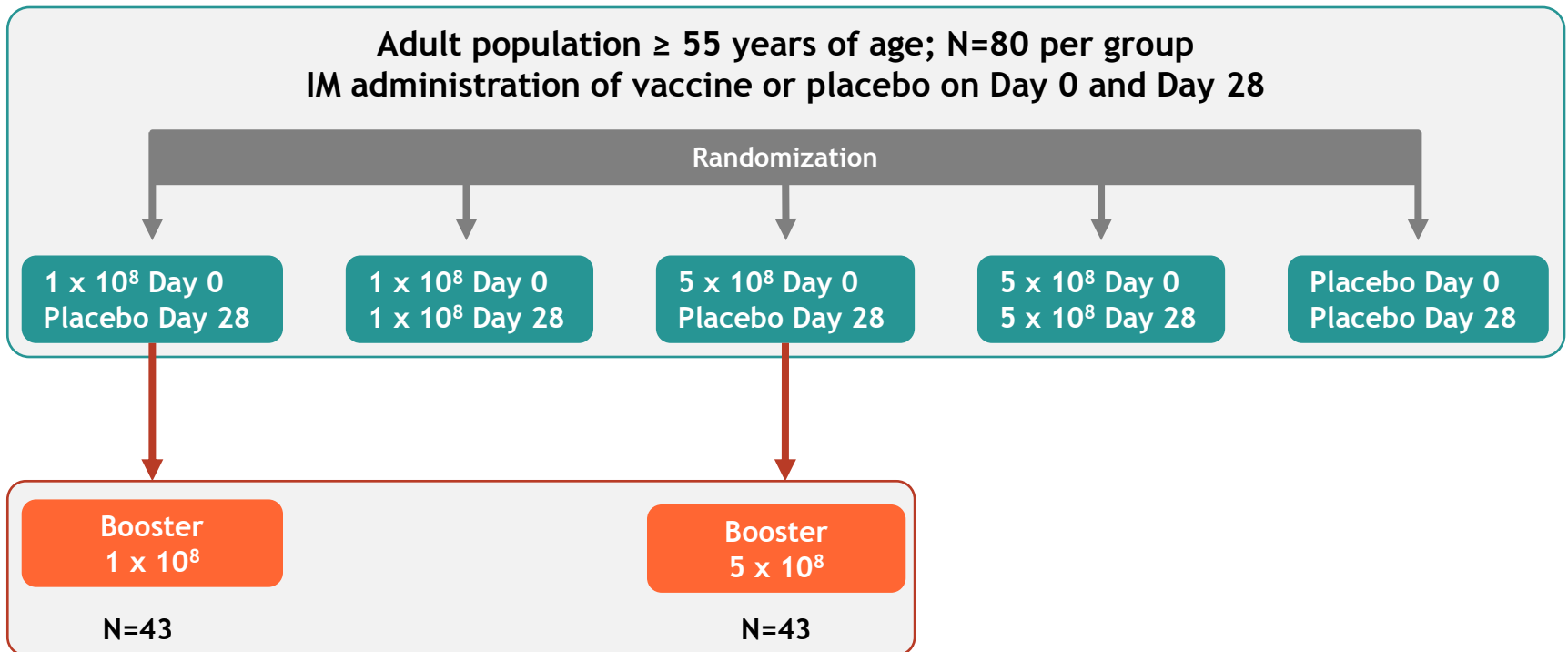
In vaccinated individuals MVA-BN RSV has demonstrated the ability to generate serum & nasal IgA as well as virus specific T-cells in peripheral blood

- [Am J Respir Crit Care Med.](#) 2015 May 1; 191(9): 1040-1049.
- [Nature Communications](#) 6, Article number: 10224 (2015)
- [Clin. Vacc. Immunol.](#) 2013, 20: 239-247.

# PHASE 2 BOOSTER STUDY: DATA MID 2018

## Key objectives of booster study

- Obtain clarity on long-term durability of immune response (12 months)
- Evaluate effect of a single booster dose after primary vaccination with a single shot using same doses as in the main study (N=86)



# DEVELOPING A HUMAN CHALLENGE TRIAL FOR RSV

## Succeeding where others have not:

- Prior human challenge studies based on a substantially weakened strain of RSV (memphis37) which has highly variable infection rates (range 33%-77%)
- BN has identified a primary isolate of RSV and has partnered with a WW leader in human challenge studies (SGS) to develop a more virulent RSV challenge

## BN is exploring the feasibility of using this strain in a MVA-BN RSV vaccine efficacy trial this year:

While still awaiting data from the Phase 2 booster study, BN is currently developing a phase 3 field efficacy protocol and preparing to meet with regulators to discuss an appropriate pathway to licensure.

# CV301 - THE STRATEGY UNFOLDS

- During 2018, four Phase 2 trials will evaluate the combination of CV301 and checkpoint inhibitors across three indications

## Non-small cell lung cancer (NSCLC)

Proof-of-concept study of CV301 plus KEYTRUDA (pembrolizumab) as first-line maintenance therapy (n=176)

## Colorectal & Pancreatic cancers

Phase 2 study of CV301 plus IMFINZI (durvalumab) and maintenance chemotherapy (n=54)

## Bladder cancer

Roche

Phase 2 study of CV301 plus TECENTRIQ (atezolizumab) (n=60)

## Colorectal cancer

Bristol-Myers Squibb

Phase 2 study of CV301 plus OPDIVO (nivolumab) in micro satellite stable mCRC (n=74)

## Other potential indications

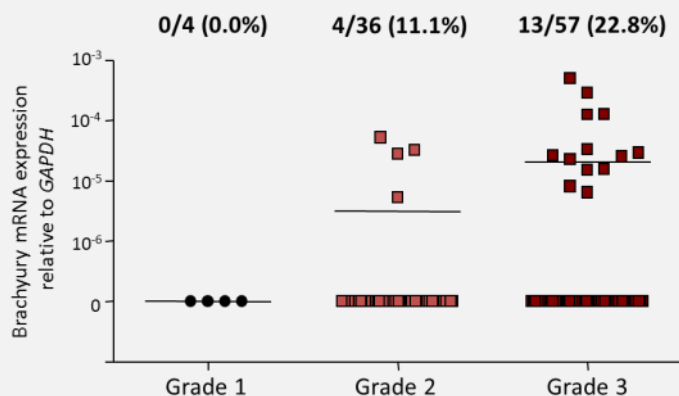
In addition to NSCLC, bladder and colorectal, Bavarian Nordic retains all commercial rights in pancreatic, breast, ovarian, gastric, liver and renal cancer

# BN-BRACHYURY: DRUGGING THE “UNDRUGGABLE”

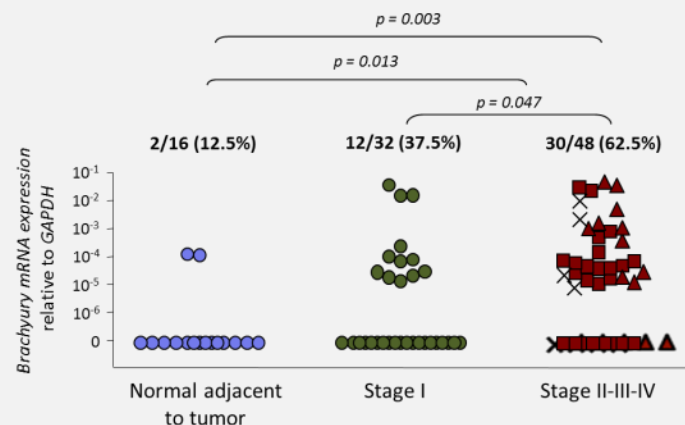
## What is brachyury?

- Brachyury is responsible for epithelial to mesenchymal transition (EMT), which is a major driver of metastasis
  - Brachyury is not expressed in most normal tissue
  - Brachyury expression is highly correlated with metastatic disease, and multi-drug resistance

### BRACHYURY EXPRESSION IN BREAST TUMOR TISSUES CORRELATES WITH TUMOR GRADE



### BRACHYURY EXPRESSION IN LUNG TUMOR TISSUES CORRELATES WITH TUMOR STAGE



A Phase 1 study of 38 patients receiving MVA-BN Brachyury showed presence of brachyury specific T cells in vast majority of patients, post-treatment\*

Ongoing Phase 1 study is evaluating safety of prime-boost

Phase 2 planned to initiate Q3 2018

- Combination with radiation in advanced metastatic chordoma
  - Primary endpoint: Objective response rate (radiation alone <5% ORR at 6 months)
  - Potential for Breakthrough Designation

### Population

- Patients with advanced, incurable chordoma
- At least 1 measurable lesion eligible for radiation therapy

### Stage 1

- 12 patients
- Only proceed to stage 2 if at least 2 objective responses occur

### Stage 2

- Enroll additional 13 patients.
- ORR goal = 20% (5/25 patients)

# ANTICIPATED SELECTED MILESTONES



## IMVAMUNE

- Filing of BLA (H2, 2018)
- Award of Priority Review Voucher upon approval (2019)

## RSV

- Results from booster-study (H1, 2018)
- Decide on the feasibility of a human challenge study (H2, 2018)

## JANSSEN

- Initiate Phase 1 study of MVA-BN HIV+AdVac (H2, 2018\*)
- Initiate Phase 1 study of MVA-BN HPV+AdVac (H2, 2018\*)

*\* Janssen is responsible for the clinical development*

## CV301

- Initiate Phase 2 study in combination with atezolizumab in bladder cancer (mid 2018)
- Initiate Phase 2 study in combination with durvalumab in colorectal cancer (H1, 2018)
- Initiate Phase 2 study in combination with nivolumab in colorectal cancer (H1, 2018)
- Initial Phase 2 results (ORR) from combination with pembrolizumab in NSCLC (H2, 2018)

## BRACHYURY

- Results from Phase 1 booster study (H2, 2018)
- Initiate Phase 2 study in Chordoma (H2, 2018)
- Initiate Phase 2 study in second indication (H2, 2018)

## PROSTVAC

- Initial results from combination study of PROSTVAC and nivolumab in mCRPC (H1, 2018)

# Q&A

