# vaccibody

## Preclinical VB10.COV2 data summary and Infectious Disease Strategy

December 11<sup>th</sup> 2020



# Forward-looking statement

This announcement and any materials distributed in connection with this presentation may contain certain forwardlooking statements. By their nature, forward-looking statements involve risk and uncertainty because they reflect the company's current expectations and assumptions as to future events and circumstances that may not prove accurate.

A number of material factors could cause actual results and developments to differ materially from those expressed or implied by these forward-looking statements.



# Agenda

1

2

3

4

5

## Vaccibody introduction

VB10.COV2 - preclinical data

The infectious disease vaccine market

Infectious disease strategy

Outlook and Q&A

# **Presenting today**

**CEO** Michael Engsig

vaccibody



M.Sc. Biochemistry and B.Sc. Commerce.

More than 20 years professional experience in biotech and pharma:

- KLIFO (EVP, Drug Development Counselling)
- PPD (Executive Director, Area Head Clinical Management, CEE)
- Takeda and Nycomed (managerial roles, broad international drug development track record in Denmark, Germany, Russia)

#### President & Chief Scientific Officer Agnete B. Fredriksen



M.Sc. and Ph.D. in Immunology.

- Created the first Vaccibody molecules
- for her Ph.D. thesis on vaccibodies
- Co-founder of Vaccibody AS (2007)
- Responsible for the scientific strategy selecting and developing the first clinical product candidates based on the Vaccibody platform

#### **Director Infectious Diseases** Gunnstein Norheim



M.Sc. and Ph.D. in pharmaceutical microbiology

- Preclinical and clinical dev. of vaccines for meningococcal vaccines, Ebola
- Research experience in epidemiology, immunology and vaccine evaluation
- Part of initiating CEPI. First vaccine science director
- Responsible for the scientific strategy dev. for infectious diseases in Vaccibody

## **Corporate overview**

- Clinical stage immunotherapy company (market cap. of approx. EURO 2 billion)\*
- Leading vaccine platform technology "targeting antigens to antigen presenting cells, generating unique rapid, strong and long-lasting immune response"
- Developing products within cancer and infectious diseases
- Vaccibody's individualized neoantigen cancer vaccine, VB10.NEO, has shown best in class CD8 T cell responses in a clinical Phase I/II trial
- Recently announced a global collaboration and license agreement with Genentech regarding our individualized cancer vaccine, VB10.NEO
- Vaccibody's VB10.16 cancer vaccine towards HPV-driven cancer types is investigated in a Phase II trial enrolling patients with advanced cervical cancer

\* Listed on Euronext Growth Oslo, a trading platform operated by Euronext,. Market cap. as per 10 December 2020



# **Pipeline**

Broad oncology coverage and strong partnerships. Leveraging platform within infectious diseases

Program	Indication	Discovery	Preclinical	Phase I	Phase II	Phase III	Partnerships
Oncology and precancer							
Individualized							
VB10.NEO	Melanoma, lung, bladder, renal, head & neck	$\bigcirc$					Genentech <sup>1</sup> Nektar <sup>2</sup>
VB10.NEO	Locally advanced and metastatic tumors	$\bigcirc$					Genentech 1, 3
Off the shelf							
VB10.16	HPV16 positive cancers Cervical cancer <sup>4</sup>	$\bigcirc$					
Undisclosed	Undisclosed targets within shared antigens						
VB10.COV2	SARS-CoV-2	$\bigcirc$					
Undisclosed	Undisclosed targets within infectious disease						

vaccibody

1) Genentech has an exclusive license to VB10.NEO; 2) Collaboration with Nektar Therapeutics on combining NKTR-214 (bempegaldesleukin) with VB10.NEO in trial arm 5B (SCCHN); 3) In combination with atezolizumab; 4) Roche supplies atezolizumab

# Strategy in brief

Leveraging Vaccibody's validated technology platform for maximum value generation

## Vision

- Leading vaccine technology company
- Game changing
   medicines
- Multiple therapeutic areas



# Vaccibody platform technology

The Vaccibody technology platform is developed based on the concept of targeting antigen to Antigen Presenting Cells (APCs) in order to create more efficacious vaccines

### **Target Antigen to Antigen Presenting Cell**

- Attract and deliver antigen to optimal cell type
- Control delivery through chosen receptor to tailor the immune response profile (e.g. antibody, CD4/CD8)
- Induce rapid response with low and few doses

#### Dimerization

- Improve attraction
- Induce activation and internalization by crosslinking receptors
- Form effective APC-B cell synapse

### Antigen

- Tolerate large globular Antigens and multiple T cell epitopes
- Derived from Cancer cell or Pathogens



# Vaccibody mechanism of action

The Antigen Presenting Cell (APC) targeting vaccine technology platform creates unique rapid, strong and broad immune responses that can be tailored to each disease





# Agenda

1

2

3

4

5

Vaccibody introduction

VB10.COV2 - preclinical data

The infectious disease vaccine market

Infectious disease strategy

Outlook and Q&A



Targeting unit LD78β

Dimerization unit Hinge + C<sub>H</sub>3 from hlgG3

Antigen unit (one of the following):

- RBD short (aa 331 524): VB2049
- RBD long (aa 319 542): VB2060
- S protein without furin cleavage: VB2065



## vaccibody

Non-Confidential

RBD: receptor binding domain, ACE2: angiotensin-converting enzyme-2

## VB10.COV2: APC targeted 2<sup>nd</sup> generation vaccine candidates

- 3 candidates with either modified Spike or 2 variants of the smaller RBD domain in the antigenic unit
- VB2060 RBD candidate was superior in expression levels, binding and neutralizing antibody responses selected as lead candidate
- RBD binds human ACE2 and is main target for neutralizing antibodies. Reduced risk of antibody-dependent enhancement.

VB10.COV2 induce rapid, high and persistent levels of antibodies in blood and lungs even after a single dose

### Antibody responses in blood and lung:

Rapid, strong and long-lasting antibody responses induced against the RBD domain of SARS-CoV-2

Rapid: Ab detected already day 7 after one vaccination with low dose

- Long-lasting:
  - Reaches plateau from day 28
  - no clear decreasing trend at day 100
- Strong: 10<sup>5</sup> 2.5 x 10<sup>6</sup> endpoint titer
- Antibodies detected also in the lung even after 1 low dose VB2060

#### **One dose potential**





Days post 1 vaccination

81482'82°82'

514 52 52 52

814 82, 828 87,

514 52 52 52 52

## VB2060 elicit rapid neutralizing antibody responses 7 days after 1 dose

- Live neutralization assay provides indication of the ability of the antibodies to protect against infection
- Strong neutralizing antibody responses elicited
- Rapid: neutralizing Ab responses already at day 7 that increase to day 28
- Stabilizes at high levels at or above the level observed in NIBSC 20/130 convalescent plasma standard for at least 3 months

Rapid and long-lasting neutralizing activity can be elicited with a single dose

Neutralizing Ab responses over time after a single vaccination



#### RBD-specific IFN-y T cell responses in splenocytes



Spike-specific IFN-y T cell responses in splenocytes



## Rapid and Strong, dose dependent T cell responses

- Strong T cell responses induced to multiple pools of RBD from day 7 post 1<sup>st</sup> dose
- The response is dose-dependent and increase by day 28 (after 2<sup>nd</sup> vaccination at d21)
- VB2065 which includes the longer Spike antigen induces very strong, CD8+ T cell dominated responses (16000 SFU/10<sup>6</sup> splenocytes)

#### Position of immunodominant epitopes in RBD



splenocytes

SFU/10<sup>6</sup> e

## VB10.COV2 induces broad and CD8 dominated T cell responses

Strong, dominating CD8 T cell responses against RBD

- 4 distinct CD8 epitopes
  - 1 described by others\*
- 3 distinct CD4 epitopes
  - 2 described by others\*

Consistent with Vaccibody's platform data MIP-1 $\alpha$  targeting ensure processing of presentation of a broader set of epitopes than seen with other vaccine technologies.

#### RBD-specific IFN-y T cell responses in splenocytes



The T cell response is long-lasting and effective memory responses are generated

- Vaccine-induced T-cell dose response remains strong even at day 89 post 1 or 2 doses VB2060
- A boost at day **89** induce strongly increased T cell response (day 99) which indicate effective memory responses



# VB2060 induce attractive T cell profile

CD4: VB2060 1x50ug

CD4: VB2060 2x25ug

CD8: VB2060 1x50ug

CD8: VB2060 2x25ug

- High percent of CD4<sup>+</sup> and CD8<sup>+</sup> T cells responding to RB
  - 2-6% RBD-specific CD8 T
  - 1-3 % RBD-specific CD4 T

 The response is dominated by multifunctional CD8 + T cells and Th1 CD4+ T cells The most significant stability parameter tested at stressed conditions (37°C) over 4 weeks



## Initial data indicate long-term thermal stability

- Data show that VB10.COV-2 is stable at 37°C for ~4 weeks
- VB10.COV-2 is predicted to be stable for
  - more than 52 weeks at 2-8°C
  - ~10 weeks at 25°C

• Preliminary data indicate that a change of formulation or parameters like pH or head space is likely to further improve the stability and hence increase the shelf life significantly

## **In summary**

- Preclinical data indicate VB2060 is a promising 2<sup>nd</sup> generation Covid-19 vaccine candidate and provides strong proof of concept for Vaccibody's potential to make a difference with vaccines against infectious diseases
  - Rapid onset of neutralizing antibody and T cell immune responses (day 7)
  - One dose potential
  - Responses increase with time and are long-lasting
  - Broad responses with neutralizing antibodies, Th1 skewed and dominating CD8+ T cell responses
  - Preliminary stability data indicate potential long-term storage at +2-8° C

# Grant from the Research Council of Norway to support second-generation COVID-19 vaccine



Oslo, 11 December 2020

Today, Vaccibody has been granted NOK 14.7 million (EURO 1.47 million) from the Norwegian Research Council's competitive programme "Innovation Project for the Industrial Sector" for the project entitled:

Launching the Vaccibody platform technology against COVID-19 by developing a competitive second-generation vaccine

Innovation Projects for the Industrial Sector are company-driven projects and is intended to promote innovation.



# Agenda

1

2

3

4

Vaccibody introduction

VB10.COV2 - preclinical data

## The infectious disease vaccine market

Infectious disease strategy

Outlook and Q&A

# Infectious disease market





# Agenda

1

2

3

4

5

Vaccibody introduction

VB10.COV2 - preclinical data

The infectious disease vaccine market

Infectious disease strategy

Outlook and Q&A

# Vaccibody's strategic playing field





Identify the sweet spot where Vaccibody's technological advantages meets unmet medical need and market potential

Achieving a balanced portfolio (low and high risk, innovation) Further balance risk through partnering

# Vaccibodies Key Differentiating Factors

## **Infectious diseases**

- Raj
  - Rapid onset of immunogenicity
  - Vaccine platform enabling complex and multiple antigen design
    - Attractive manufacturing, administration and formulation
- •
- Tailored to each disease's correlate of protection



# **Rapid onset of Immunogenicity**



• Neutralizing, protective Ab and T cell responses within 1 week after a single dose

# **Enabling Complex and Multiple Antigen design**



Versatile format enables expression of multiple antigens in one construct

Variable size, structure and origin

Induces broad antibody and T cell responses against multiple antigens

# **Tailored to each Disease's Correlate of Protection**



- VB has a unique targeting unit that binds surface receptors on APC
- · Adapting the APC targeting unit affects the immune response profile
- Vaccibody can match targeting unit and antigen to the disease's correlate of protection



# Non-complex manufacturing and formulation, painless administration

- ~50 patient-specific batches produced on demand within weeks
- 100% manufacturing success rate independent of antigenic sequences
- Patient friendly, needle-free, pain-less administration
- Stability data indicating + 2-8°C long-term storage



- Rapid and robust vaccine design
- Scalable manufacturing process
  - Painless administration
- Indication of long-term storage at +2-8°C

# Key Differentiating factors and their Applicability

	Rapid onset of immune responses	Complex and mulitple antigen design	Tailored to each disease's correlate of protection	Non-complex manufacturing process and formulation, painless administration
Opportunity	• One dose efficacy	<ul> <li>Include multiple antigens from same or different pathogens</li> <li>Inclusion of conserved epitopes</li> </ul>	Match targeting unit and antigen to the disease's correlate of protection	<ul> <li>Rapid response time</li> <li>Global distribution</li> <li>Thermostability</li> <li>Low CoGs</li> </ul>
Applicability	<ul> <li>Pandemics and other emerging diseases, travel, biodefense</li> <li>Therapeutic potential post exposure</li> </ul>	<ul> <li>Vaccine against complex pathogens and pathogens with high Ag variability</li> <li>Pan-pathogen vaccines</li> <li>Immunocompromised patients</li> </ul>	Pathogens particularly sensitive to specific immune responses	<ul><li>Pandemics and other emerging diseases</li><li>LMIC</li></ul>

# Significant unmet medical need remains within infectious disease



Respiratory infections with insufficient efficacy/lack of vaccines (e.g. Flu/RSV)

Requiring strategies to handle Ag variability, and selection of protective antigens



Pathogens requiring multi-antigen vaccines, IgG + T cells due to diversity, stages (e.g. malaria, tuberculosis, HepC)

Requiring broad immune responses against multiple antigens Prophylactic and therapeutic need



Ongoing threats where rapid protection and distribution is important (travel, LMICs, pandemics)

Requiring one dose efficacy, robust global distribution of stable product Rapid manufacturing process

# **3 Strategic Focus Areas**

Explore and exploit technology platform versatility	Develop innovative vaccines based on the technology's key differentiating factors	Prepare for emerging diseases including pandemics		
<ul> <li>Leverage Vaccibody's unique APC-targeting technology to customize the immune response profile to each disease and it's correlate of protection</li> <li>Leverage versatile vaccine format and internal proprietary bioinformatic tools to inform optimal antigen design</li> </ul>	<ul> <li>Vaccines where single antigen protection is insufficient</li> <li>Vaccines where both humoral and T cell responses are needed</li> <li>Vaccines with pan-pathogen potential</li> <li>Vaccines for post-exposure/therapy</li> </ul>	<ul> <li>Proof of Concept with VB10.COV2</li> <li>Optimize and streamline manufacturing process</li> <li>Explore, formulations, kinetics, doses, dose regimens etc</li> <li>Ensure fast turnaround time from discovery to clinic</li> </ul>		

# Infectious Disease Strategy supports the overall Vaccibody Strategy

The infectious disease strategy is a direct extension of the overall Vaccibody strategy

Further leverage the technology platform

Accelerate and expand the pipeline

Explore and exploit technology platform versatility

Prepare for emerging diseases including pandemics Develop innovative vaccines based on the technology's key differentiating factors

Seek strategic partnerships to compliment our strengths



# Agenda

1

2

3

4

5

Vaccibody introduction

VB10.COV2 - preclinical data

The infectious disease vaccine market

Infectious disease strategy

Outlook and Q&A

## **2021** Priorities

- - Execute on the collaboration with Genentech
  - Execute on the Infectious disease strategy
  - Accelerate new off-the shelf cancer vaccines with shared antigens
  - Explore and leverage the full potential of the technology platform
  - Build a world-class organization to deliver on the commitment

## **2021 Priorities and News-flow**

- 1H 2021 VB10.16 Safety data for first patients VB10.16 Interim clinical data for first patients from VB C-02 trial in cervical cancer
- 1H 2021 VB10.NEO Initiation of VB N-02, Phase 1b trial

1H 2021 VB10.COV2 - preclinical update

2H 2021 VB10.16 - Fully enrolled VB C-02 trial in cervical cancer

2H 2021 VB10.16 - Interim clinical data for first patients from VB C-02 trial in cervical cancer

2H 2021 Pre-clinical update from the infectious disease initiative



Q&A