

# Vaccibody AS

## **Capital Markets Day**

November 12, 2019

Agnete B Fredriksen President & CSO

**&** 

Michael Engsig CEO

### Capital Markets Day - Program

- 14.00-14.10 Introduction
- 14.10-15.00 Update on the VB N-01 study including the clinical data
- 15.00-15.45 Status of the cancer vaccine field and development of novel immunotherapies
- Company update • 15.45-16.05
- 16.05-16.30 Questions & Answers
- 16.30-17.30 Mingling, snacks and drinks



### Michael Engsig

### Agnete Fredriksen

## Ulrich Granzer

### Michael Engsig

### All

### All











## **Experienced International Management Team with Solid Drug Development Experience**

- Privately-held clinical stage immuno-oncology company, 28 employees





## Vaccibody Product Pipeline

PROGRAM	DISCOVERY	PRE-CLINICAL	PHASE I	Pŀ		
MELANOMA LUNG (NSCLC) BLADDER RENAL HEAD AND NECK	VB10.NEO					
HEAD AND NECK	VB10.NEO + NKTR-214					
PRECANCEROUS CERVICAL LESIONS	VB10.16					
CERVICAL	VB10.16 + At	ezolizumab (CPI)				















## Vaccibody – Proprietary Vaccine Technology Platform

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 to Antigen Presenting Cell** 

**Dimerization for** crosslinking target receptor

### **Antigen moiety**

## Mechanism of Action: the Multiple Effects of MIP-1 $\alpha$ as Targeting Unit



Targeting is elicited by the MIP-1a chemokine



### vaccibody Strong Correlation Between Strength of Induced HPV16-Specific Immune Response and Lesion Size Reduction in the Dosing Phase



- All 9 patients with strong HPV16-specific T cell responses (>650 spots/mill) experienced reduction of the lesion size after • vaccination with VB10.16
- A fourth vaccination at week 16 was implemented in phase IIa to boost and prolong T cell responses

Patients with lesion size reduction (red)

Patients with no lesion size reduction (black)

## Adding an Extra Dose Increased the Immune Response



- The vaccination regimen from cohort I (week 0, 3 and 6) plus a booster vaccination at week 16 was introduced in the Expansion Cohort. Stronger, long-lasting responses
- 16 of 17 patients (94%) from the Expansion Cohort elicited increased HPV16-specific T cell responses after vaccination with • VB10.16



## Promising Clinical Efficacy with Excellent Safety; Improved in Expansion Phase





VB10.16 as a monotherapy in HPV16-positive, precancerous cervical lesions induces:

- Lesion size reduction in all patients followed >4 months ٠
- CIN regression to CIN1 or no CIN in 10 patients •
- HPV16 and/or p16 clearance in 8 patients •



## VBI0.NEO Has a Unique Ability to Induce Strong Neoepitope-Specific **CD8T-Cell Responses**



-VBI0.NEO induces a strong CD8T cell response, combined with a CD4 response to 5 of 6 MC38 neoantigens. -Three of these neoepitopes have been shown to be non-immunogenic delivered as peptide + adjuvant -VBI0.NEO has a unique ability to induce strong CD8 responses to neoantigens (Confirmed in multiple models)

Yadav et al., 2014

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## Neoepitope-Specific CD8 T-cells Are Crucial for Tumour Protection



Depletion of CD8T cells prohibit tumour protection in VBI0.NEO vaccinated mice, indicating a crucial role of neoepitope-specific CD8T cells for anti-tumour efficacy

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## VBI0.NEO Has Proven to Induce an Effective Anti-Tumour Response



### Strong scientific rational and proven mechanism of action leading to anti-tumor efficacy



## Proprietary NeoSELECT Was Developed to Match VBI0.NEO's Mode of Action





## VB N-01 Clinical Trial Was Designed to Evaluate VB10.NEO in Five Indications

**VB N-01**: An open labelled first human dose phase 1/2a study to evaluate safety, feasibility and efficacy of multiple dosing with individualized VB10.NEO immunotherapy in patients with locally advanced or metastatic melanoma, NSCLC, clear renal cell carcinoma, urothelial cancer or squamous cell carcinoma of head and neck, who did not reach complete responses with current standard of care immune checkpoint blockade



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## High focus on successful and fast manufacturing

- So far, 100% manufacturing success rate for patients providing a successful biopsy Best in class
  - Top choice of 20 neoepitopes used for every patient
  - Proven feasibility and stability data from all initial batches
- Confidence in reaching best in class manufacturing time before reaching market
  - Good dialogue with regulatory authorities
  - One roof strategy to be implemented before market approval







## Nine Leading Clinical Sites in Germany Are Engaged & Aimed for Initiation by Q4





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ous nklin, Berlin ter	07	<b>Universitätsklinikum Ulm</b> Dr. Laban
linik	08	<b>Universitätsklinikum Tübingen</b> Dr. Mauz
nedizin	09	<b>Universitätsklinkum Halle</b> <b>(Saale)</b> Dr. Eisenmann

Site not yet activated

## Treatment Schedule for Patients Enrolled in the VB N-01 Trial



- Inclusion criteria: previous treatment with checkpoint inhibitor for >12 weeks at enrollment.
- With ~12 weeks manufacturing time, patients have been treated at least 6 mnths on CPI before 1st dose VB10.NEO
- Limited tumour reduction expected from continous checkpoint inhibitor treatment after 6 months.



eeks at enrollment. mnths on CPI before 1<sup>st</sup> dose VB10.NEO creatment after 6 months.

## Treatment Design Allows Evaluation of VBI0.NEO-Induced Clinical Responses



• After 6 months on CPI treatment, most patients are stable or relapse (progressive) If they progress, they normally continue to progress 

Tsimberidou et al., 2018

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### Not Vaccibody data

## vaccibody Heavily Pre-Treated Patients Treated with CPI Monotherapy for 9-32 Months Before Adding VBI0.NEO

							months CPI	Best		status at	
							before	response on	status at	start	
patient	indication	diagnosed	age	prior therapy	TNM	TMB	VB10.NEO	СРІ	screening	VB10.NEO	
01-002	SCCHN	2005	53	S, Rt, T, ct, o	N2M1	low	32	SD	SD	PD	
01-004	SCCHN	2015	69	S, Rt, ct, ch	T4Nx	low	15	SD	SD	SD	S: Surgery Rt: Radiotherapy T: Targeted Therapy
01-006	SCCHN	2017	68	S, ch, ct, ipi	T2N2M1	med	18*	SD	SD	PD	
01-010	SCCHN	2015	60	S, Rt, ct	T4N2M1	low	12	SD	SD	PR	
											Ct: Cetuximab
02-003	melanoma	2000	81	S	M1	high	10	PR	SD	SD	Ch: Chemotherapy
					•			• •	•		O: Other
02-007	NSCLC	2018	54	S, Rt, ch	T2N1M1	med	9	SD	SD	PD	
			-						•		Burden
01-001	RCC	2014	69	S	T1N1M1	low	16	SD	SD	SD	SD: Stable Disease PD: Progressive Disease PR Partial Response * Stopped CPI
01-003	RCC	2005	64	S, T, o	T1aN1M1	low	5*	PD	PD mixed	PD	
01-005	RCC	2006	58	S, Rt, T	T1bN1M1	low	11	SD	SD	SD	
02-002	RCC	2013	76	S <i>,</i> IT	T3bN0M0	low	8+15	PR	SD	PD	
01-007	RCC	2017	55	S <i>,</i> T	T3aN1M1	low	14	PR	SD	SD	
01-008	RCC	2017	62	S <i>,</i> T	T2N1M1	low	14	SD	SD	SD	
01-009	RCC	2011	57	S, Rt, o	T1bNXM1	low	31	SD	SD	SD	
01-011	RCC	2007	58	S, o	T2N0M0	low	26	PR	SD	SD	

14 patients have been evaluated for clinical response to VB10.NEO (2-9 months follow up time) •

All patients had been treated with CPI for 9-32 months before adding VB10.NEO. 5 patients relapsed before the first vaccination

II patients showed low TMB, 2 medium TMB (SCCHN, NSCLC) and I high TMB (melanoma)

### vaccibody SCCHN (Head & Neck): Clinical Responses Observed After VBI0.NEO Initiation in All Patients



### Head & Neck (SCCHN; 4 patients)

VBI0.NEO induced strong immune responses leading to clinical responses in all assessed SCCHN patients 

SCCHN: Squamous Cell Carcinoma of the Head and Neck

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## Vaccibody SCCHN (Head & Neck): Change in All <u>Individual</u> Target Lesions <u>Before and</u> <u>After VBI0.NEO Treatment</u>



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### Key Learnings (Head & Neck)

- All SCCHN patients show a positive change in the lesion size development after VBI0.NEO treatment start
- Multiple lesions respond
- The lesion used to select neoepitopes responds best. Next best response is seen in lesions from the same region

## Melanoma (Skin): VBI0.NEO Induce Several de novo T Cell Responses and Increased Tumour Shrinkage



### Melanoma (1 patient)

- VBI0.NEO induces an increased T cell response against several of the selected neoepitopes
- Immune responses are weaker than tested in SCCHN so far, but the majority are *de novo* responses
- An increased reduction in is observed after the first dose VBI0.NEO in the large target lesion (81-72mm)

epitopes e *novo* responses rget lesion (81-72mm

## NSCLC (Lung): Rapid Reduction in Target Lesion Size after VBI0.NEO Treatment



\* Immune response not yet assessed (too early)

NSCLC (Lung Cancer):

Rapid reduction in the target lesion (lung lesion used to select neoantigens) 9 weeks after VBI0.NEO was started 



**—** 02-007 \*

[wks] 24

## RCC (Renal): Reduced Growth and Long-Term Continuous Stable Lesions



Renal Cell Carcinoma:

- Limited changes were observed in the RCC patients post VBI0.NEO treatment
- Importantly, none of the lesions used to select neoantigens have progressed (>20%) post 1st dose VB10.NEO

RCC: Renal Cell Carcinoma

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Data shown for the two RCC patients with strongest immune response

## vaccibody RCC (Renal): Change Was Seen in All Individual Target Lesions Before and After Treatment with VBI0.NEO



RCC: Renal Cell Carcinoma

- [wks]
- [wks]

### **Key Learnings (Renal Cancer)**

- Most RCC patients enrolled so far have multiple large target lesions.
- More limited changes observed so • far after vaccination.
- Interestingly, none of the lesions used to select neoepitopes have progressed (>20%)

## SCCHN Case study: A Closer Look at Tumour Cells (patient 01-002)



- Both cervical LN lesions were growing before the first dose of VBI0.NEO; Both lesions stabilized up to at least week 37
- One of these lesions was used to select neoepitopes for vaccine design  $\bullet$
- Tumour cells that were found at screening were no longer found 6 months after starting VBI0.NEO

SCCHN: Squamous Cell Carcinoma of the Head and Neck

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## Summary of Clinical Observations: VBI0.NEO Causes Shrinkage of Tumours and Stabilization of Progressing Lesions

VBI0.NEO is the first cancer vaccine to show a strong ability to shrink tumours in multiple patients with advanced metastatic disease

- Kinetics: Shrinkage occurs 9-24 weeks after first dose VBI0.NEO
- Lesion: Optimal shrinkage in lesion used to select neoepitopes
- Tumour cells with neoantigens targeted by vaccine are specifically killed.
- •Other parameters?



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## Patients with High TMB Responds Better to Immunotherapies



Our patient population is at the lower end of the TMB scale for their indications (and did not have a objective response on CPI alone)

Source: Yarchoan et al., 2017 NEJM TMB: Tumor Mutational Burden

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Strong relationship between Tumor Mutational Burden (TMB) and response to CPI

Limits response to already existing neoantigenspecific T cell repertoire

Patients with low TMB have worse prognosis

## Clinical Response Was Seen Even in Patients with Low TMB, Indicating Potential in a Broad Setting and Large Number of Indications



• The Renal Cell Cancer patients in our VB N-01 trial have the lowest TMB and the largest tumour burden among all included patients

Data indicates a broad potential for vaccine-induced clinical responses 



Broad potential for vaccine-induced clinical responses identified

## Patients with Clinical Response Had a Higher Number of Neoepitopes - and Thus a Better Opportunity to Select High-Quality Neoepitopes



SCCHN: Squamous Cell Carcinoma of the Head and Neck NSCLC: Non Small Cell Lung Cancer

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## Lower Quality Neoepitopes in Renal Cancer Patients Make It More Difficult to Develop a Potent Vaccine



RCC: Renal Cell Cancer

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## Patients With Clinical Responses Have the Strongest Immune Response Profile and Highest Frequency of High-Quality Neoepitopes



### Patients with clinical response after VBI0.NEO vaccinations have

• Highest frequency of high quality neoepitopes

Patients with clinical reponse after VBI0.NEO vaccinations have • A) Highest frequency of immunogenic neoepitopes B) Highest frequency of increased response after vaccination C) Highest frequency of de novo immune responses

Clinical response is here defined as reduction in the sum of target lesions by at least 10% or stabilization of prior progressing lesions

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## Strong, Dominating CD8 T Cell Responses Are Correlated with Clinical Responses



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## vaccibody Neoepitope-specific CD8 dominating immune responses in SCCHN patients with clinical response



The strongest de novo responses\* were characterized as dominating CD8 T cell responses by FACS analysis in SCCHN patient 01-004. Also secreting IL-2.

<sup>\*</sup> As identified by IFN-γ ELISpot

## Key Highlights

	Breakthrough data with Neoantigen Oncology Vaccine	Ongoing basket trial across 5 solid tumour indications
		<ul> <li>VB10.NEO is the first cancer vaccine to show a strong abili with advanced metastatic disease</li> </ul>
51		<ul> <li>Tumour shrinkage is observed even after long-term PD-1 / longer expected to provide further response</li> </ul>
	multiple	<ul> <li>A strong correlation is found between high quality neoanticlinical responses</li> </ul>
	indications	In-house, proprietary best in class neoantigen selection to
		Safe and well-tolerated intramuscular delivery of DNA vace
	Differentiated	Rapid, robust manufacturing process with competitive COC
2	Manufacturing	Proven 100% success rate with all patient-specific vaccine
	Process	Proprietary NeoSELECT platform to quickly identify tumour
	Vaccine platform	Unique targeting of antigen presenting cells providing best
	with unique	Proven ability to induce rapid and strong CD8 responses the strong C
5	mechanism of	Platform technology provides potential for expansion beyo
	action	variety of infectious diseases and tumour models.



lity to shrink tumours in multiple patients

/ PD-L1 treatment (CPI) where CPI is no

gens, CD8+ T cell immune responses and

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### GS

s with top 20 selected neoantigens

r neoantigens

t in class immune responses hat correlates with clinical efficacy and oncology into. Preclinical data within a











## Vaccibody Achievements

### Clinical proof of principle established from VB C-01

- Ability to raise an antigen specific immune response in humans
- Immune response translate into meaningful clinical improvement in precancer setting
- Promising initial data from VB N-01
  - Developed a promising concept for addressing patients own immunogenic somatic mutations in cancers
  - Proven feasibility in value chain from biopsy to patient specific cancer vaccine product
  - Well tolerated product for IM administration
- Demonstrated neoantigen vaccine can raise best in class specific immune response against somatic mutations and resulting best in class clinical responses across tumour types
- Technology platform that can be applied to a range of diseases with unmet medical need

VB10.NEO is the first neoantigen cancer vaccine to demonstrate induction of strong cancerspecific immune responses which leads to clinical responses in several patients with locally advanced or metastatic disease.

Interim results from phase I/IIa clinical trial suggests a clear link between selection of highquality neoepitopes, generation of strong neoepitope-specific CD8+ T cell responses and clinical responses.



PRESS RELEASE

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### VACCIBODY ANNOUNCES INITIAL POSITIVE CLINICAL RESPONSES IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC CANCER TREATED WITH VB10.NEO **NEOANTIGEN CANCER VACCINE**

## Vaccibody's Solid Base

- 299 mNOK in cash and cash equivalents as of Sept 30, 2019
- Diverse and active shareholder base, approx. 280 shareholders
- Raised 509 mNOK in equity since inception
- Traded "over the counter" by Arctic, ABG, DNB, Carnegie

- Solid IP base with multiple layers of protection
- Experienced and engaged team



## Update since September Capital Markets Day

### **VBI0.NEO**

- First VB10.NEO clinical data released\* major de-risking factor
- 100% manufacturing success rate
- On track to initiate enrollment in NEKTAR arm of VB N-01 during Q4 2019
- Accelerating efforts to progress VB N-01 trial opening 6 new clinical sites (total of 9)

### **VBI0.16**

- On track to vaccinate first patient in QI 2020 in VB C-02
  - First Central approval by an Ethics Committee (Bulgaria, first of six countries incl Norway)

### Organization

New Chief Medical Officer to begin in January 2020



<sup>\*</sup> http://www.vaccibody.com/portfolio\_page/vb10-neo-an-individualized-neoepitope-car induces-positive-clinical-responses-in-patients-with-locally-advanced-or-metastatic-solid-tumoursmaryland-november-2019/

## Outlook next 6 months

### Clinical trial for cancer neoantigen vaccine (VBI0.NEO)

• Decision of design for 1st expansion cohort

### **Nektar collaboration**

- Approval of additional arm with combination of VBI0.NEO and NKTR-214
- First patient dosed in clinical trial evaluating the combination

## Clinical trial in cervical cancer combining VBI0.16 and checkpoint inhibitor atezolizumab

• First patient dosed in the clinical trial evaluating the combination of VB10.16 and atezolizumab



## In Summary

## **Achievements**

- Vaccibody technology platform provides best in class broad and strong immune response translating into clinical response across indications
- Clinical proof of concept for both VBI0.16 and VBI0.NEO
- Cutting edge experience in manufacturing and supply chain
- Strong collaboration partners to improve positioning

## Key priorities to drive asset value

- Progress clinical activities
- Expand footprint
- Strengthen manufacturing setup
- Leverage our technology platform



## Vaccibody team ready to execute and deliver!



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