Vaccibody

CAPITAL MARKETS DAY

Oslo, tirsdag den 3. April, 2018

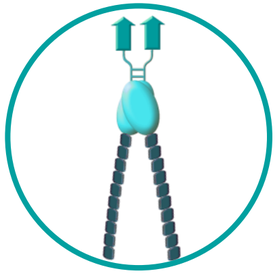
Agnete Fredriksen, PhD
President & CSO
abfredriksen@vaccibody.com

Martin Bonde, BComm, PhD
CEO
mbonde@vaccibody.com

Agenda

1. Background

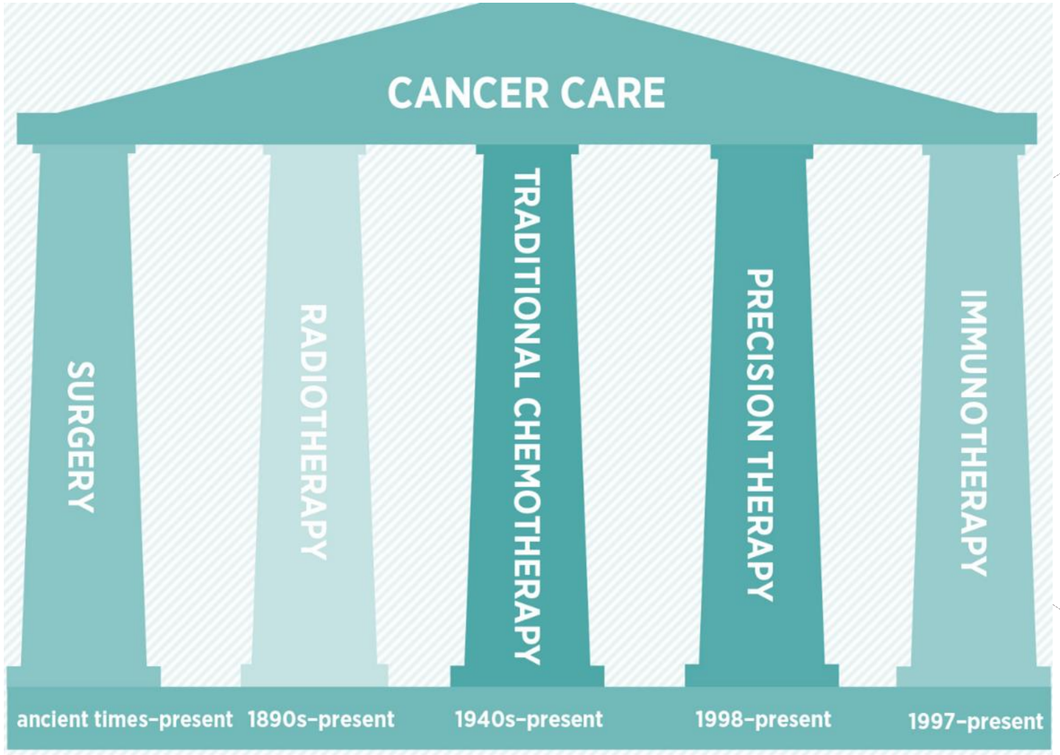
2. Vaccibody’s Cancer Vaccine Strategy



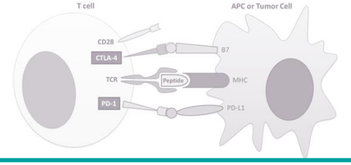
3. Neoantigen Prediction Tools

4. Vaccibody’s Clinical Trial Experience and Future Plans

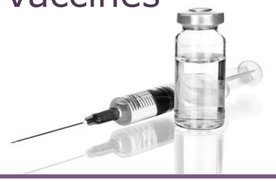
Immunotherapy: The next Wave of Cancer Therapy



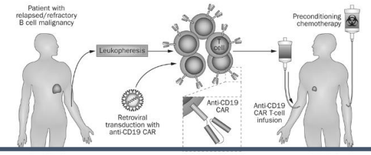
Checkpoint Inhibitors



Vaccines



Cell Therapies



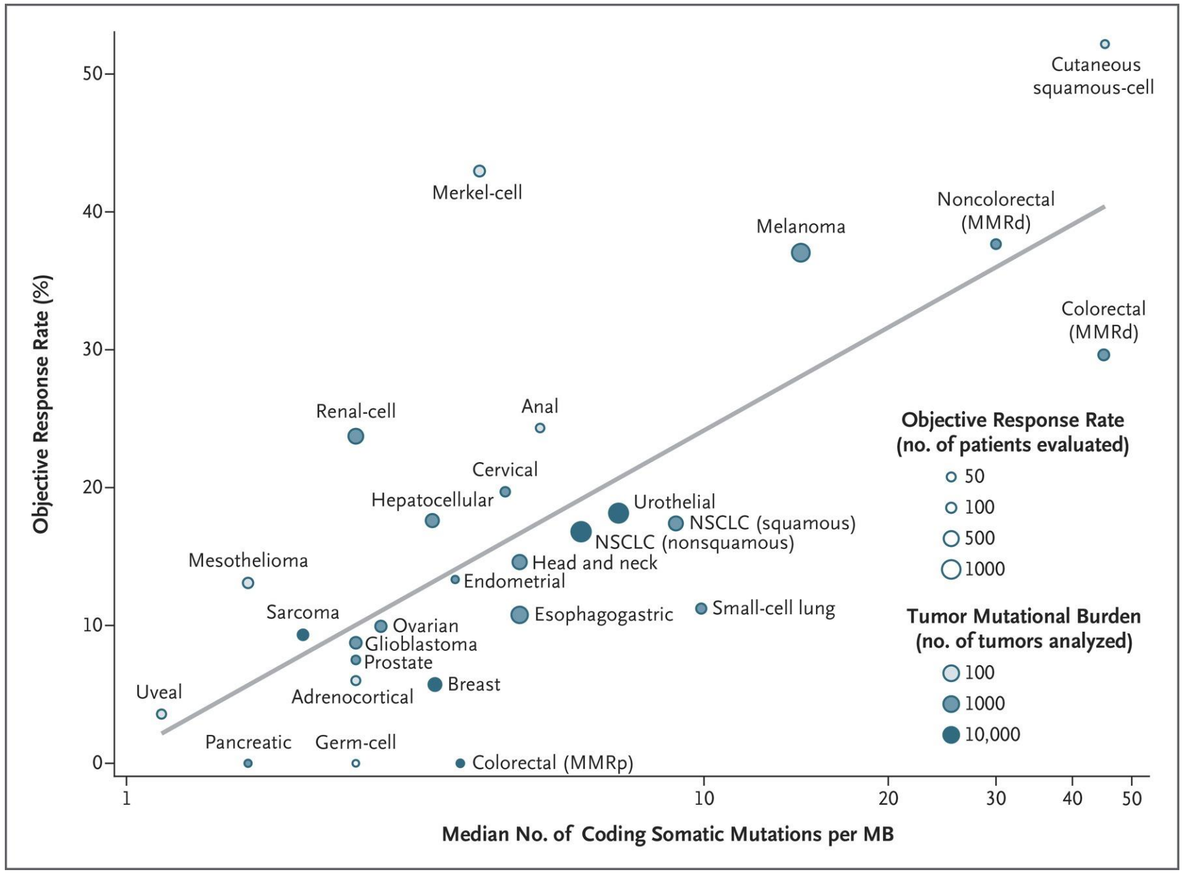
Others, e.g.

- Oncolytic viruses
- Cytokines
- Bi-specific antibodies
- Small molecules
- Adjuvants

Various Immuno-Therapy Modalities

Vaccination is best suited to stimulate a controlled and TRULY specific individualised immune response

CheckPoint Inhibitors – Their Promise and their Limitations



- Strong relationship between number of mutations (neoantigens) and response to CPI
- Limits response to already existing neoantigen-specific T cell repertoire
- Reveals an important role of immune response to neoantigens in cancer immunotherapy

Cancer vaccines are the **optimal tool** to activate more effective and broader neoantigen specific T cell responses

Yarchoan et al., 2017 NEJM

The Workflow of Personalised Cancer Treatment

1. Tumour biopsy and sequencing

2. Neoepitope selection (TSNA)

3. Vaccine manufacturing (n=1)

4. Vaccine administration and immunogenicity

Time, cost, efficacy?

Proof of Concept published in Nature Letters July 2017

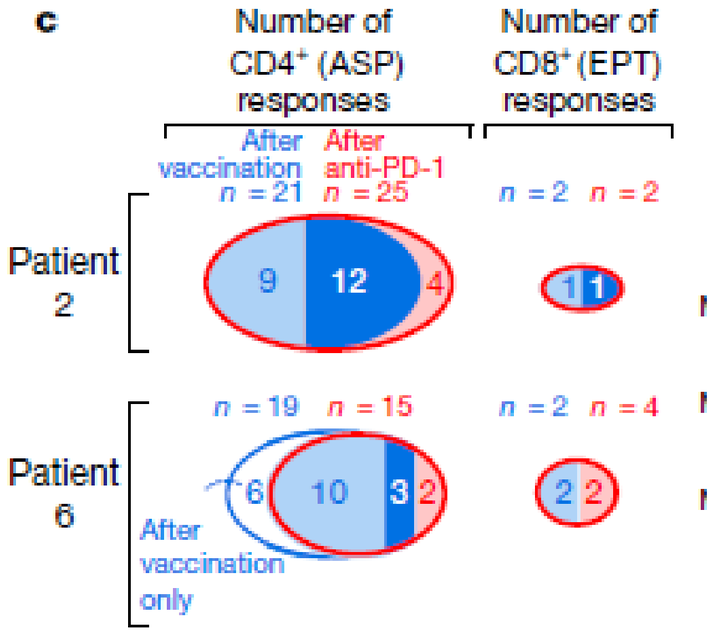
LETTER

NEON THERAPEUTICS

doi:10.1038/nature22991

An immunogenic personal neoantigen vaccine for patients with mel

Patrick A. Ott[1,2,3]*, Zhuting Hu[1]*, Derin B. Adrienne Luoma[5], Anita Giobbie-Hurder[6], Shuqiang Li[4], David J. Lieb[4], Thomas Eisen Kaliappanadar Nellaiappan[11], Andres M. Sa Charles H. Yoon[3,13], Maegan Harden[4], Niall Gad Getz[3,4,14], Kai Wucherpfennig[3,5], Doni & Catherine J. Wu[1,2,3,4]



- 6 patients wit
- 97 neoepitope with polyICLC
- 7 vaccinations
- T cell respons
- Neoepitopes s

LETTER

BIONTECH

doi:10.1038/nature23003

Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer

Ugur Sahin[1,2,3], Evelyna Derhovanessian[1], Matthias Miller[1], Björn-Philipp Kloke[1], Petra Simon[1], Martin Löwer[2], Valesca Bukur[1,2], Arbel D. Tadmor[2], Ulrich Luxemburger[1], Barbara Schrörs[2], Tana Omokoko[1], Mathias Vormehr[1,3], Christian Albrecht[2], Anna Paruzynski[1], Andreas N. Kuhn[1], Janina Buck[1], Sandra Heesch[1], Katharina H. Schreeb[1], Felicitas Müller[1], Inga Ortseifer[1], Isabel Vogler[1], Eva Godehardt[1], Sebastian Attig[2,3], Richard Rae[2], Andrea Breitkreuz[1], Claudia Tolliver[1], Martin Suchan[2], Goran Martic[2], Alexander Hohberger[3], Patrick Sorn[2], Jan Diekmann[1], Janko Ciesla[4], Olga Waksmann[4], Alexandra-Kemmer Brück[1], Meike Witt[1], Martina Zillgen[1], Andree Rothermel[2], Barbara Kasemann[2], David Langer[1], Stefanie Bolte[1], Mustafa Diken[1,2], Sebastian Kreiter[1,2], Romina Nemecek[5], Christoffer Gebhardt[6,7], Stephan Grabbe[3], Christoph Höller[5], Jochen Utikal[6,7], Christoph Huber[1,2,3], Carmen Loquai[3]* & Özlem Türeci[8]*

- 13 patients with melanoma (stage III/IV)
- 125 neoepitopes delivered as ivt-RNA (intranodal)
- 8 (+12) vaccinations per patient
- T cell responses to 75 neoepitopes (60%)
- Neoepitopes showing immunogenicity *in vivo*

Vaccinating with neoepitopes elicits a broader and stronger tumour-specific immune response

Ott et al., Nature Reviews 2017
Sahin et al., Nature Letters 2017

Deals, fundings and collaborations in the neoantigen field

Date	Company/Inst.	Comments	Phase	Acquirer/Licensor	Deal type	Size/Upfront (USDm)	Max. deal value (USDm)
Oct 2015	NEON THERAPEUTICS	Spun out from Broad Inst & Dana Faber Backed by Third Rock Ventures	Preclinical	NA	PP (series A)	USD 55m	NA
Oct 2015	gritstone ONCOLOGY	From MSKCC (US) & King's College London (UK) Backed by i.e. Versant Ventures, The Column Group, Clarus Ventures & Frazier Healthcare Partners	Preclinical	NA	PP (series A)	USD 102m	NA
Jun 2016	moderna™ messenger therapeutics	Strategic collaboration and license agreement. Multiple studies in several types of cancer. Following human POC, Merck has the right to elect to make an additional undisclosed payment. The companies will then equally share cost and profits under a WW collaboration	Pre-clinical	MERCK	Co-development and commercialisation agreement	USD 200m	**NA**
Aug 2016	ADVAXIS IMMUNOTHERAPIES™	Amgen receives exclusive WW rights to develop and commercialize ADXS-NEO. Amgen will be fully responsible for funding clinical and commercial initiatives.	Pre-clinical	AMGEN	Co-development and commercialisation agreement	USD 40m + USD 25m equity stake	**USD 540m**
Sep 2016	BIONTECH	Genentech agreeing to share profits from certain programs. BioNTech retaining copromotion rights and option to pick up programs Genentech drops.	Phase I	Genentech	Co-development and commercialisation agreement	Not disclosed ("upfront & nearterm payouts")	**USD 310m**
Jan 2017	NEON THERAPEUTICS	Led by Partner Fund Management. Joined by Third Rock Ventures, Access Industries, Fidelity, Wellington, Inbio Ventures and Nextech Invest	Phase I	NA	PP (series B)	USD 70m	NA
Jul 2017	Wash-U	Collaboration to dvance both clinical and preclinical research. Proposed clinical trials will be reviewed and approved by MedImmune.	Pre-clin/Phase I	MedImmune A member of the AstraZeneca Group	Research and clinical alliance	NA	NA
Oct 2017	gritstone ONCOLOGY	Led by Lilly Asia Ventures, joined by GV, Trinitas Capital & Alexandria Venture Investments	Pre-clinical	NA	PP (series B)	USD 93m	NA
Oct 2017	CUREVAC the RNA people®	Co-development of five vaccines against "certain neoantigens"	Pre-clinical	Lilly	Co-development and commercialisation agreement	USD 50m + USD 53m equity stake	**USD 1.8bn**
Nov 2017	nousCom	Backed by a syndicate of leading transatlantic life sciences investors led by new investor Abingworth with participation from 5AM Ventures, and existing investors LSP and Versant Ventures.	Pre-clinical	NA	PP (series B)	USD 49m	NA

Source: company data, press releases, Arctic Securities Research

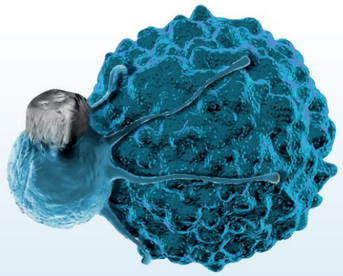
Vaccibody strongly engaged in key conferences

November 14–16, 2017
Boston, MA

Book now and save up to $800

NEOANTIGEN Summit2017

Supercharging Immunotherapies & Cancer Vaccines



Conference Day Two | Thursday, November 16

8.00 **Breakfast & Registration**

Martin Bonde, CEO, **Vaccibody**

9.00 **Chair's Opening Remarks**

Agnete Fredrickson, CSO, **Vaccibody**

3.00 **Development of safe, efficacious and cost-efficient cancer neoantigen vaccines**

- Preclinical proof-of-concept: identification of neoantigens and construction of highly immunogenic and efficacious vaccines
- Clinical studies: design consideration and execution strategy
- Cost-efficient GMP-production of personalized neoantigen vaccines

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Agnete invited speaker at numerous conferences

- Drug Discovery Virtual Event, Feb 2
- Live podcast Radforsk + Kreftforeningen, March 16
- European Neoantigen Summit, Amsterdam, April 24-26
- Annual Cancer Vaccines Summit, Prague, April 26-27
- 3rd Annual Advances in Immuno-Oncology Congress in London, May 24-25, 2018, plus upfront webinar
- 6th Annual Immuno-Oncology Summit, Boston August 30-31

2018 Speakers Include:

Kandeepan Ganeshalingam
MSD

Agnete Fredriksen
Vaccibody A/S

Stefan Gluck
Celgene

Meet Senior Decision Makers
Over 300 VPs, Directors & Professors from leading pharmaceutical organisations, biotech companies and academic institutions will attend

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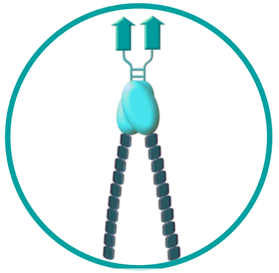
Agenda

1. Background

2. Vaccibody’s Cancer Vaccine Strategy

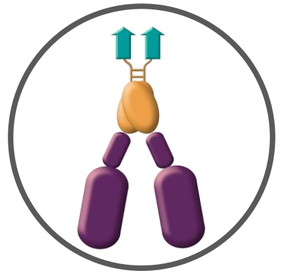


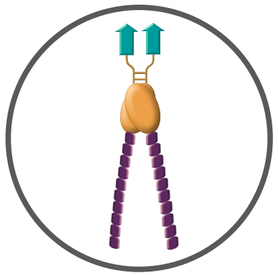
3. Neoantigen Prediction Tools

4. Vaccibody’s Clinical Trial Experience and Future Plans

Vaccibody Product Pipeline

PROGRAM	DISCOVERY	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
Precancerous cervical lesions	**VB C-01 (VB10.16)**				
MELANOMA LUNG (NSCLC) BLADDER RENAL HEAD AND NECK	**VB N-01 (VB10.NEO)***				





* Clinical Trial Application (CTA) approved March 2018.

Vaccibody – Proprietary Vaccine Technology Platform

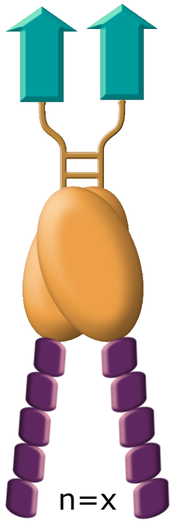
The Vaccibody Technology Platform was developed based on the concept of **targeting antigen to APC** in order to create more efficacious vaccines.

Exchangeable DNA Cassette

Vaccibody DNA Vaccine Plasmid

VB10.NEO

In vivo expression



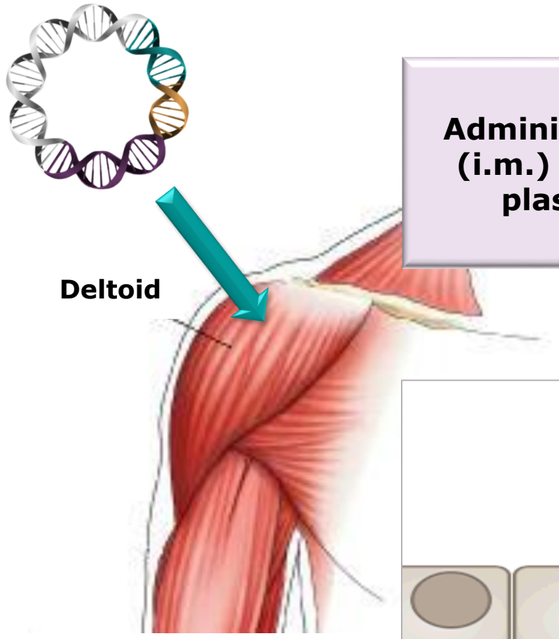
Vaccibody in Protein Format

Target to Antigen Presenting Cell

Dimerization for crosslinking target receptor

Antigen moiety

Mechanism of Action – Intrinsic Adjuvant

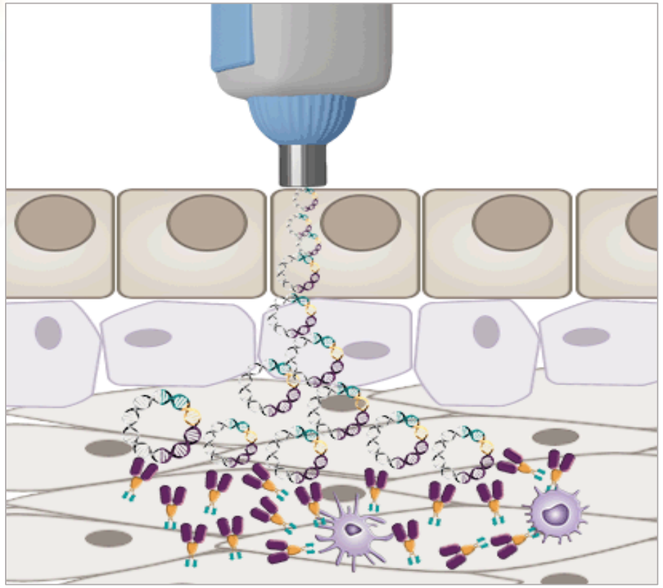


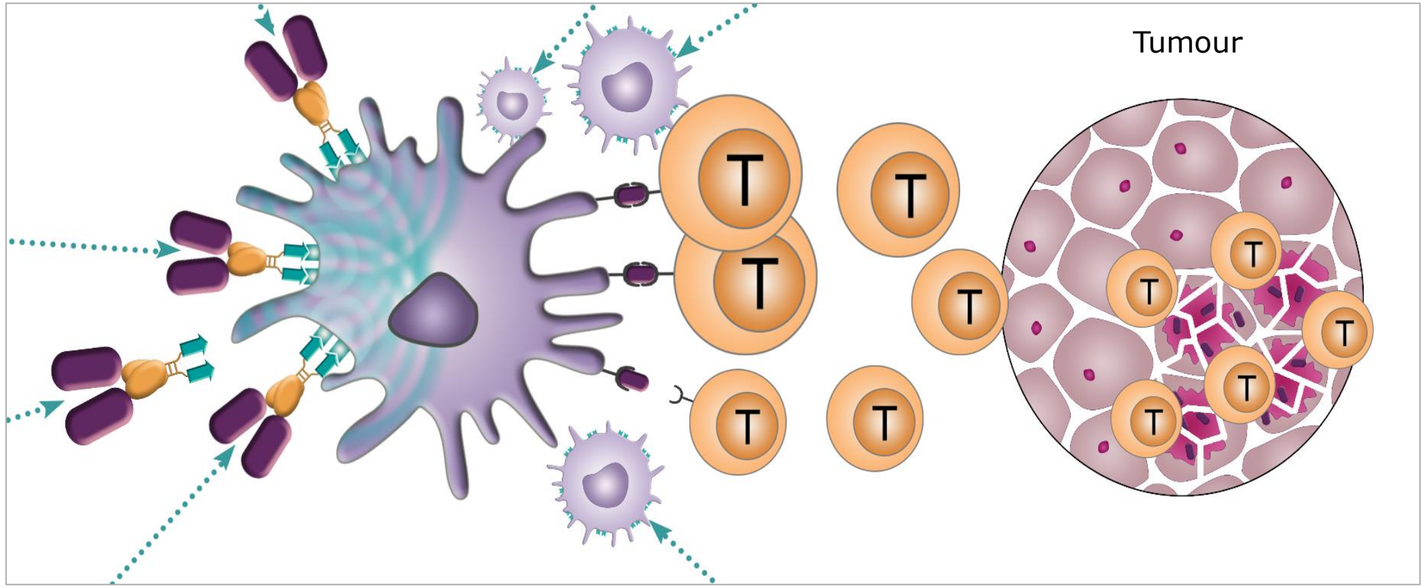
Administration (i.m.) of DNA plasmid

***In vivo* protein expression and secretion**

Chemokine MIP-1α

Target – Attract –Mature –Deliver-Cross-present



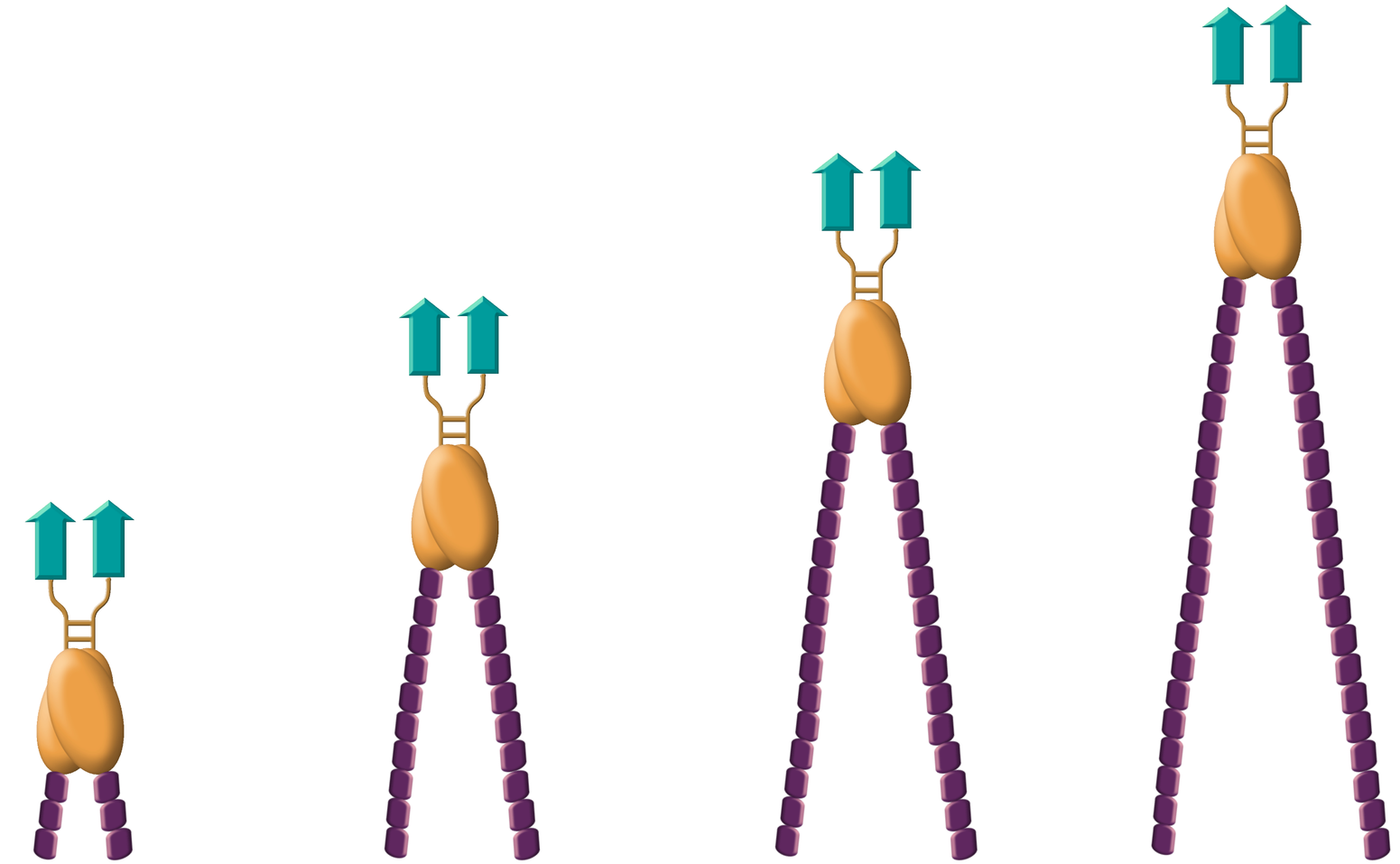


Simple Vaccine Delivery

PharmaJet®

- ✓ Needle free injection
- ✓ Small, handy, easy to use
- ✓ Minimal pain compared to electroporation
- ✓ Cost effective
- ✓ Applicable for multiple immunizations

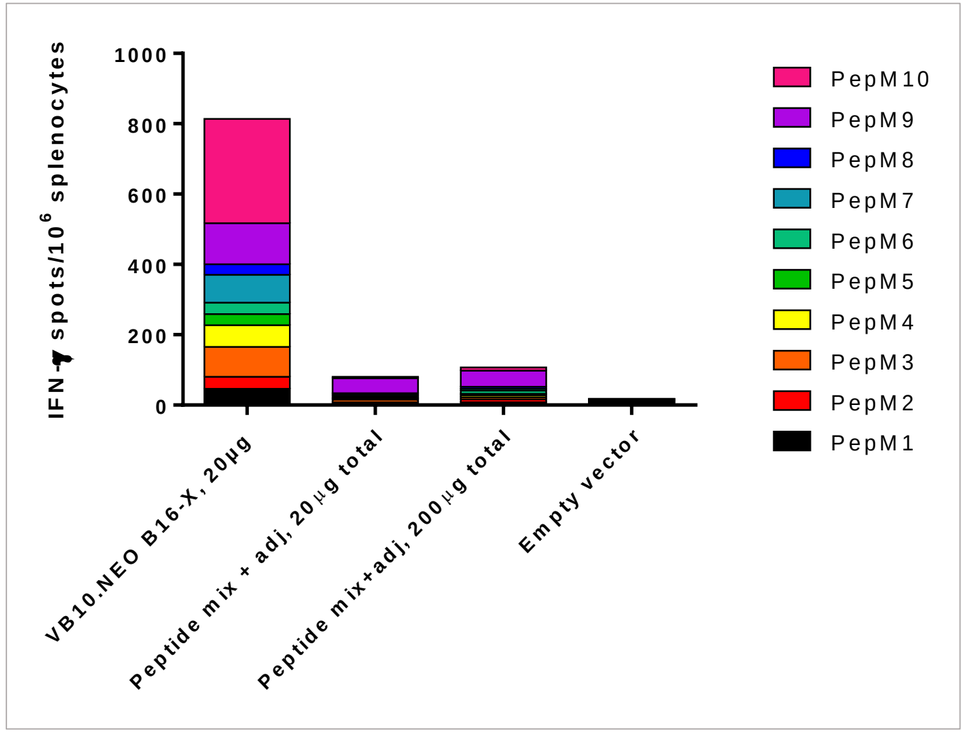
VB10.NEO – A Robust Vaccine Format



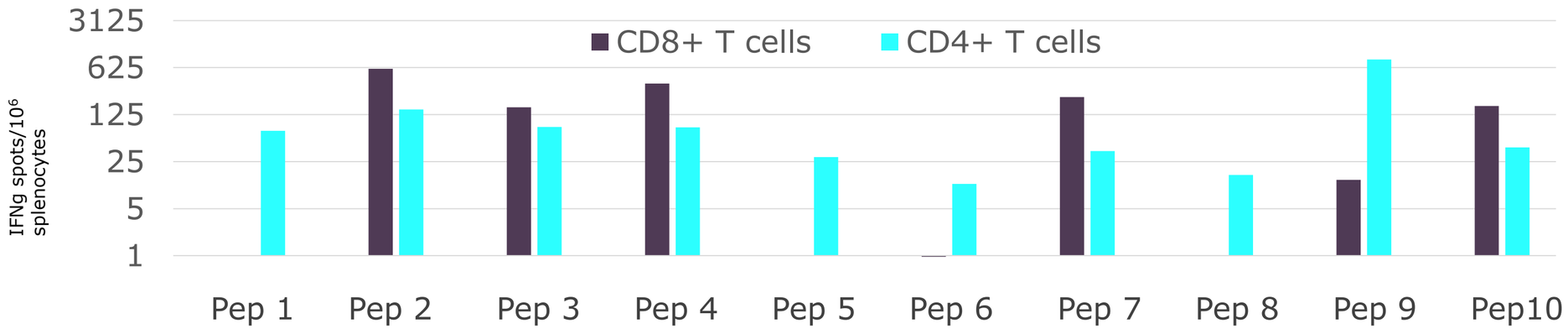
>70 different VB10.NEO constructs with ~300 neoepitopes constructed to date

VB10.NEO induces Rapid, Broad and Strong responses to multiple Neoepitopes by single Vaccination

- VB10.NEO induces a broader and stronger response than Peptide + Poly (I:C) Adjuvant vaccines after a single immunization.
- VB10.NEO vaccinated animals respond to all 10 neoepitopes after a single immunization.
- Immunodominant neoepitopes differ between delivery vehicles



VB10.NEO generates a broader immune response profile dominated by CD8+ T cells than competing technologies



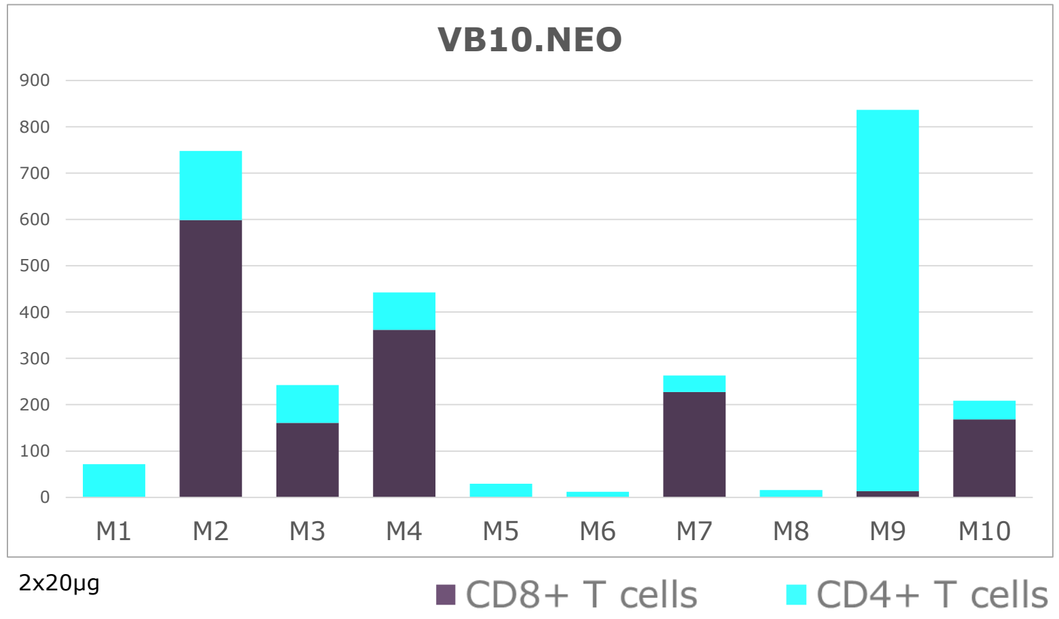
Peptide*	CD4										
	CD8										
RNA*	CD4										
	CD8										
VB10.NEO	CD4										
	CD8										

* Tested IFNγ CD4 and CD8 T cell response against 10 identical neoepitopes from B16 melanoma

*Kreiter et al., 2015

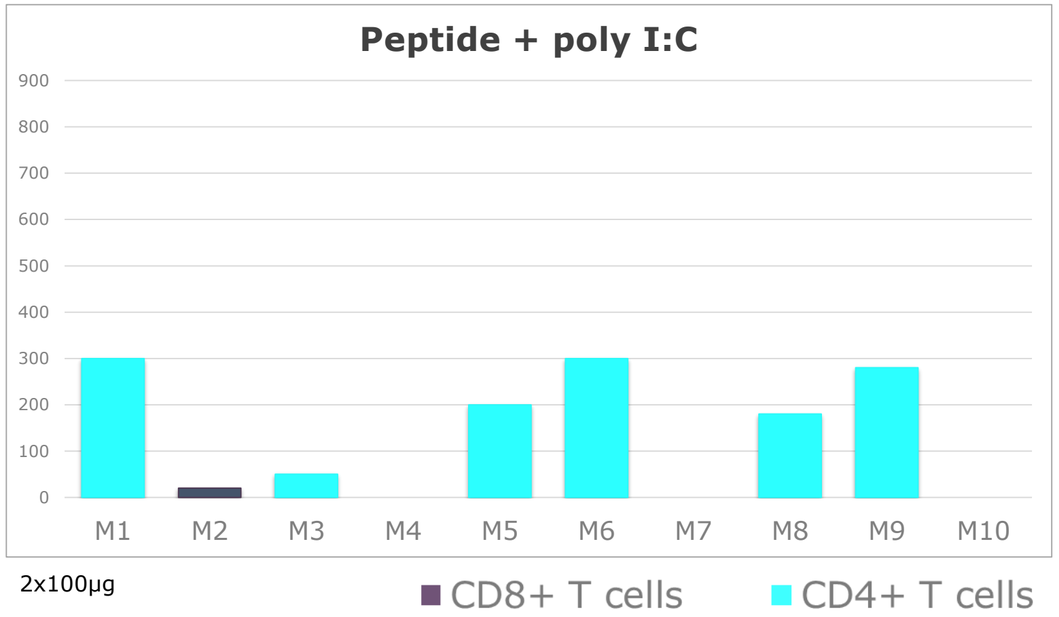
VB10.NEO leads to a unique CD8 dominated neoepitope response

VB10.NEO induces a **strong, broad** immune response **dominated by CD8+** T cells



2x20µg

Peptide + poly I:C vaccination with the **identical** neoepitopes have been reported to induce **no or weak** immune responses



2x100µg

VB10.NEO elicits a unique immune response profile

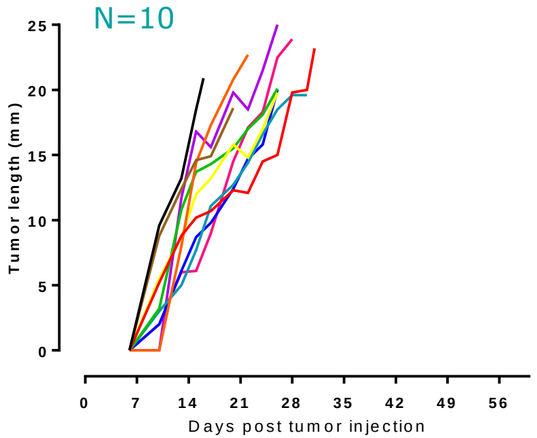
Strong, dominantly CD8+ T cell response to neoepitopes where peptide and RNA vaccines have been shown to be less efficient

* Castle et al., 2012 and Kreiter et al., 2015-adapted figure based on B16 melanoma results

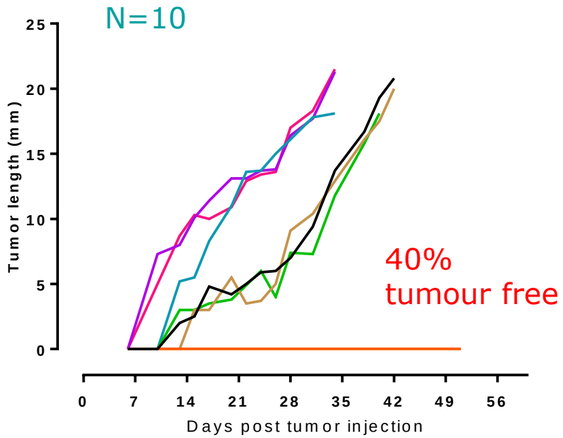
Vaccibody Induces Tumor Protection as Monotherapy

CT26 colon carcinoma model

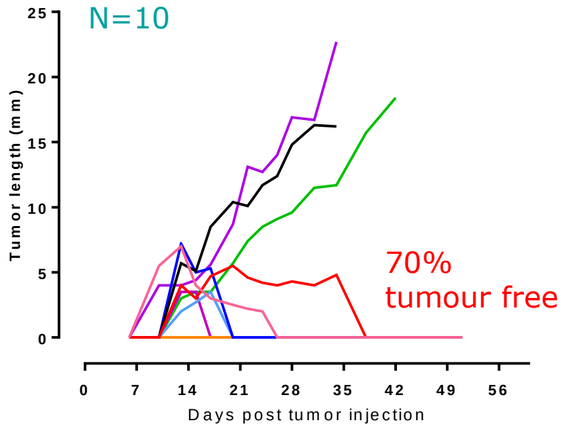
Control



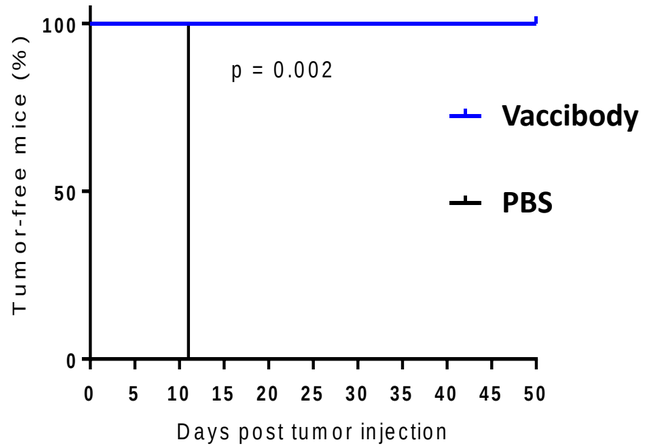
Vaccibody Monotherapy



Vaccibody Combination Therapy



Re-challenged mice are protected



- Vaccibody vaccination induces strong CD8+ T cell responses and **tumor protection as Monotherapy**
- Combination with anti-PD-1 immunotherapy induced enhanced anti-tumour responses in mice involving **complete tumour regression** of large, established tumours
- **Long-term memory responses** ensure effective anti-tumour responses after a 2nd tumour challenge in surviving mice with no sign of tumour growth

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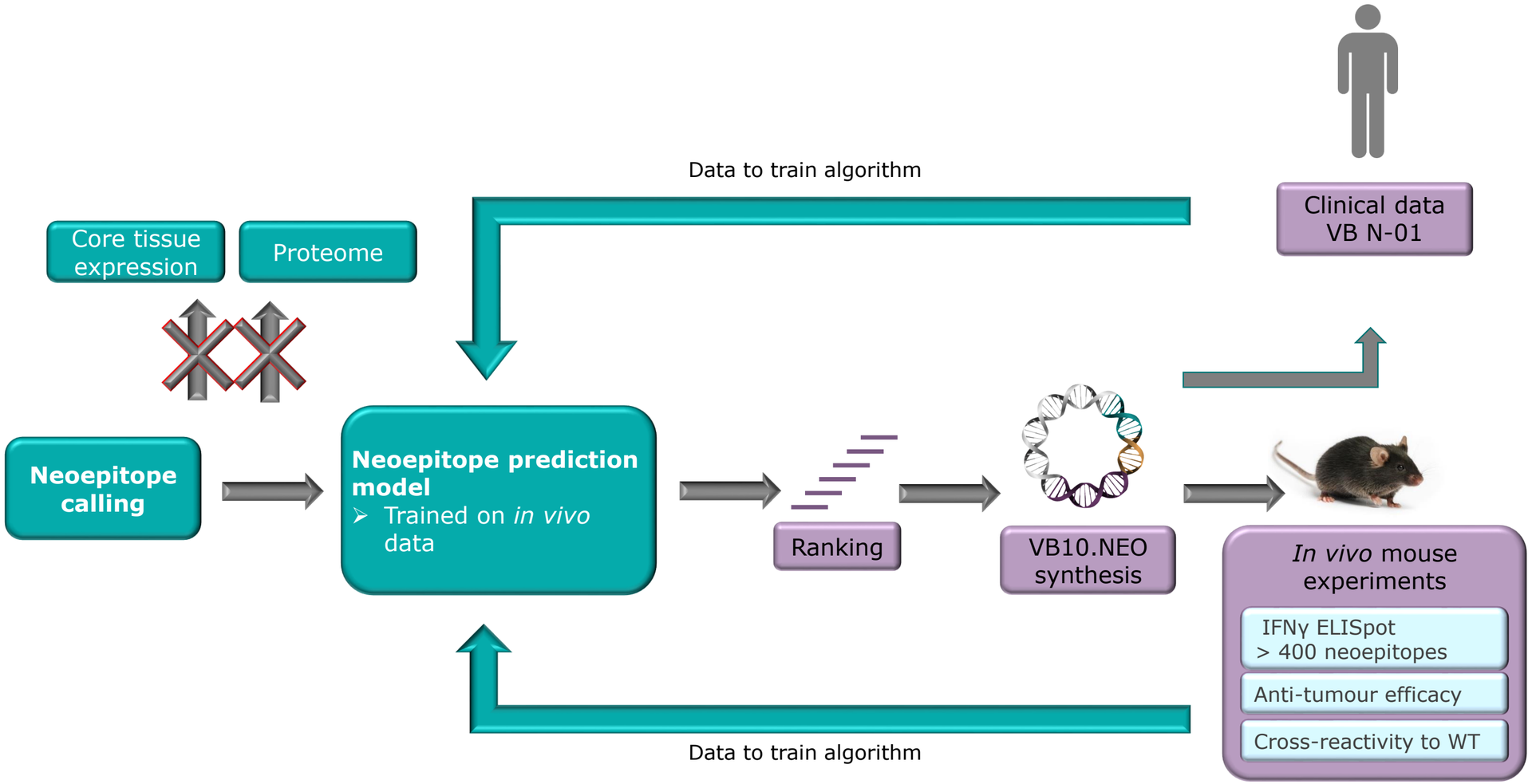
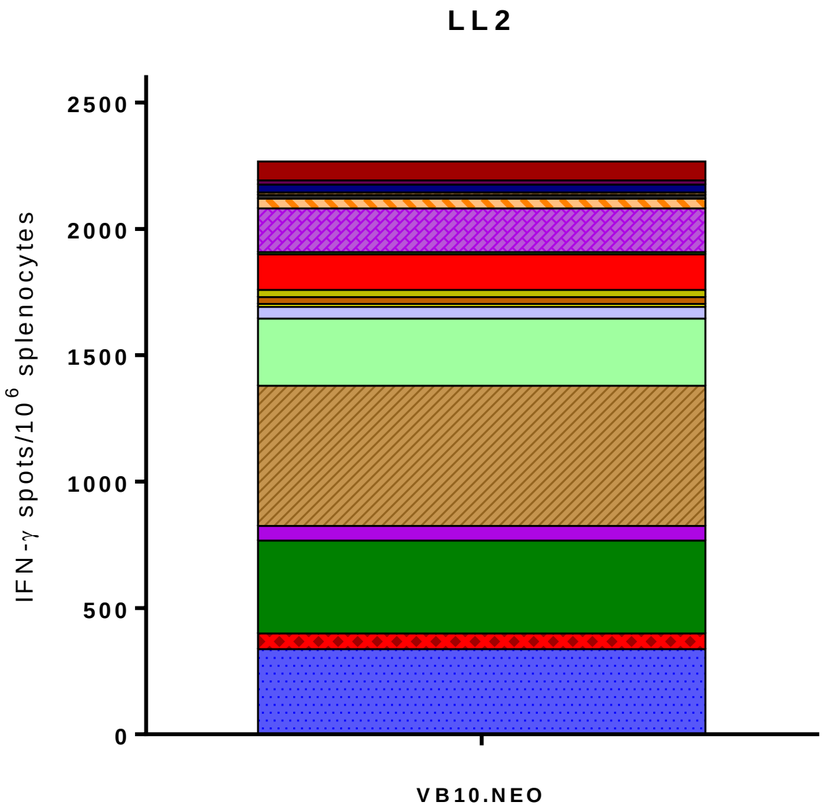
Development of VB10.NEO neoepitope prediction tool



Verification of VB10.NEO neoepitope prediction tool



VB10.NEO specific Neo-epitope Selection Tool employed in LL2 lung cancer tumour model:

= 68% immunogenic neoepitopes (14/20)

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Vaccibody Product Pipeline

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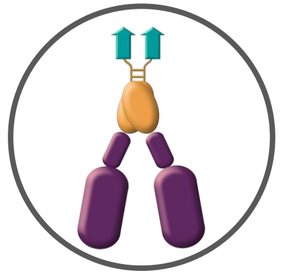
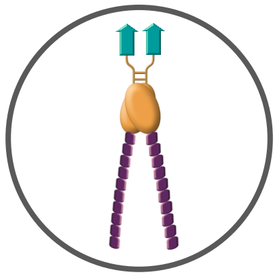
Precancerous cervical lesions	**VB C-01 (VB10.16)**				
MELANOMA LUNG (NSCLC) BLADDER RENAL HEAD AND NECK	**VB N-01 (VB10.NEO)***				



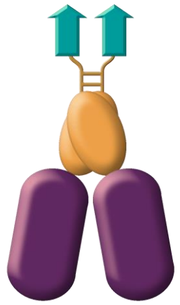


* Clinical Trial Application (CTA) approved March 2018.

Clinical Learnings – Vaccibody platform

VB10.16

- HPV16 specific therapeutic DNA vaccine (against viral neoantigens E6 and E7)
- First indication precancerous cervical lesions (CIN 2/3)
- Exploratory proof of concept clinical trial ongoing (Ph I/IIa)



SAFETY: No drug-related SAEs observed

DOSING: 3 week vaccination intervals induces strongest responses

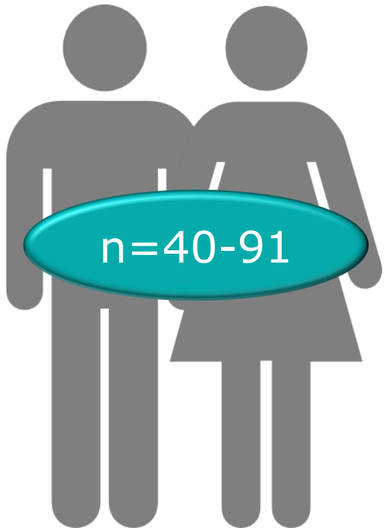
EFFECT: Clinical efficacy correlates strongly with T cell response. 6/6 patients completing 12 month follow up showed regression to CIN1 or less at some point

Clinical Trial VB N-01 planned FPI Q12018

VB N-01: An open labelled first human dose phase 1/2a study to evaluate safety, feasibility and efficacy of multiple dosing with individualised 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

VB10.NEO

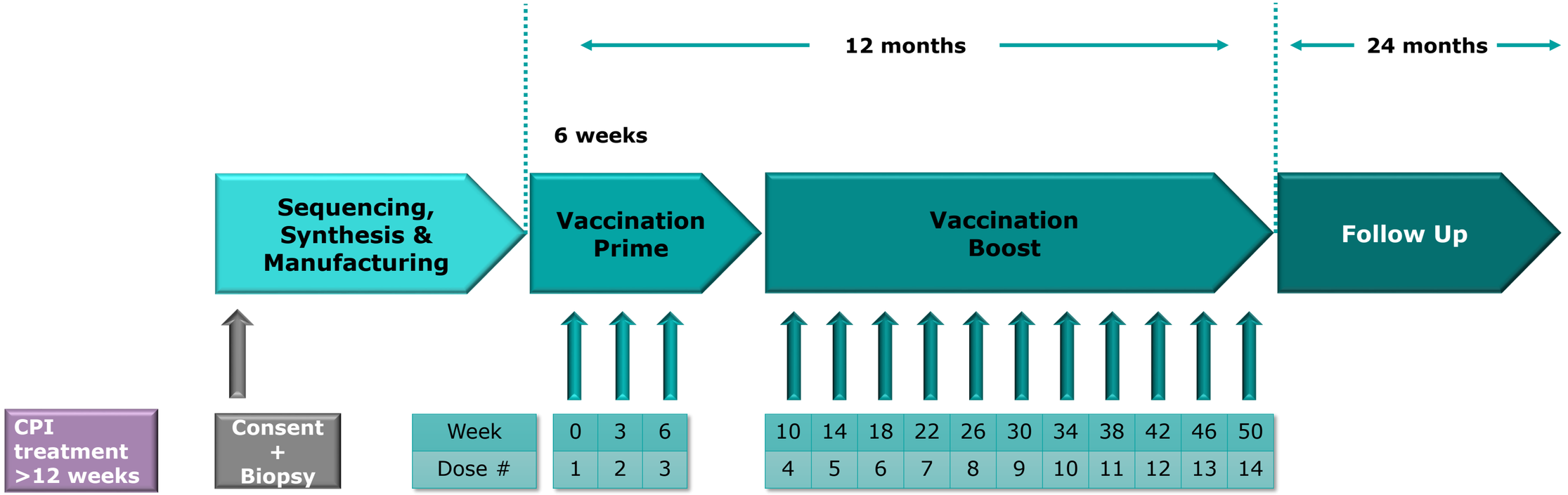
VB N-01



- **Melanoma**
- **NSCLC**
- **Clear Renal Cell Carcinoma**
- **Urothelial Cancer**
- **Squamous Cell Carcinoma of the Head and Neck**

- Approved CPI as SOC
- Moderate to high mutational load

Study Design and Treatment Schedule VB N-01



Renowned, International Clinical Sites

Prof Dr med Jürgen Krauss*
Head of Clinical Immunotherapy
National Centre for Tumour Diseases (NCT), Medical Oncology

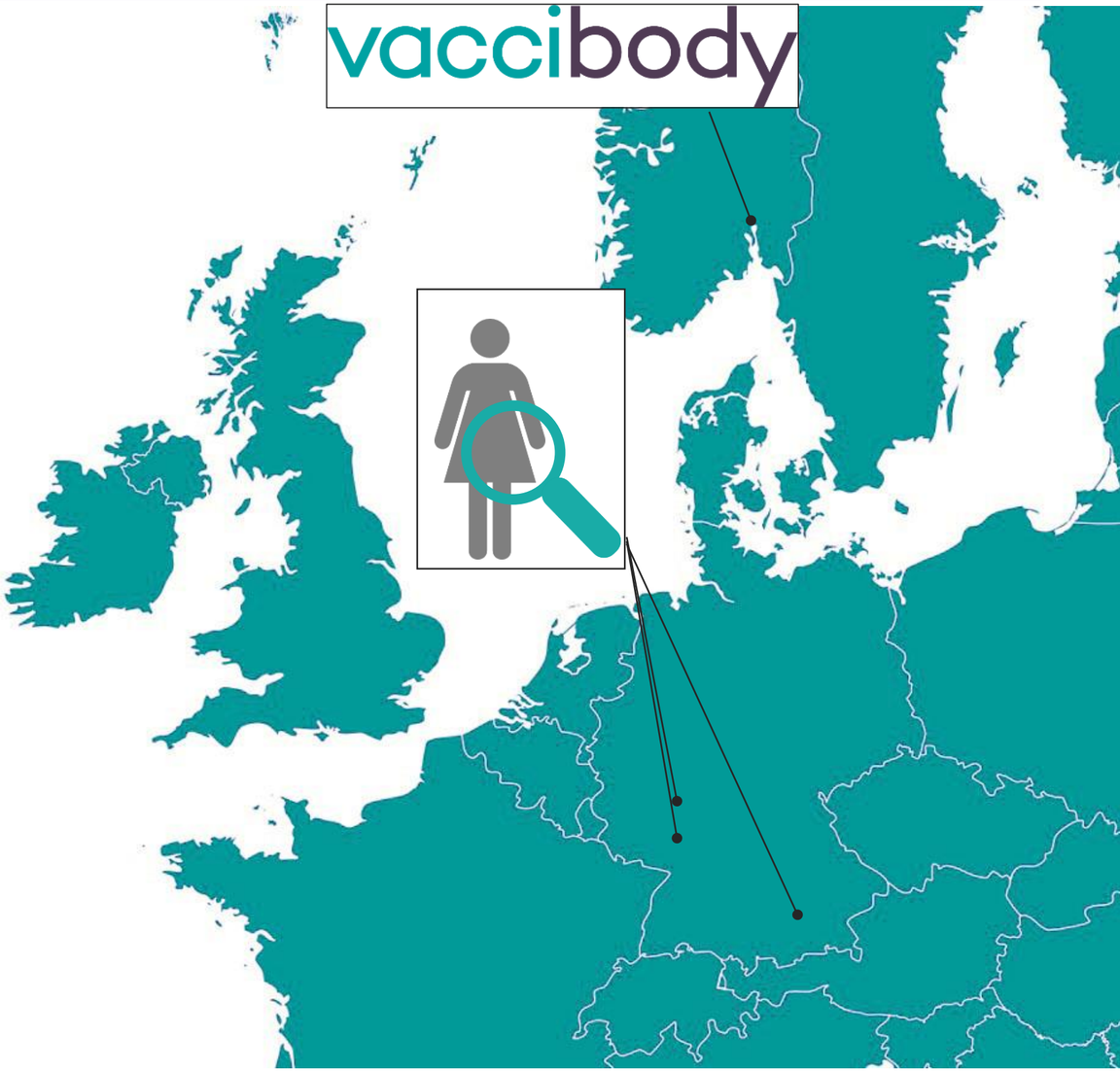
Heidelberg, Germany

Prof Dr med Angela Krackhardt
Director Tumour Immunology and Translational Immunotherapy
University Hospital Klinikum Rechts der Isar

Munich, Germany

Prof Dr med Elke Jäger
Director Department of Oncology and Hematology
Clinic Nordwest

Frankfurt am Main, Germany



* Coordinating Investigator

Vaccibody's Solution to Personalised Cancer Treatment

1. Tumour biopsy and sequencing

2. Neoepitope selection

VB10.NEO specific proprietary selection method

3. Vaccine manufacturing (n=1)

-Robust, rapid, cost-effective manufacturing
- stable, safe DNA plasmid format
-hold up to 20 neoepitopes

4. Vaccine administration and immunogenicity

-Needle-free delivery
-Rapid, strong, long-lasting
-Broad and CD8 dominated

Rapid, cost-effective, efficacious

2017 Annual accounts – P&L

(KNOK)

- **Operating revenue: 9,763**
  - Revenue 486 from Evaxion
  - BIA-grant 3,897
  - Skattefunn: 5,102
  - EU, SAPHIR: 278
- **Operating expenses: 43,731**
  - External R&D, lab expenses and IP-expenses: 22,844
  - Personnel expenses: 14,372
  - Rent, admin. and bus. dev.: 6,515
- **Net financials: 2,597**
  - Net interest income: 1,605
  - Net currency gain: 992
- **Ordinary result –31,371**

Income statement

	Note	2017	2016
OPERATING REVENUE AND EXPENCES			
Operating revenue			
Revenue	1	486 180	243 149
Other operating income	2	9 277 255	8 755 464
Total operating revenue		9 763 435	8 998 613
Operating expenses			
Employee benefits expense	5	14 371 809	8 507 351
Depreciation and amortization expenses	4	82 454	84 401
Other operating expenses	5	29 277 139	16 814 918
Total operating expenses		43 731 403	25 406 669
OPERATING PROFIT OR LOSS		(33 967 968)	(16 408 056)
FINANCIAL INCOME AND EXPENSES			
Financial income			
Changes in market value of fin. cur. assets		(15 785)	322 179
Other interests	3	1 634 649	(69 794)
Other financial income	6	1 570 113	88 431
Total financial income		3 188 977	340 817
Financial expenses			
Changes in market value of fin. cur. assets		0	54 653
Other interests		13 844	933
Other financial expense	6	577 786	97 361
Total financial expenses		591 630	152 947
NET FINANCIAL INCOME AND EXPENCES		2 597 347	187 870
ORDINARY RESULT BEFORE TAXES		(31 370 621)	(16 220 187)
Tax on ordinary result	7	0	0
ORDINARY RESULT		(31 370 621)	(16 220 187)
TO MAJORITY INTERESTS		(31 370 621)	(16 220 187)
APPLICATION AND ALLOC.			
Uncovered loss	9	(31 370 621)	(16 220 187)
TOTAL APPLICATION AND ALLOCATION		(31 370 621)	(16 220 187)

2017 Annual accounts – Balance Sheet

(MNOK)

- Cash and equivalents: 207
- Receivables, mainly grants: 7
- Fixed assets: 0.4

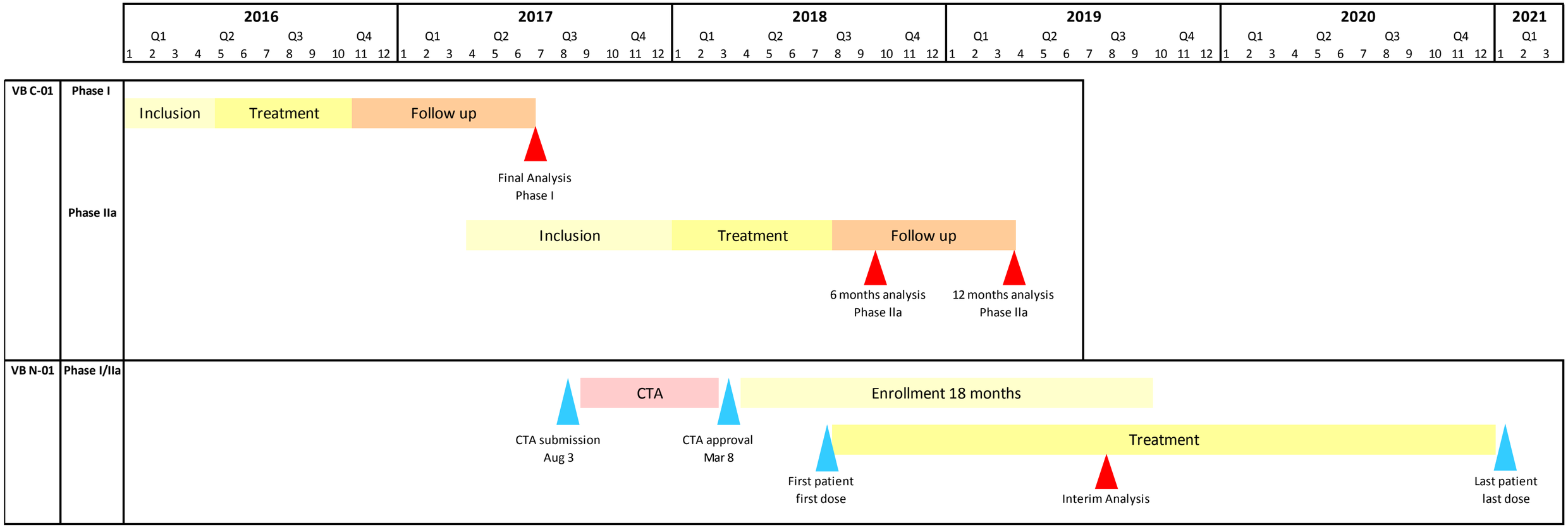
- Equity: 203 *(95%)*
- Current liabilities: 11

	Note	31.12.2017	31.12.2016
ASSETS			
FIXED ASSETS			
Intangible assets			
Concessions, patents, licenses, trade marks	10	299 700	299 700
Total intangible assets		**299 700**	**299 700**
Tangible assets			
Machinery and plant	4	29 166	97 485
Fixtures and fittings, office machinery etc.	4	60 059	0
Total tangible assets		**89 225**	**97 485**
Financial fixed assets			
Other long-term receivables		45 926	0
Total financial fixed assets		**45 926**	**0**
TOTAL FIXED ASSETS		**434 851**	**397 185**
CURRENT ASSETS			
Receivables			
Trade receivables		0	237 243
Unpaid subscribed capital	9	0	220 000 000
Other short-term receivables	2	6 958 485	6 370 972
Total receivables		**6 958 485**	**226 608 215**
Investments			
Quoted bonds	3	40 097 817	0
Other quoted financial instruments	3	126 698 744	5 368 996
Total investments		**166 796 561**	**5 368 996**
Bank deposits, cash in hand, etc.	8	40 276 141	19 633 377
TOTAL CURRENT ASSETS		**214 031 188**	**251 610 588**
TOTAL ASSETS		**214 466 038**	**252 007 774**

	Note	31.12.2017	31.12.2016
EQUITY AND LIABILITIES			
EQUITY			
Paid-in equity			
Share capital	9	2 417 064	1 529 649
Share premium reserve	9	287 444 579	78 784 384
Other paid-in equity	9	0	209 050 000
Total paid-in equity		**289 861 643**	**289 364 033**
Retained earnings			
Uncovered loss	9	(86 332 842)	(54 962 221)
Total retained earnings		**(86 332 842)**	**(54 962 221)**
TOTAL EQUITY		**203 528 801**	**234 401 811**
LIABILITIES			
CURRENT LIABILITIES			
Accounts payable		6 084 410	3 410 732
Public duties payable		861 270	633 276
Other currents liabilities	9	3 991 557	13 561 954
TOTAL CURRENT LIABILITIES		**10 937 237**	**17 605 962**
TOTAL LIABILITIES		**10 937 237**	**17 605 962**
TOTAL EQUITY AND LIABILITIES		**214 466 038**	**252 007 774**

vaccibody

Important milestones 2018-2020



Conclusions – take home messages

- Vaccibody has established itself as a leader in the rapidly developing field of cancer neoantigen vaccines
- Vaccibody has built a strong team over the last 15 months and filled key positions within medical, production and research – now 16 employees
- Vaccibody has a strong cash position (runway until end of 2020) and is expecting important value inflections in the next 18 month both for neoantigen clinical trial as well as for the HPV clinical trial

Vaccibody team ready to execute and deliver

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