vaccibody

Targeting antigens to antigen presenting cells induce effective anti-tumor efficacy as monotherapy and as combination therapy

European Neoantigen Summit

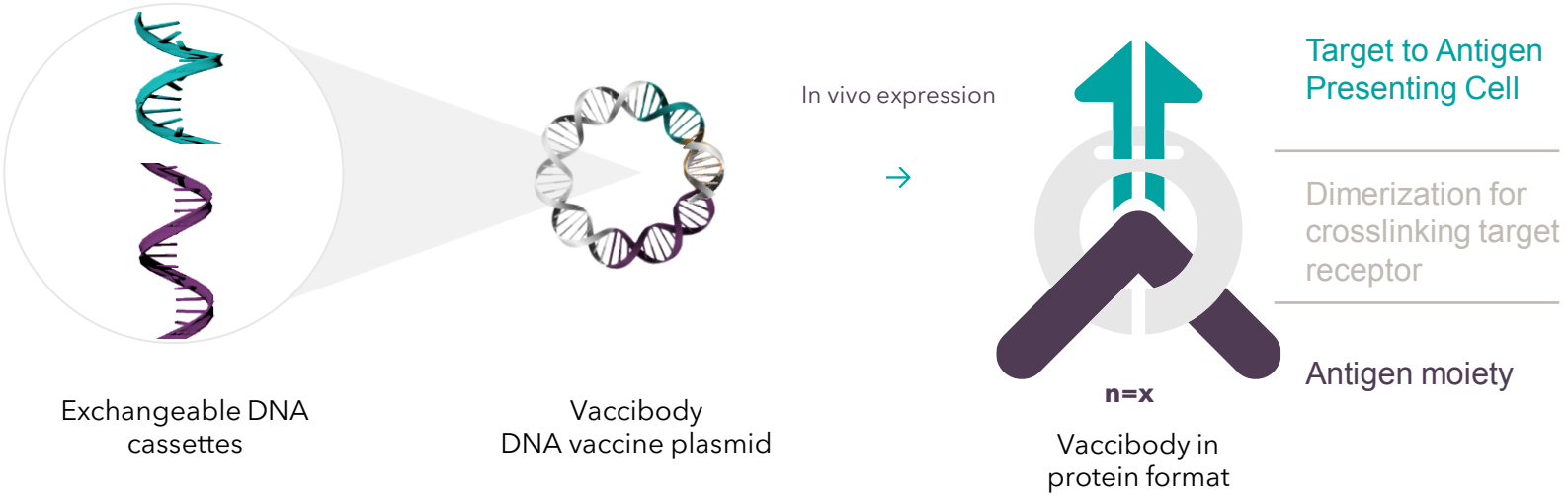
22 April 2021

Agenda

1. **Vaccibody™ platform for induction of rapid, strong and broad immune responses**
2. Tailoring the immune response profile by targeting different APC
3. Combinations and applicability within personalized and off-the shelf cancer vaccines and beyond

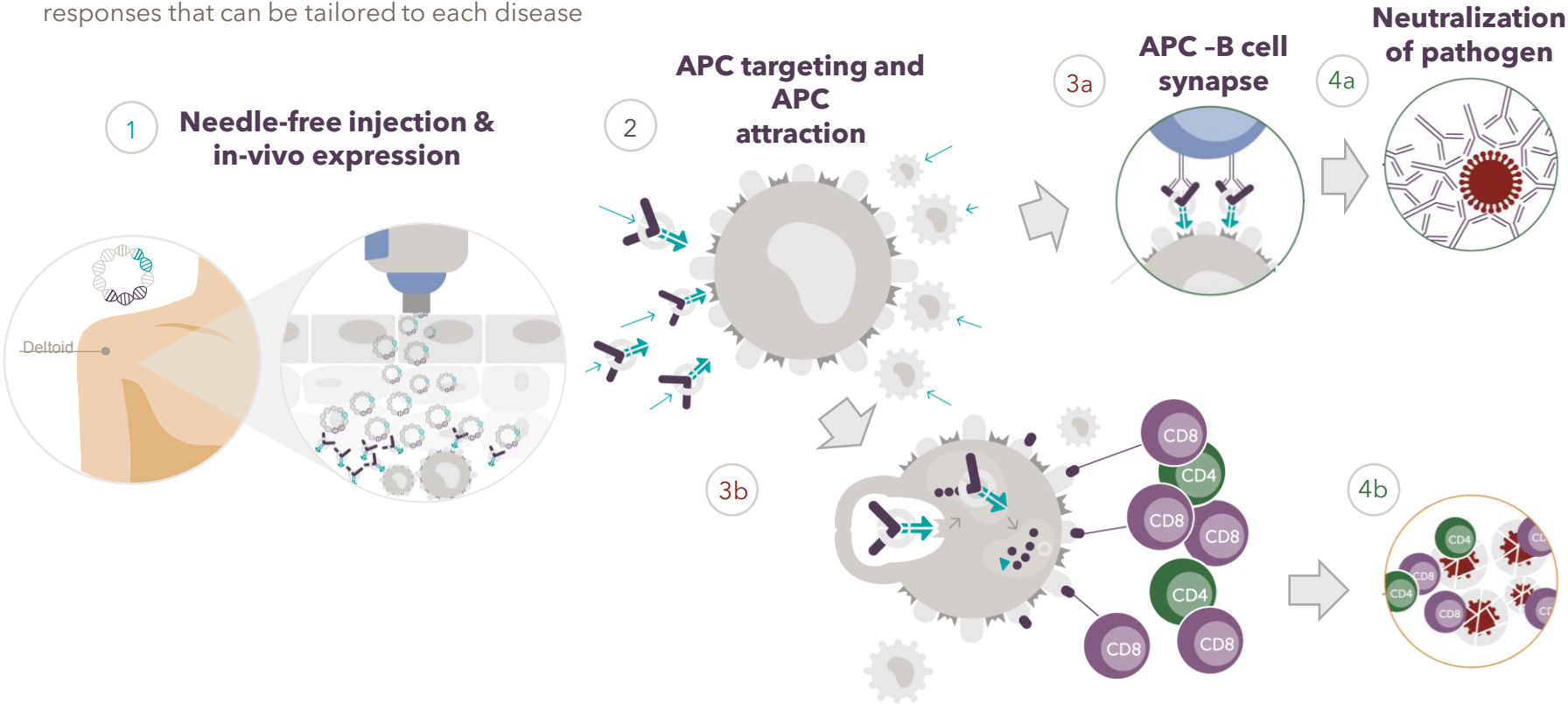
Flexible Vaccibody™ format can fuel multiple products customized for each indication

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



Vaccibody mechanism of action

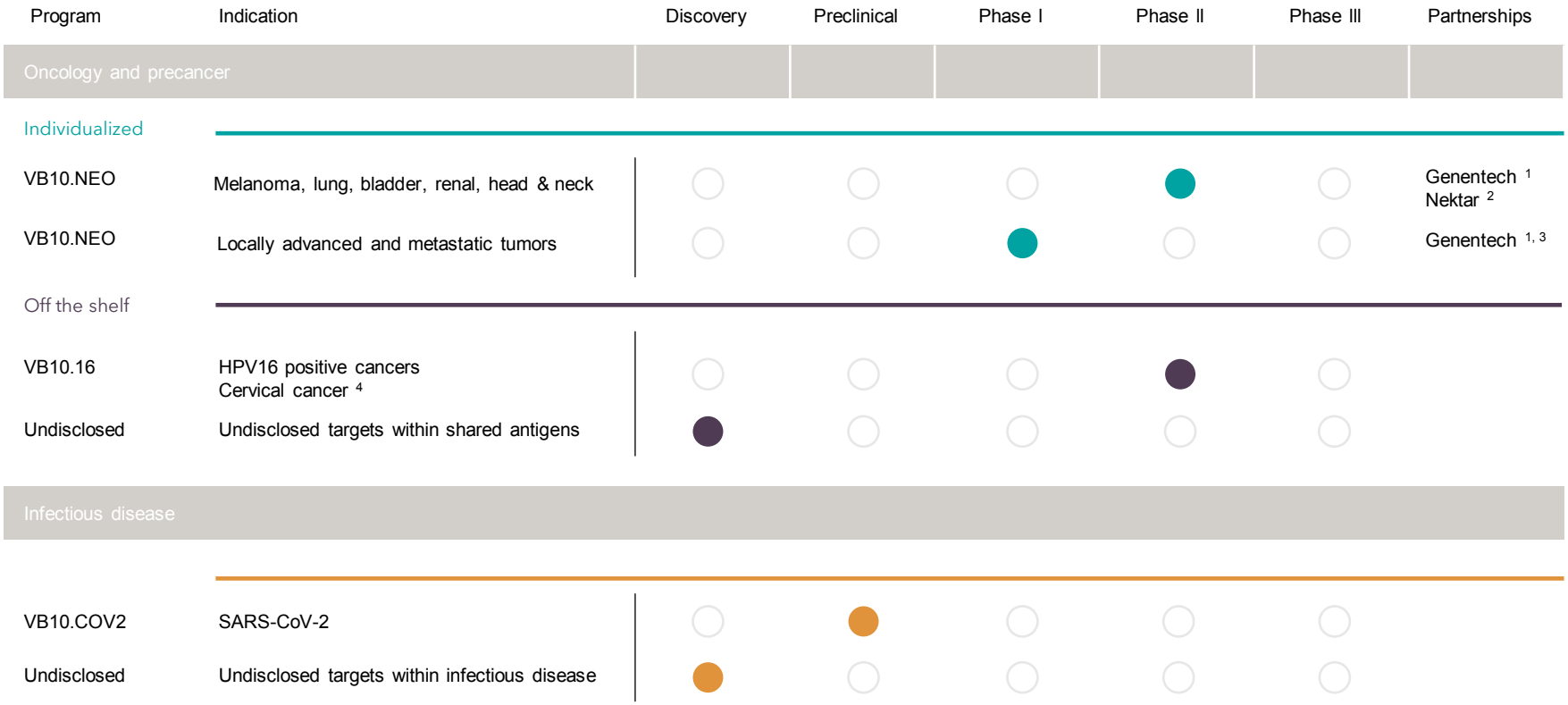
The APC targeting vaccine technology platform creates unique rapid, strong and broad immune responses that can be tailored to each disease



vaccibody

Pipeline

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

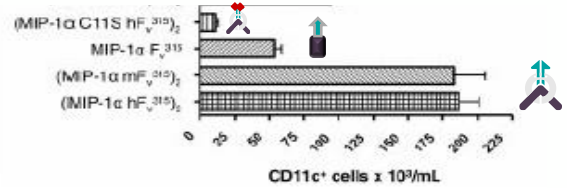


vaccibody

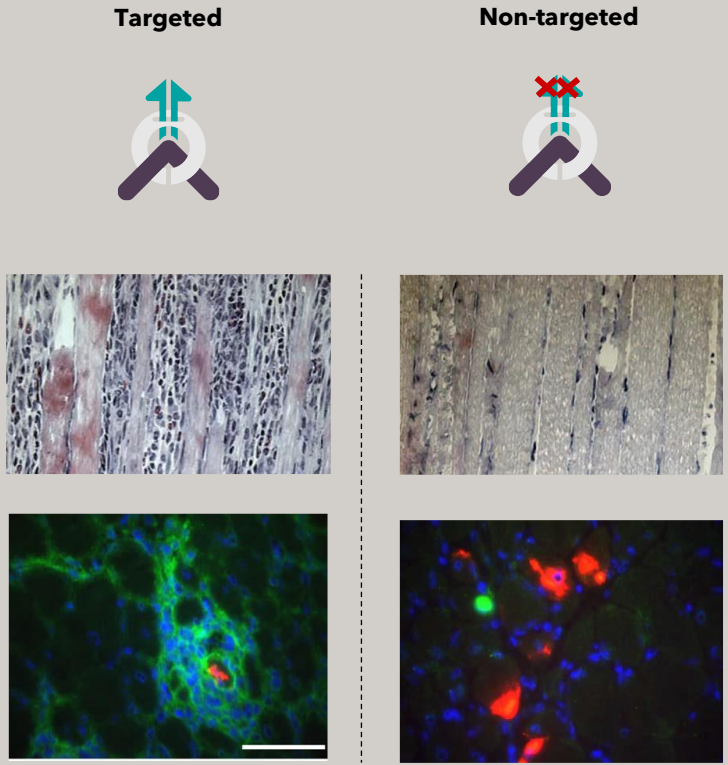
1) Genentech has an exclusive license to VB10.NEO; 2) Collaboration with Nektar Therapeutics on combining NKTR-214 (bempegaldesleukin) with VB10.NEO in trial arm 5B (SCCHN); 3) In combination with atezolizumab; 4) Roche supplies atezolizumab

Targeting ensures efficient attraction of APC

- Targeting Vaccibody™ protein secreted from transfected myocytes **attracts APCs** through chemokine induced migration of APC
- High local concentration of vaccine and APC
- Ensure rapid and efficient **loading of antigen to APC**
- This feature is dependent on a functional **targeting module**



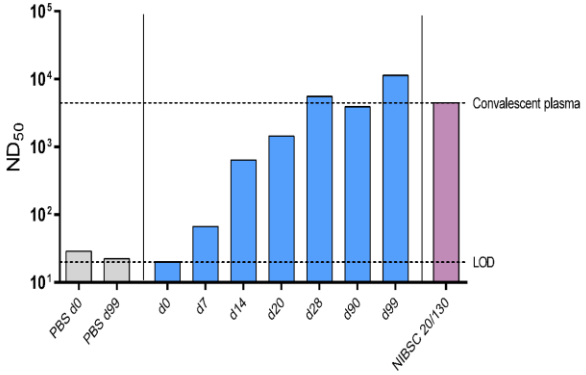
Homodimerization improves chemotaxis



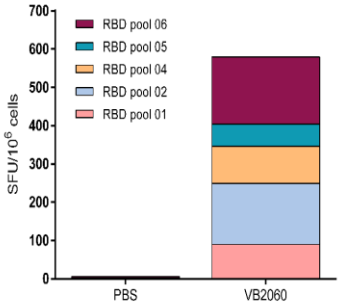
Fredriksen et al., 2007; Løvås et al., 2014.

Rapid onset of Immunogenicity

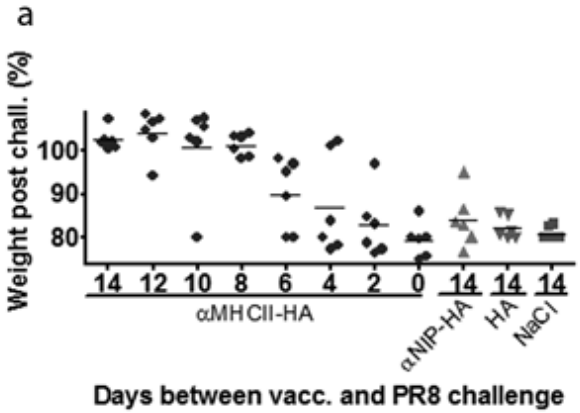
SARS-CoV-2 neutralization from d7



RBD-specific T cell responses d7



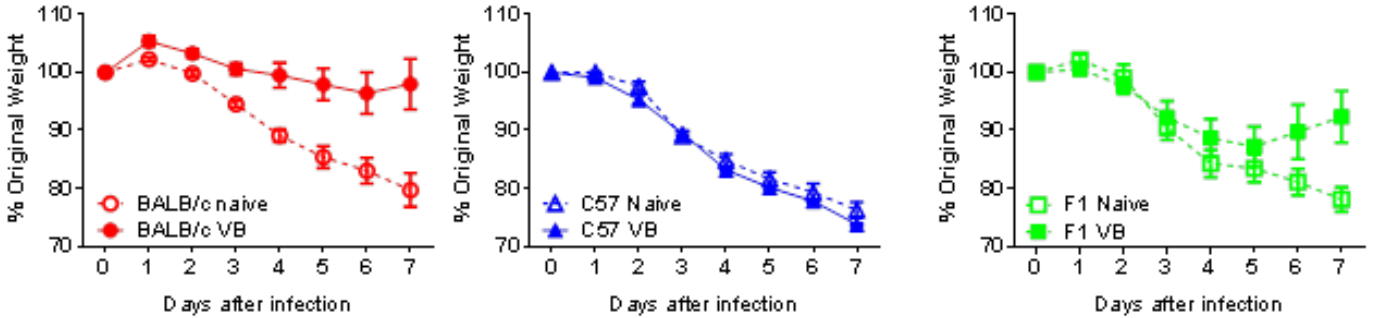
Rapid protection against influenza
(1 week post 1 vaccination)



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

Norheim_2020, Grodeland_2013

Protection is dependent on proper targeting to APC



- Vaccibody™ constructs targeting I-E^{d} bind APC receptor in BALB/c, but not C57BL/6 mice
  Protection against influenza is dependent on functional targeting to APC

Lambert et al., 2016

Standard manufacturing process 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

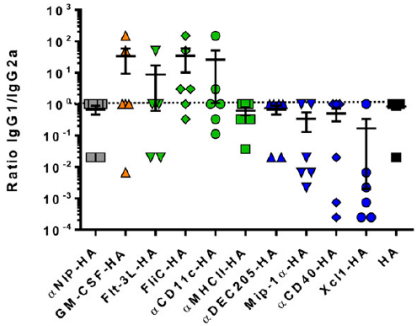
- Rapid and robust vaccine design
- Scalable manufacturing process
- Painless administration
- Indication of long-term storage at +2-8°C

Agenda

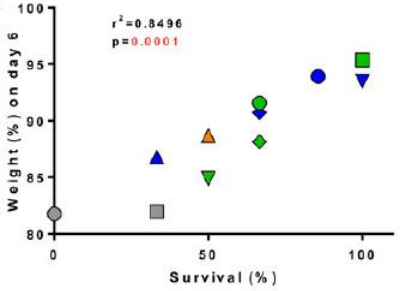
1. Vaccibody™ platform for induction of rapid, strong and broad immune responses
2. **Tailoring the immune response profile by targeting different APC**
3. Combinations and applicability within personalized and off-the shelf cancer vaccines and beyond

Choice of targeting unit affects the immune response profile

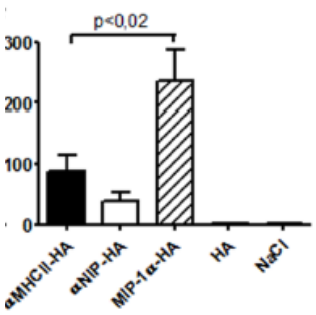
Targeting unit affects Th1/Th2 balance



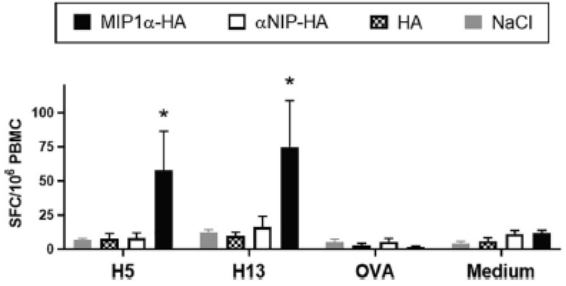
Targeting unit affects level of protection



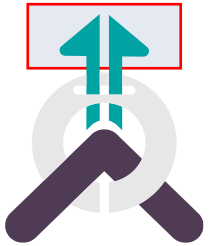
Targeting unit affects level of CD8 T cell response



MIP-1a induces cross-reactive T cell responses

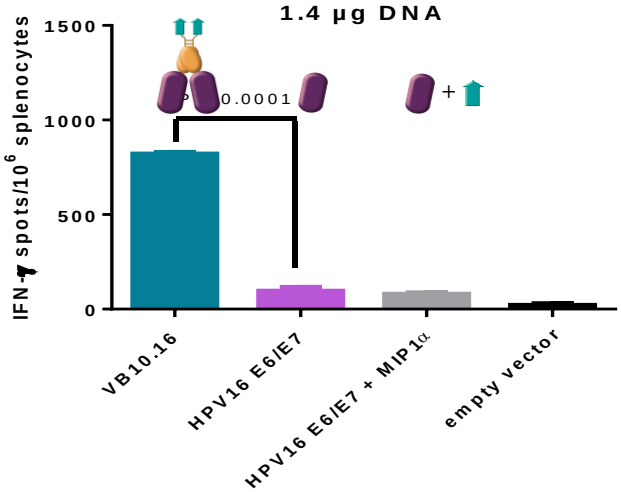


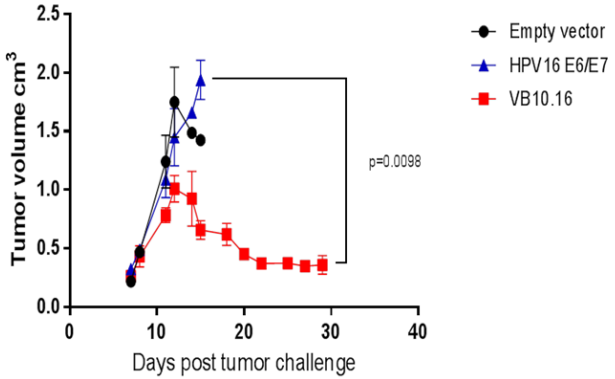
- VB has a unique targeting unit that binds surface receptors on APC
- Adapting the APC targeting unit affects the immune response profile
- **Vaccibody can match targeting unit and antigen tailored to each disease**



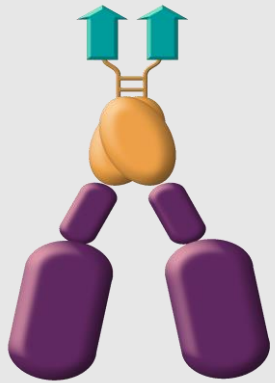
Braathen, 2018, Grodeland_2013, 2020

Induction of Strong CD8 responses using MIP-1α





VB10.16



VB10.16 compared to other vaccine formats:

- Induction of significantly stronger HPV16 specific IFN-γ T cell responses at very low doses
- Strong anti-tumor efficacy with regression of large established tumours
- Dependent on the Vaccibody vaccine format covalently linking MIP-1α to HPV antigens in dimeric format

VB10.NEO: Exclusively licensed to Genentech

Global, oncology collaboration between Vaccibody and Genentech to develop individualized neoantigen cancer vaccines across multiple tumor types

vaccibody

Conduct clinical Phase1b trial combining VB10.NEO with *atezolizumab*

→

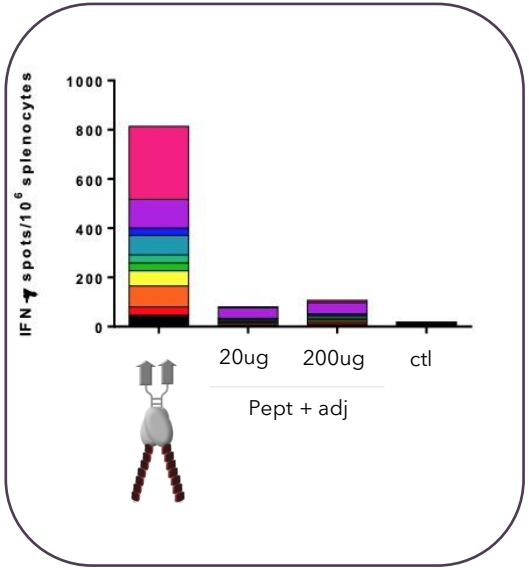
Genentech
A Member of the Roche Group

Responsible, and bear all costs, for all further clinical, regulatory, manufacturing and commercialization activities for VB10.NEO

The Genentech collaboration was announced October 1st, 2020

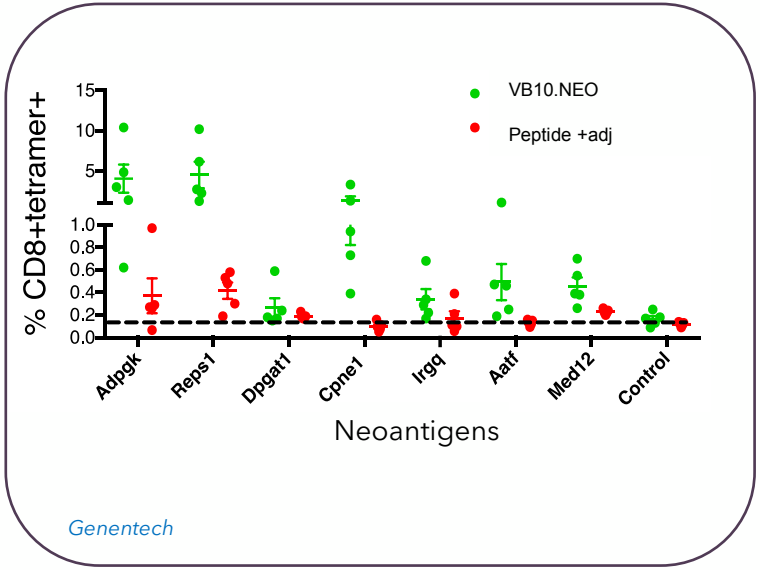
VB10.NEO exhibits superior T cell priming activity after a single dose

VB10.NEO exhibits superior priming after single dose



B16 melanoma model

VB10.NEO elicit a potent and broad CD8 T cell response



MC38 colon carcinoma model

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

B16 melanoma model

		Pep 1	Pep 2	Pep 3	Pep 4	Pep 5	Pep 6	Pep 7	Pep 8	Pep 9	Pep10
Peptide*	CD4										
	CD8										
RNA*	CD4										
	CD8										
Non-targeted DNA	CD4				nt		nt			nt	nt
	CD8										
VB10.NEO	CD4										
	CD8										

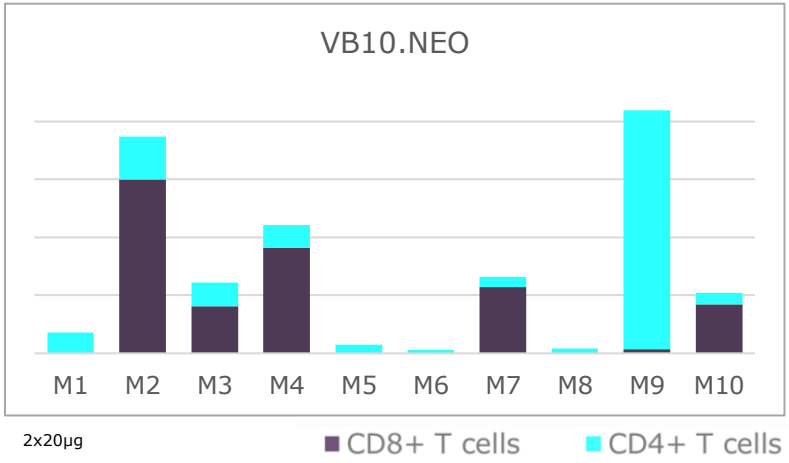
Peptide and RNA vaccines induces primarily CD4 T cell responses, while VB10.NEO induces strong, dominating CD8 responses to the identical neoepitope sequences

Non-targeted DNA vaccines induced a CD8 response towards 1 of 6 tested neoepitopes

- Castle et al., 2012 and Kreiter et al., 2015
- Aurisicchio et al., 2019

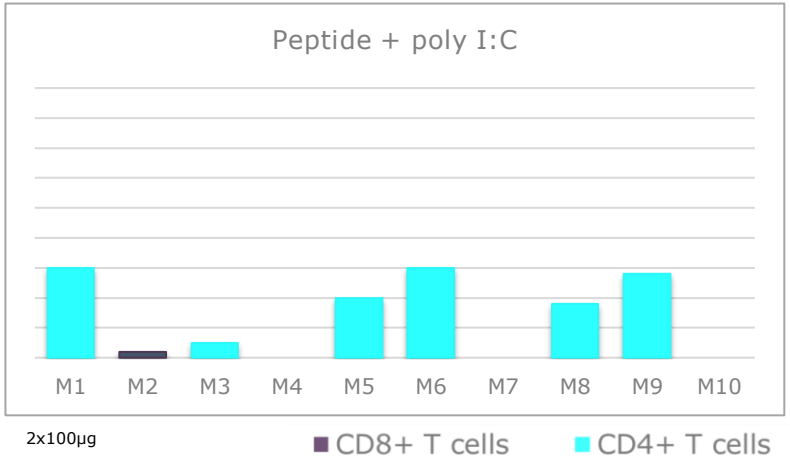
VB10.NEO leads to a unique immune response pattern

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



Peptide + poly I:C vaccination has been reported to induce **dominantly CD4 T cell responses**

B16 melanoma model



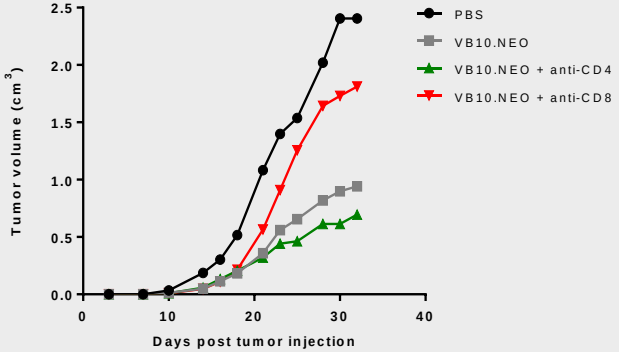
VB10.NEO induces a different immune response pattern adding strong, dominantly CD8+ T cell responses to identical neoepitopes that induces **no or weak** immune responses if delivered as peptide vaccine

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

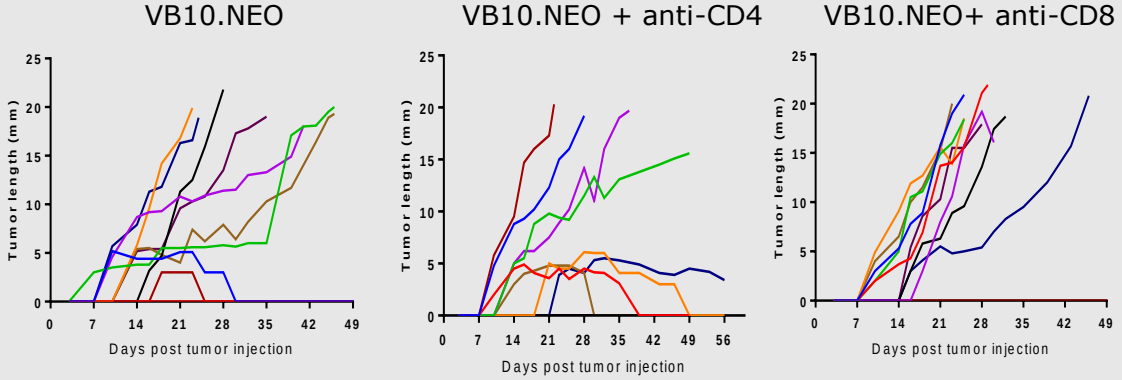
Neoepitope-specific CD8 T cells are crucial for tumour protection

CT26 colon carcinoma model

Average, all groups



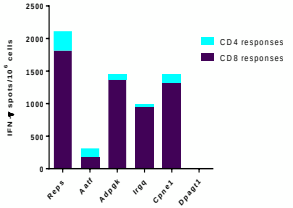
Individual growth curves



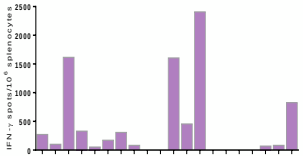
Depletion of CD8 T cells prohibit tumor protection in VB10.NEO vaccinated mice, indicating a crucial role of neoepitope-specific CD8 T cells for anti-tumor efficacy

VB10.NEO has proven to induce an effective anti-tumor response

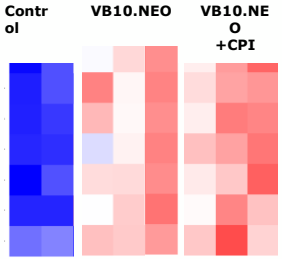
Neoepitope-specific CD8+ T cell response in spleen



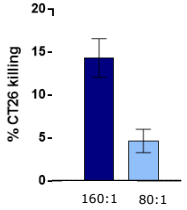
Neoepitope-specific T cell response in tumor



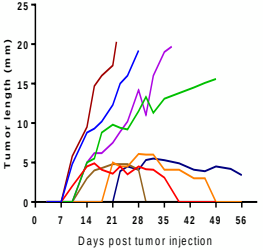
Influx of cytotoxic T cells in tumor (TILs)



TILs recognize and kill tumor cells



Tumor protective immune responses elicited in vaccinated mice (CD8 dependent)



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

Agenda

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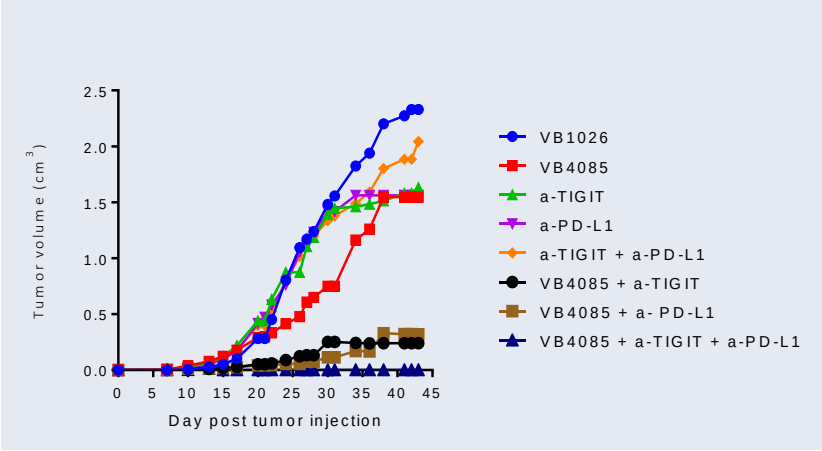
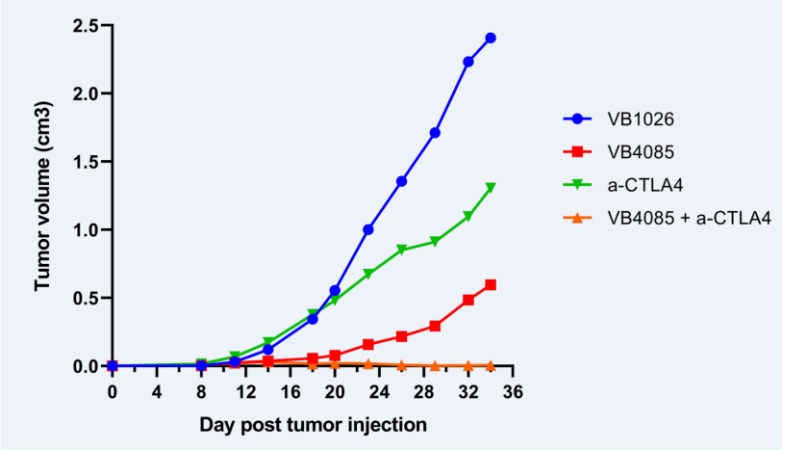
Synergistic effects adding Vaccibody™ to CPI regimen(s)



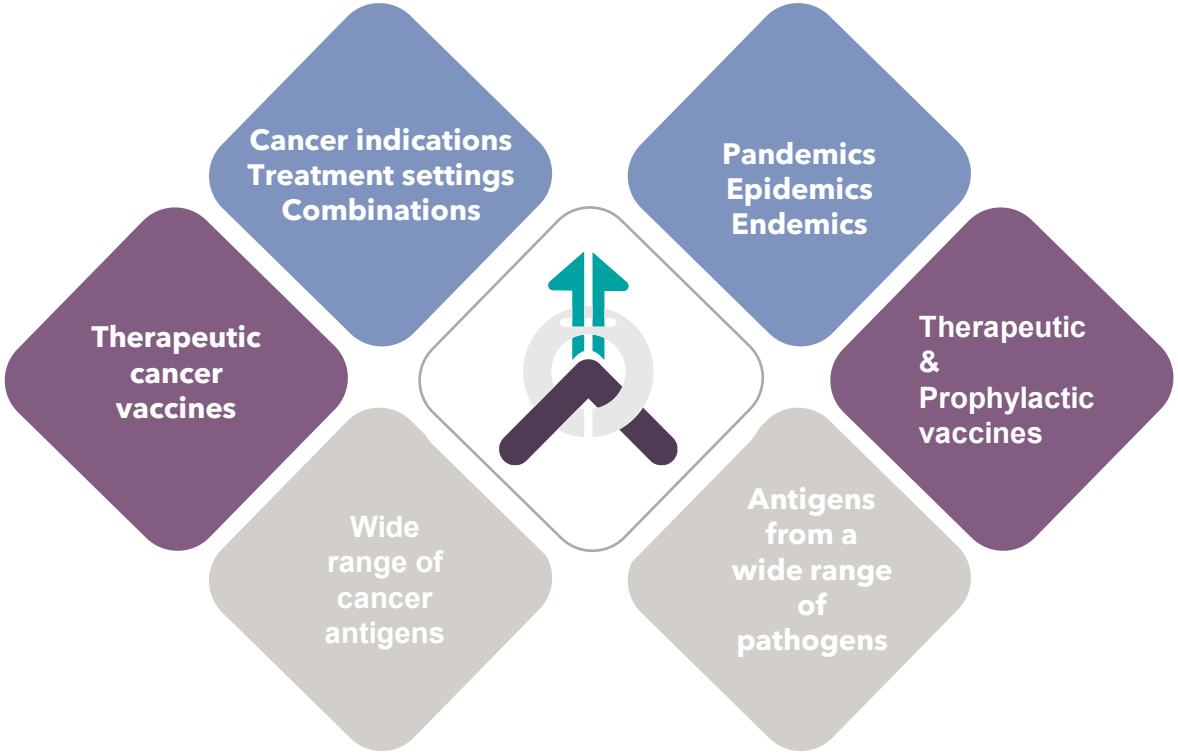


- VB plus anti-PD-L1, anti-TIGIT and anti-CTLA-4 mAbs all leads to synergistic anti-tumor efficacy
- Triple combination of VB plus anti-PD-L1 and anti-TIGIT leads to 100 % complete responses with significant contribution of VB

Future plans

Accelerate and expand of the pipeline across an increasing range of therapeutic areas and therapeutic modalities, with selected strategic partnerships

Shared off-the-shelf cancer vaccines



Vaccines against Infectious diseases

Acknowledgements

vaccibody

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Mark McCarron
Siri Tahtinen
Lelia Delamarre
Ira Mellman

vaccibody

President and CSO Agnete Fredriksen

ABFredriksen@vaccibody.com