vaccibody

Development of a Cost-effective Personalized cancer Neoantigen vaccines inducing a unique CD8-dominated T cell response

World Immunotherapy congress
Festival of Biologics

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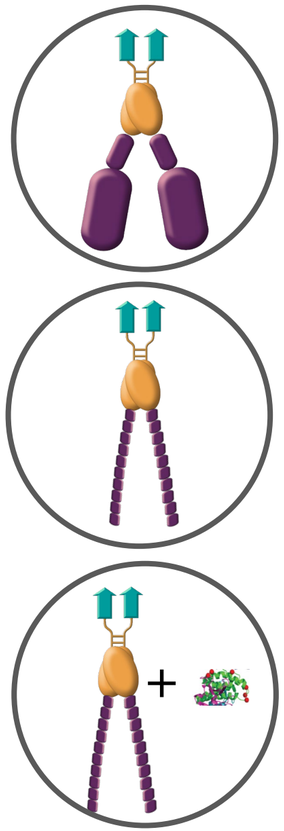
Agnete Fredriksen, PhD
President & CSO
Vaccibody AS

abfredriksen@vaccibody.com

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)				
HEAD AND NECK	VB10.NEO + NKTR-214		NEKTAR®		



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?

Vaccibody – Proprietary Vaccine Technology Platform

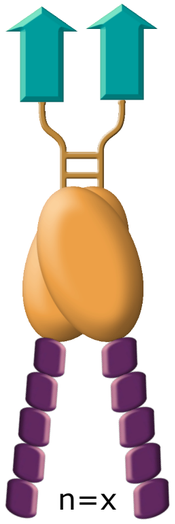
The Vaccibody Technology Platform was developed based on the concept of **targeting antigen to APC** in order to create more efficacious vaccines.

Exchangeable DNA Cassette

Vaccibody DNA Vaccine Plasmid

VB10.NEO

In vivo expression



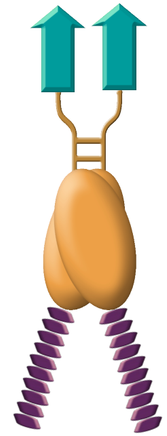
Vaccibody in Protein Format

Target to Antigen Presenting Cell

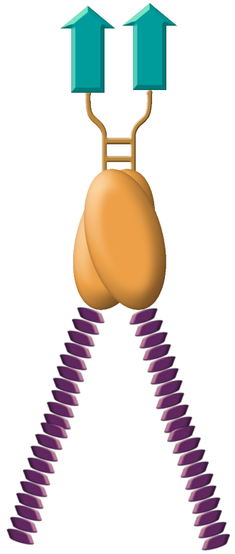
Dimerization for crosslinking target receptor

Antigen moiety

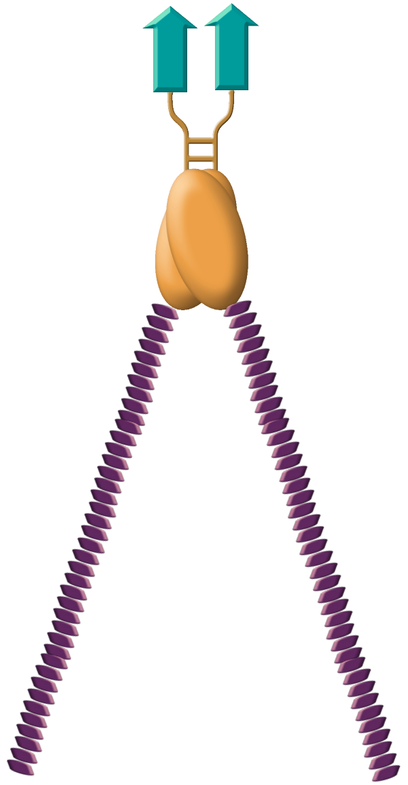
VB10.NEO – A Robust Vaccine Format



VB10.NEO-X



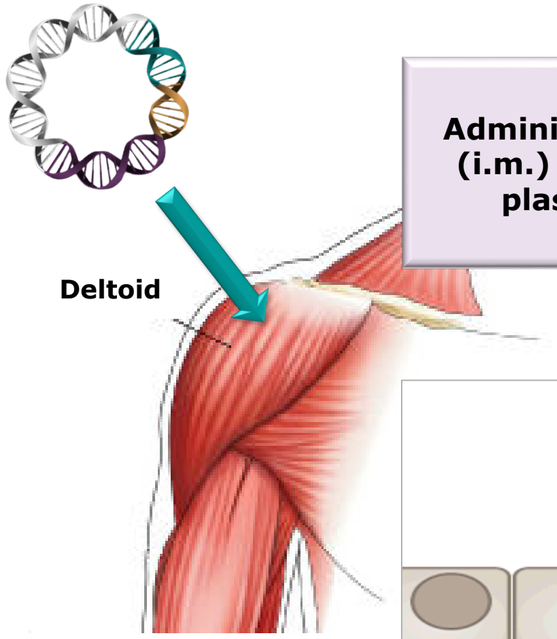
VB10.NEO-XX



VB10.NEO-XD

>90 different VB10.NEO constructs with >450 neoepitopes constructed to date with up to 40 neoepitopes

Mechanism of Action – Intrinsic Adjuvant

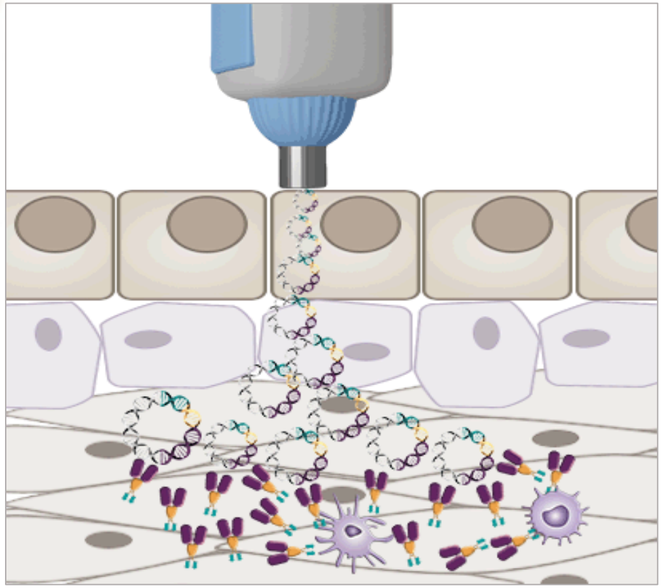


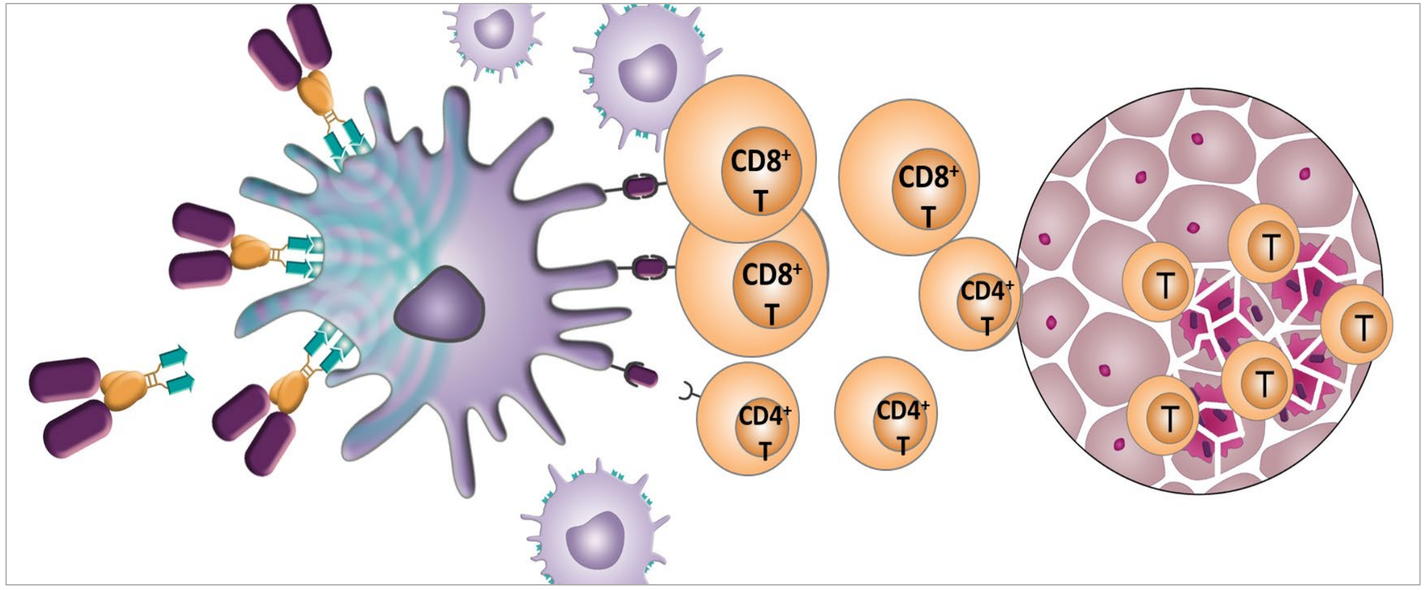
Administration (i.m.) of DNA plasmid

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

Chemokine MIP-1α

Target – Attract –Mature –Deliver-Cross-present





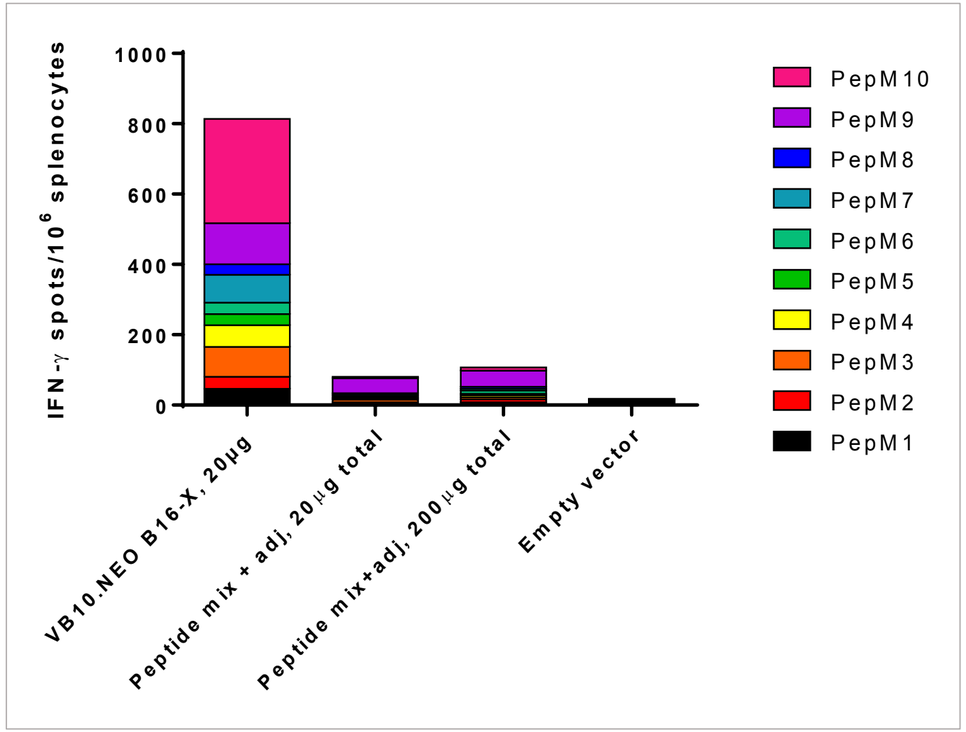
Patient Friendly, simple Vaccine Delivery

PharmaJet®

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

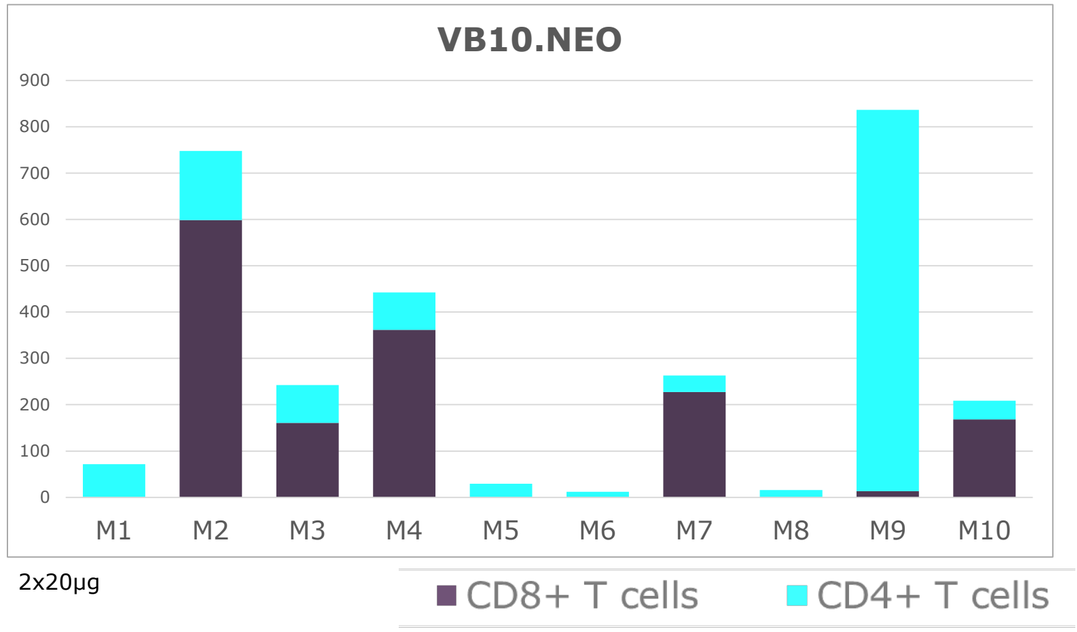
VB10.NEO induces Rapid, Broad and Strong responses to multiple Neoepitopes by single Vaccination

- 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



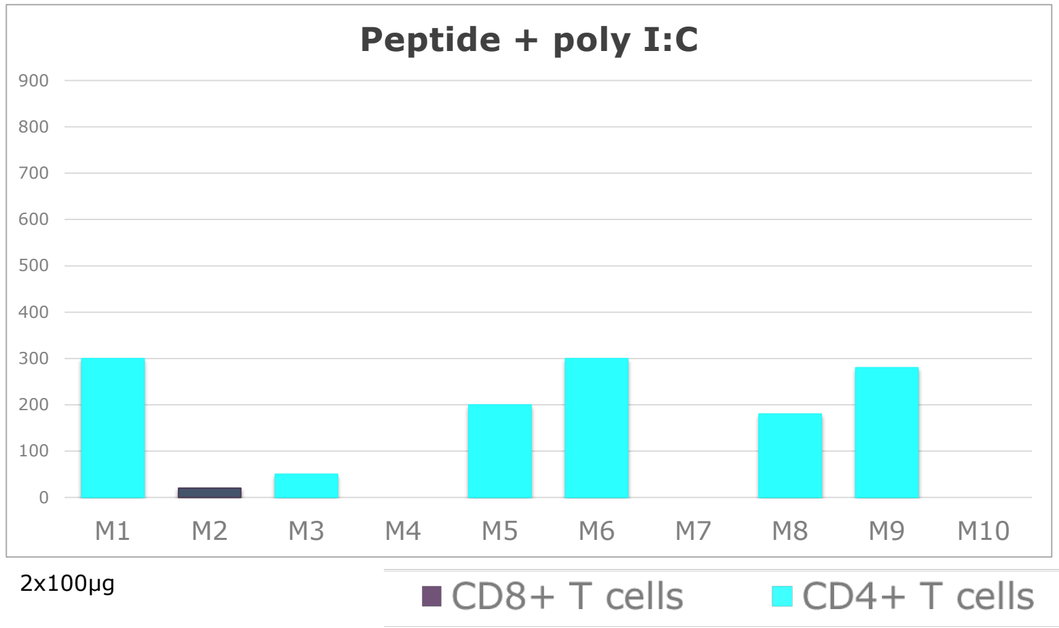
VB10.NEO leads to a unique CD8 dominated neoepitope response

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



2x20µg

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



2x100µg

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

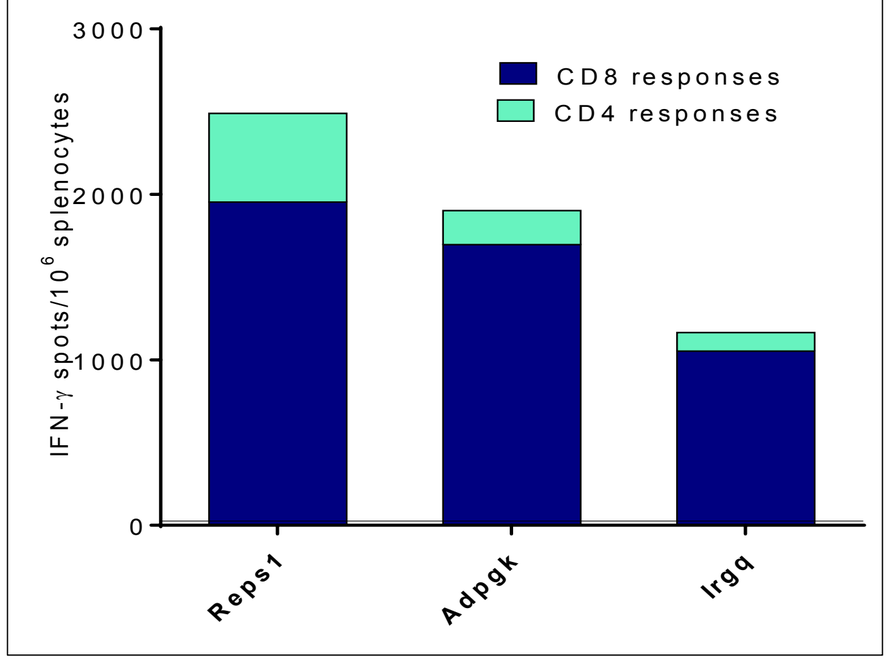
* Castle et al., 2012 and Kreiter et al., 2015-adapted figure based on B16 melanoma results

Confirmation of VB10.NEO's unique ability to induce strong neoepitope-specific CD8 responses

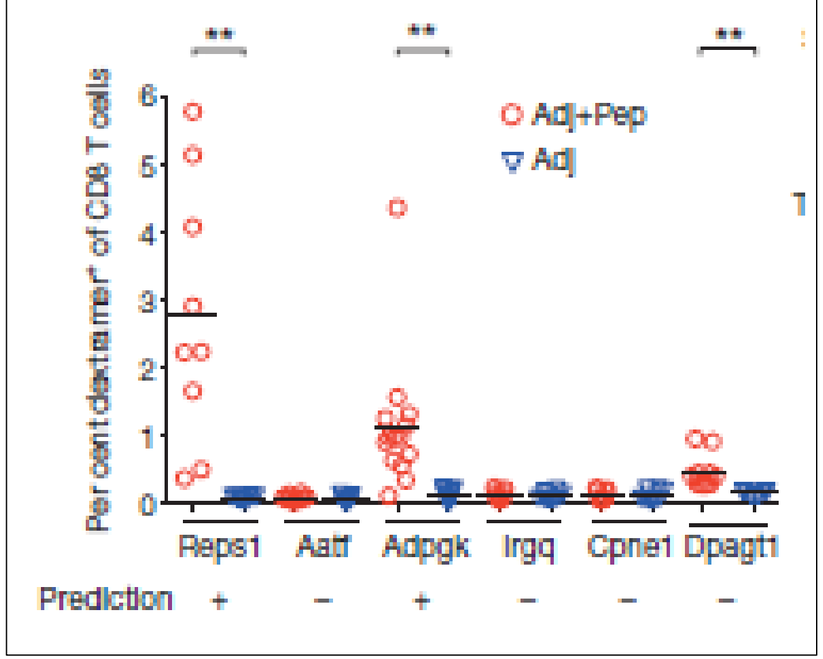
MC38 colon carcinoma

Yadav et al., 2014

VB10.NEO



Peptide + poly I:C + anti-CD40 mAb



-VB10.NEO induces a strong CD8 T cell response, combined with a CD4 T cell response **to all** peptides tested for MC38 colon carcinoma.

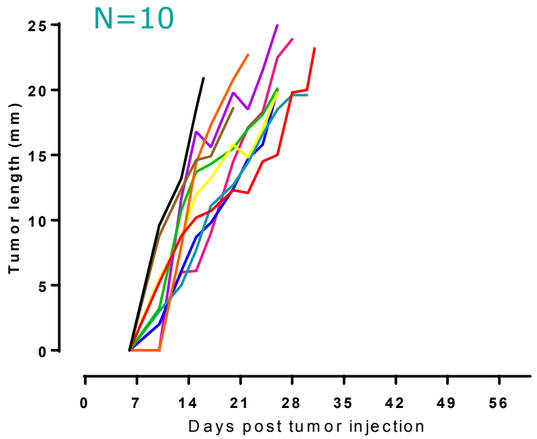
-1/3 of these neoepitopes have been shown to be **non-immunogenic delivered as peptide + adjuvant**

-Confirmation of VB10.NEO's ability to induce stronger CD8 responses to neoantigens

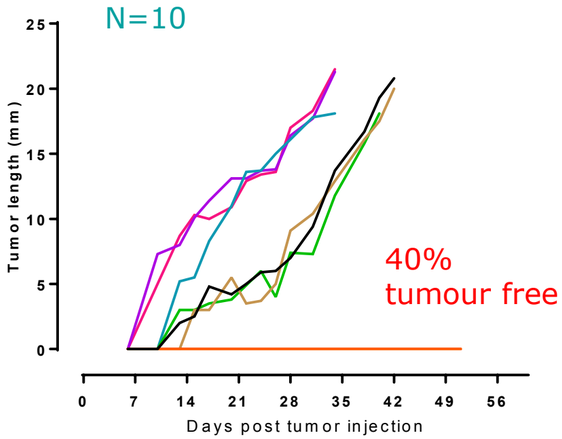
Vaccibody Induces Tumor Protection as Monotherapy

CT26 colon carcinoma model

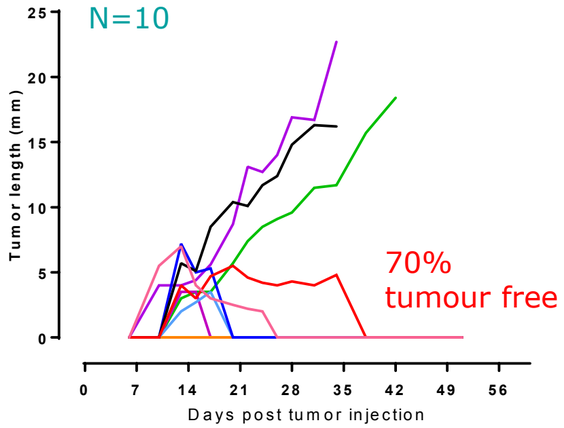
Control



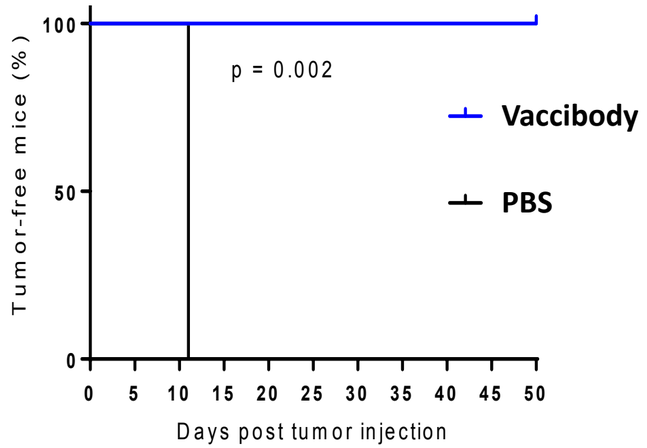
Vaccibody Monotherapy



Vaccibody Combination Therapy



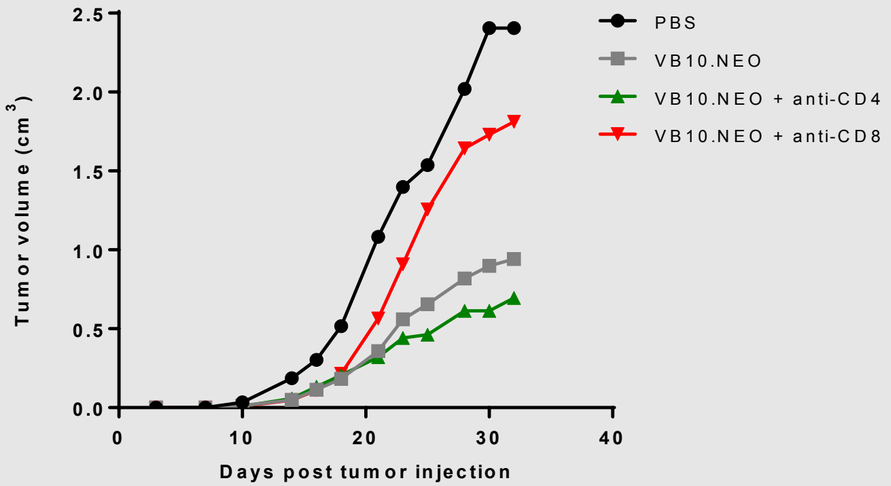
Re-challenged mice are protected



- 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

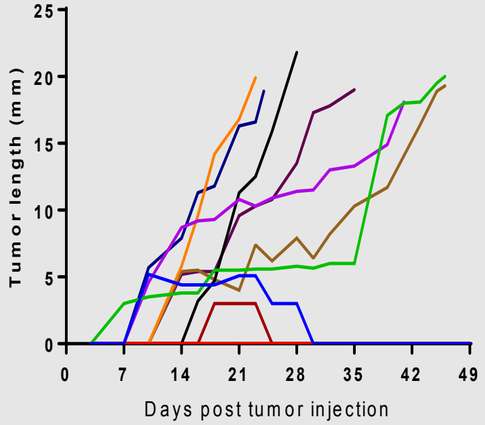
Neoepitope-specific CD8 T cells are crucial for tumour protection

Average, all groups

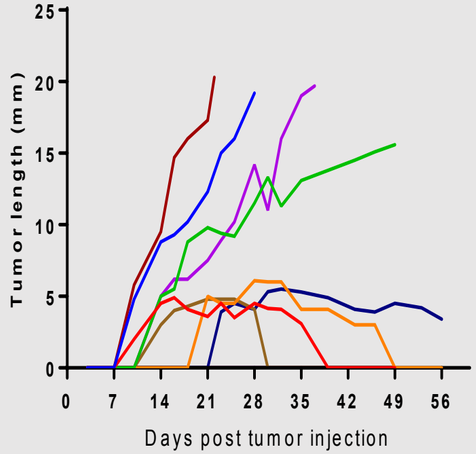


Individual growth curves

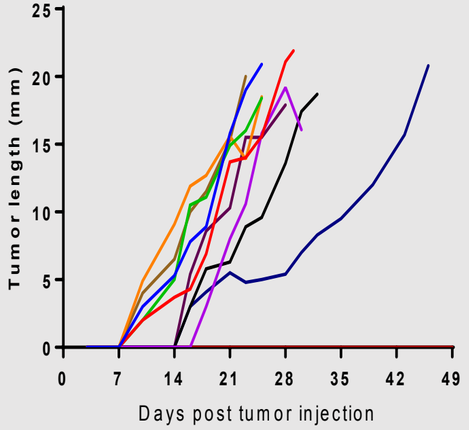
VB10.NEO



VB10.NEO + anti-CD4

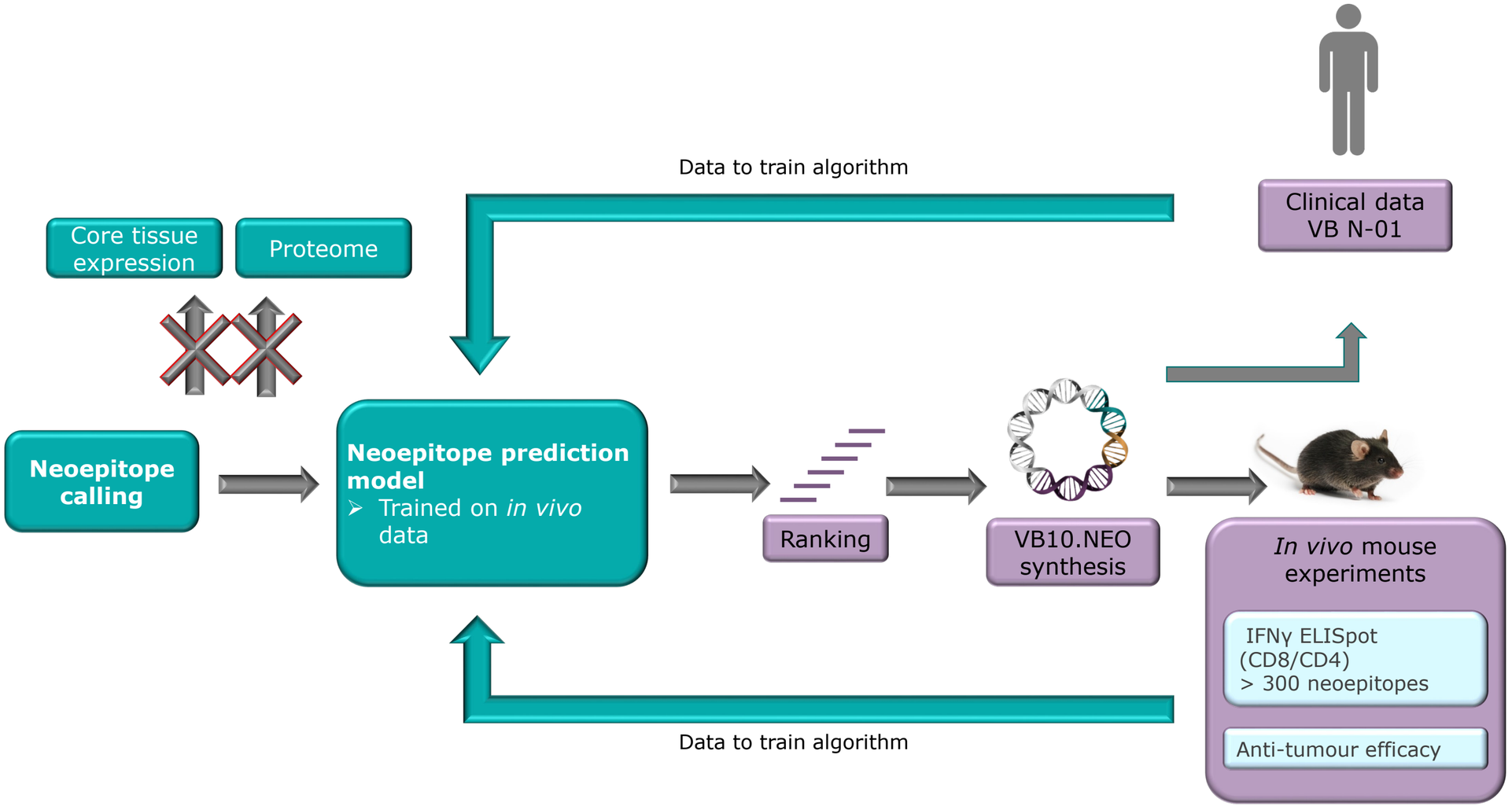


VB10.NEO+ anti-CD8



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

Developing VB10.NEO specific Neoepitope Selection



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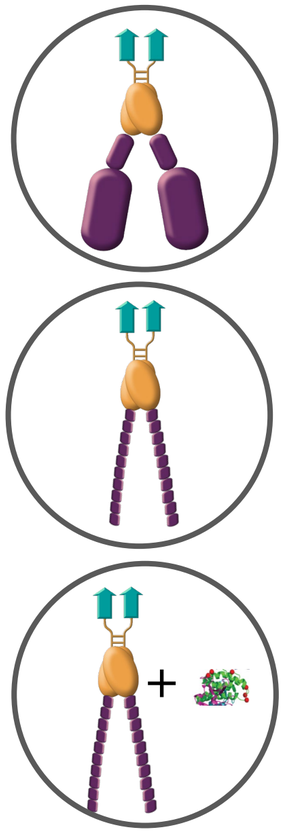
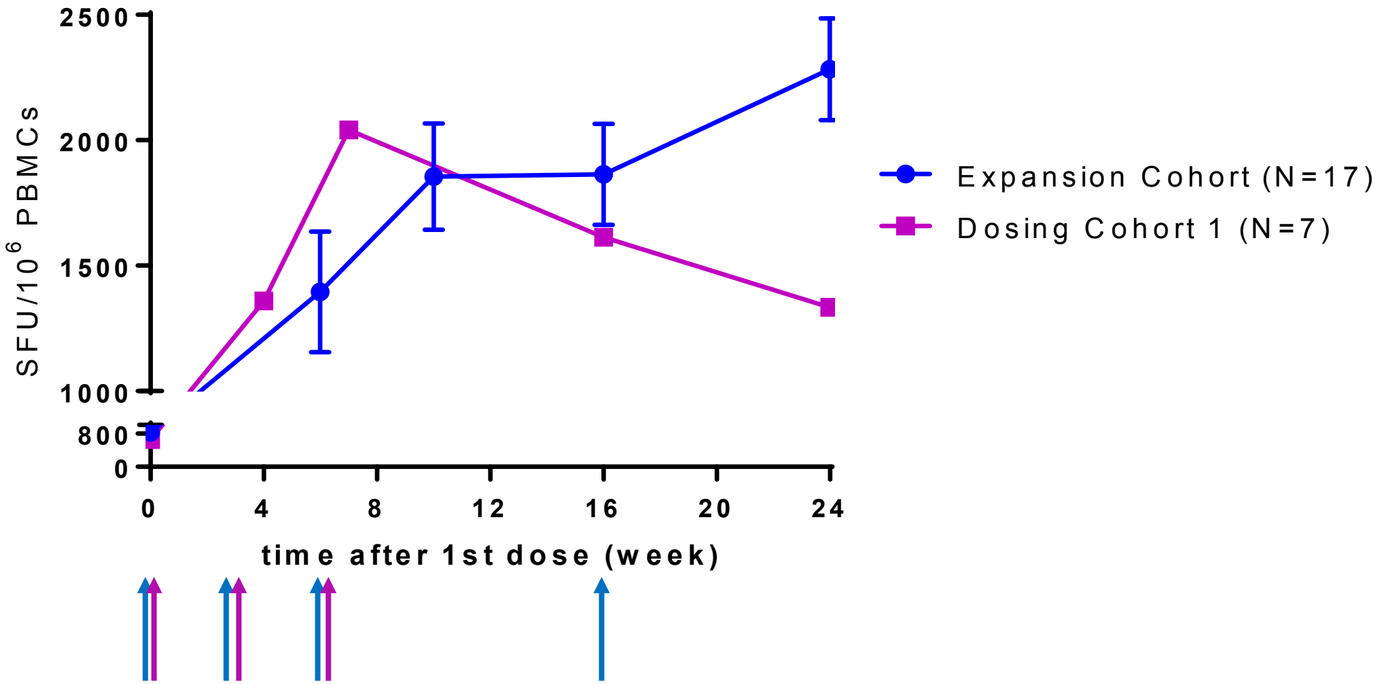
HEAD AND NECK	VB10.NEO + NKTR-214		NEKTAR®		

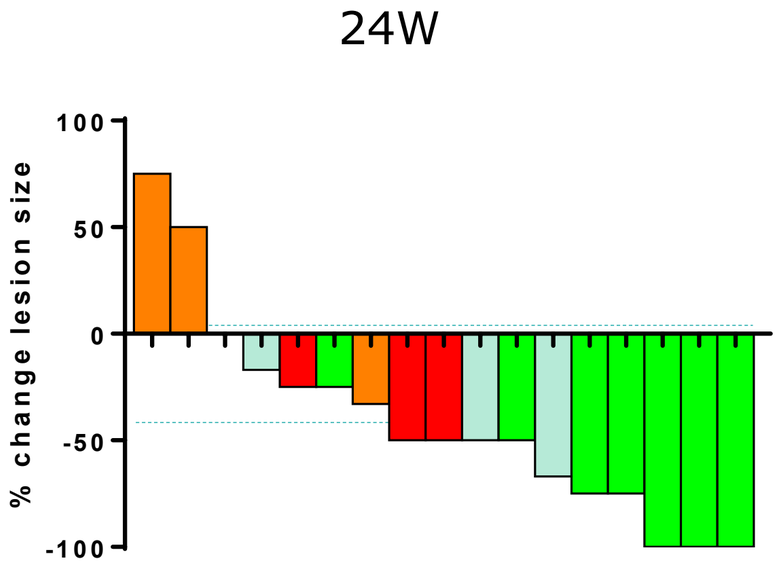


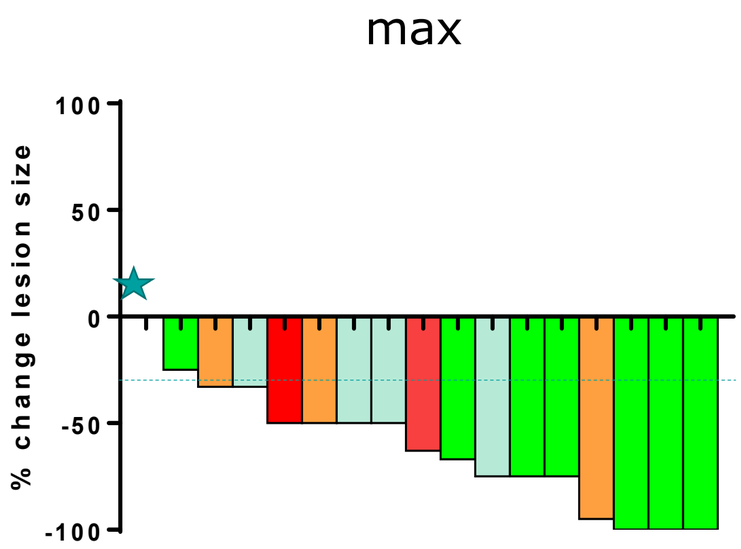
Strong, long-lasting immune responses elicited to HPV16, VB C-01



- The vaccination regiment from cohort 1 (week 0, 3 and 6) plus a booster vaccination at W16 was introduced in phase IIa
- 16 of 17 patients (94%) from phase IIa elicited increased HPV16-specific T cell responses after vaccination with VB10.16.
  - Rapid, strong and long-lasting

Lesion size reduction observed in majority of patients, VB C-01

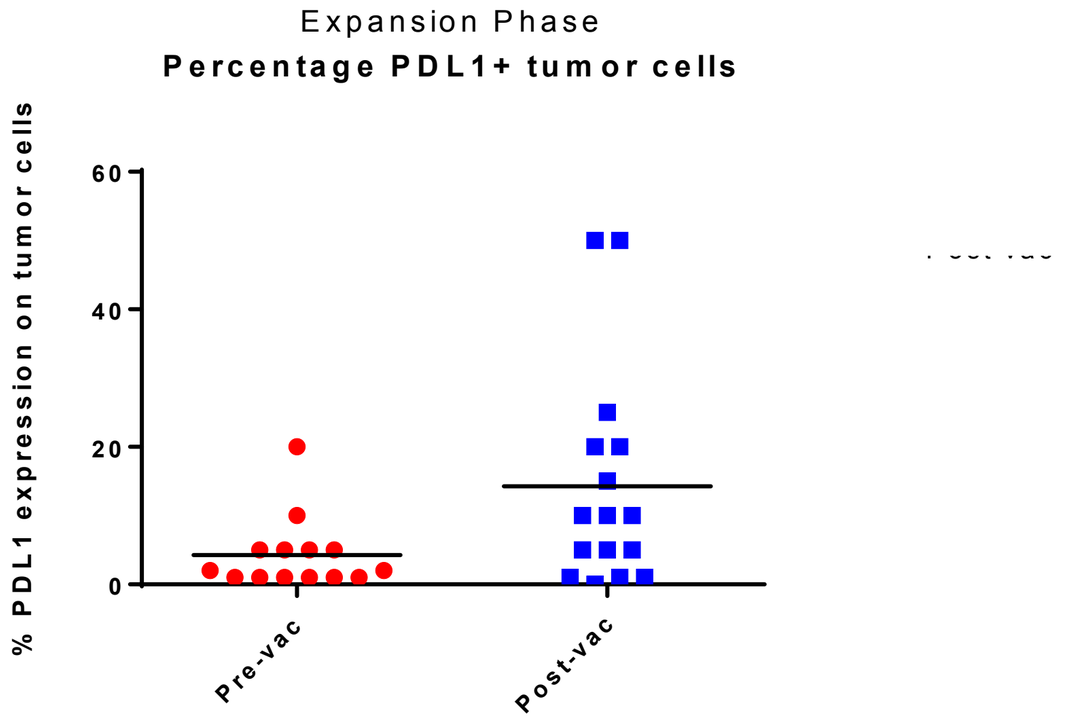




Green - no CIN
Blue - CIN1
Orange - CIN2
Red - CIN3

- 16 of 17 patients from phase IIa showed reduction in lesion size
- ★ The one patient without lesion size reduction chose early conization (week 16)
- At 24 weeks, 14 patients showed decreased lesion size 2 patients an increase
- 13 PR, 2 CR, 2 SD (one of these were conizated eary)

VB10.16 upregulates PD-L1 locally, VB C-01



- 6 of 8 patients that did not regress to CIN1 or no CIN uprgeulated PD-L1
- Strong rationale for combination with anti-PD-1/PD-L1 to improve effect of CPI, especially in PD-L1 negative patients

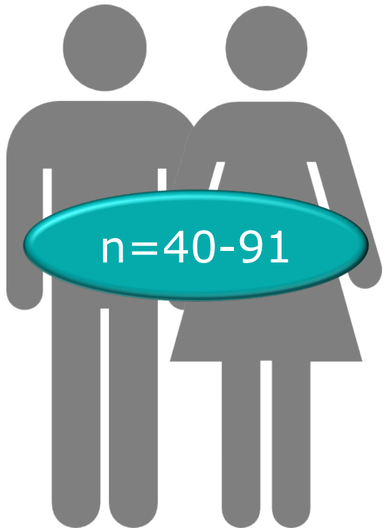
Clinical Trial VB N-01

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

Oct 10, 2018:
- 10 pt enrolled.
- Vaccination phase started

VB10.NEO

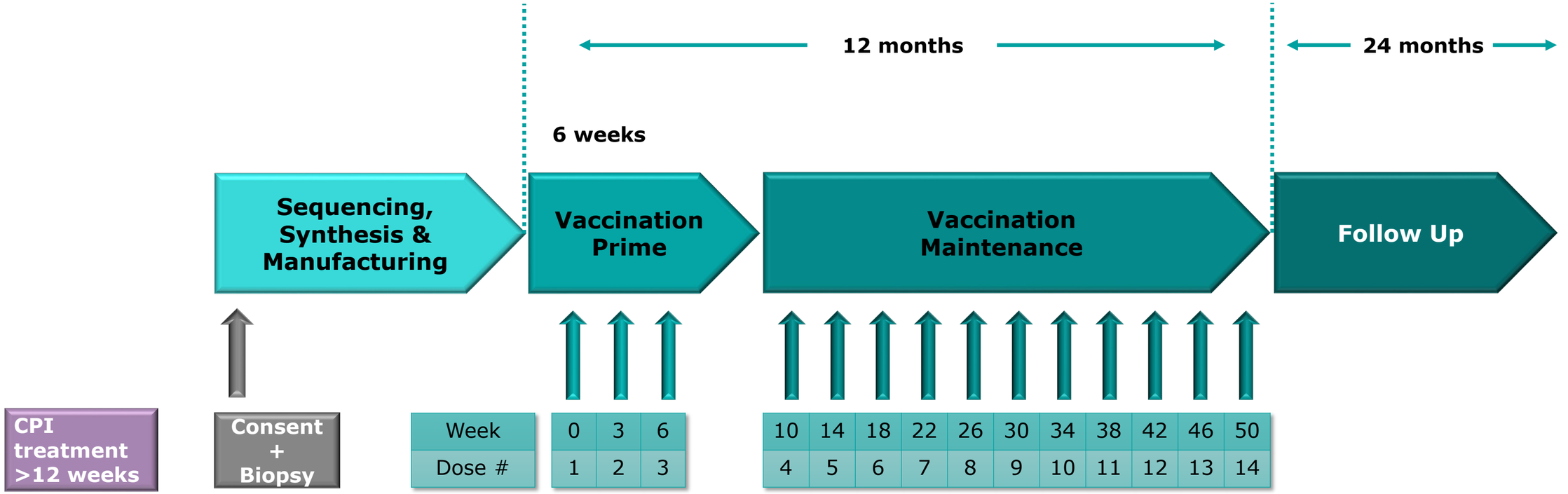
VB N-01



- 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



Vaccibody's Solution to Personalised Cancer Treatment

1. Tumour biopsy and sequencing

2. Neoepitope selection (TSNA)

NeoSELECT™

3. Vaccine manufacturing (n=1)

-DNA: Robust, rapid, cost-effective, stable, safe, up to 40 neoepitopes

-up to 40 neoepitopes

4. Vaccine administration and immunogenicity

-Needle-free

-Target, Attract, Mature, Deliver, Cross-present

-Rapid, strong, long-lasting

-CD8 dominated

Vaccibody provide a Rapid, Cost-effective and Efficacious solution

vaccibody

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