

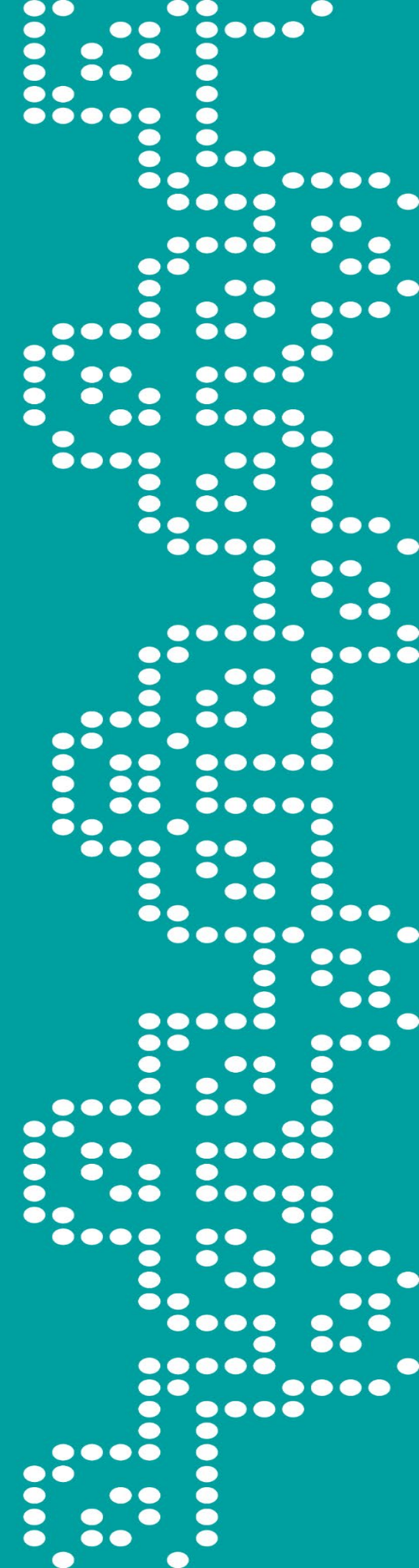
Individualised cancer neoantigen vaccines: the promise and the challenges

Immuno-Oncology Summit, Vienna

October 3, 2018

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Agenda

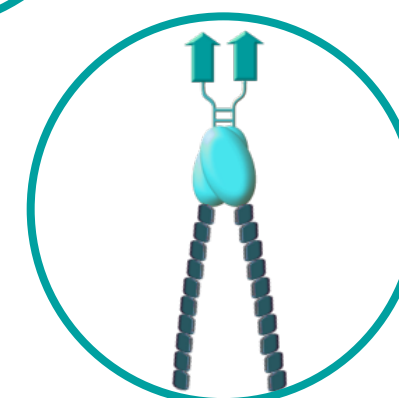
1.

Background Cancer Neoantigens



2.

Vaccibody's Cancer Vaccine Strategy



3.

Neoantigen Prediction Tools
NeoSELECT™

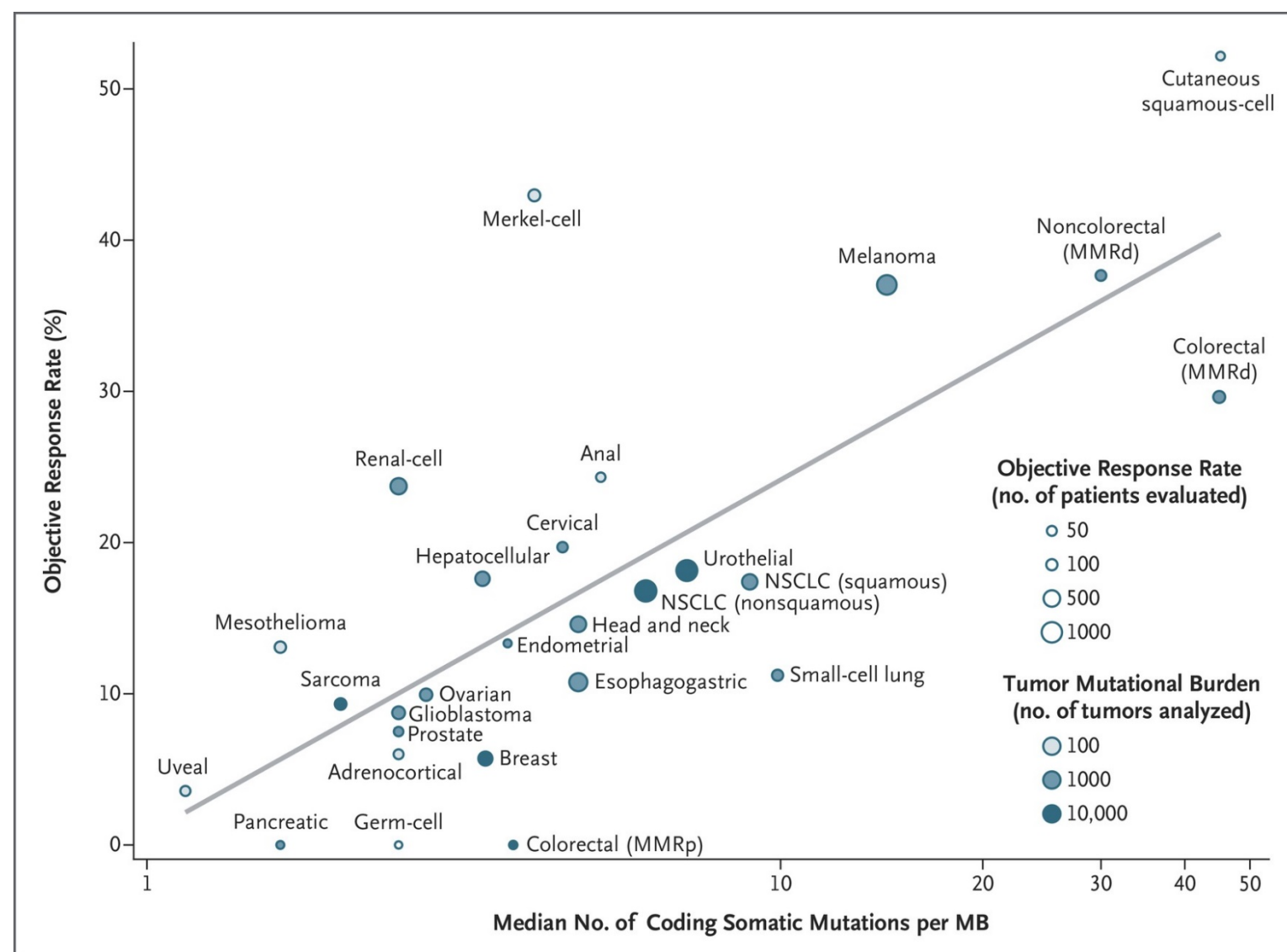


4.

Vaccibody's Clinical Trial Experience
and Future Plans



CheckPoint Inhibitors – relationship to neoantigens



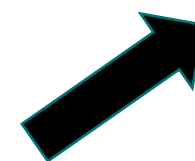
Strong relationship between mutational burden and response to CPI

Limits response to already existing neoantigen-specific T cell repertoire

Reveals an important role of immune responses to neoantigens in cancer immunotherapy

Cancer neoantigen vaccines are the **optimal tool** to activate a truly specific, strong and broad neoantigen specific T cell responses

The Workflow of Personalised Cancer Treatment



Time, cost, efficacy?

Proof of Concept published in Nature Letters July 2017

LETTER

doi:10.1038/nature22991

An immunogenic personal neoantigen vaccine for patients with melanoma

Patrick A. Ott^{1,2,3*}, Zhuting Hu^{1*}, Derin B. Keskin^{1,3,4}, Sachet A. Shukla^{1,4}, Jing Sun¹, David J. Bozym¹, Wandu Zhang¹, Adrienne Luoma⁵, Anita Giobbie-Hurder⁶, Lauren Peter^{7,8}, Christina Chen¹, Oriol Olive¹, Todd A. Carter⁴, Shuqiang Li⁴, David J. Lieb⁴, Thomas Eisenhaure⁴, Evisa Gjini⁹, Jonathan Stevens¹⁰, William J. Lane¹⁰, Indu Javeri¹¹, Kaliappanadar Nellaippan¹¹, Andres M. Salazar¹², Heather Daley¹, Michael Seaman⁷, Elizabeth I. Buchbinder^{1,2,3}, Charles H. Yoon^{3,13}, Maegan Harden⁴, Niall Lennon⁴, Stacey Gabriel⁴, Scott J. Rodig^{9,10}, Dan H. Barouch^{3,7,8}, Jon C. Aster^{3,10}, Gad Getz^{3,4,14}, Kai Wucherpfennig^{3,5}, Donna Neuberg⁶, Jerome Ritz^{1,2,3}, Eric S. Lander^{3,4}, Edward F. Fritsch^{1,4†}, Nir Hacohen^{3,4,15} & Catherine J. Wu^{1,2,3,4}

- 6 patients with melanoma (stage III/IV)
- 97 neoepitopes delivered as long-peptides with polyICLC (SC)
- **CD4 dominated responses**

LETTER

doi:10.1038/nature23003

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

Ugur Sahin^{1,2,3}, Evelyn Derhovanessian¹, Matthias Miller¹, Björn-Philipp Klocke¹, Petra Simon¹, Martin Löwer², Valesca Bukur^{1,2}, Arbel D. Tadmor², Ulrich Luxemburger¹, Barbara Schrörs², Tana Omokoko¹, Mathias Vormehr^{1,3}, Christian Albrecht², Anna Paruzynski¹, Andreas N. Kuhn¹, Janina Buck¹, Sandra Heesch¹, Katharina H. Schreeb¹, Felicitas Müller¹, Inga Ortseifer¹, Isabel Vogler¹, Eva Godehardt¹, Sebastian Attig^{2,3}, Richard Rae², Andrea Breikreuz¹, Claudia Tolliver¹, Martin Suchan², Goran Martić², Alexander Hohberger³, Patrick Sorn², Jan Diekmann¹, Janko Ciesla⁴, Olga Waksman⁴, Alexandra-Kemmer Brück¹, Meike Witt¹, Martina Zillgen¹, Andree Rothermel², Barbara Kasemann², David Langer¹, Stefanie Bolte¹, Mustafa Diken^{1,2}, Sebastian Kreiter^{1,2}, Romina Nemecek⁵, Christoffer Gebhardt^{6,7}, Stephan Grabbe³, Christoph Höller⁵, 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)
- **CD4 dominated responses**

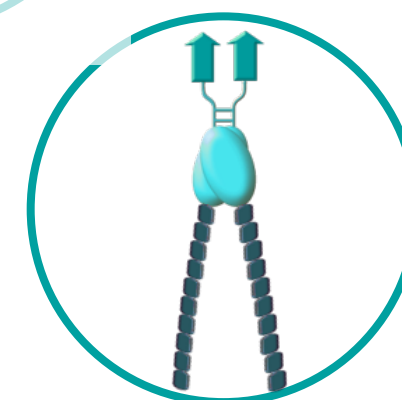
- Vaccinating with neoepitopes elicits a broad and strong tumour-specific immune response
- Both peptide and RNA neoantigen based vaccines elicits predominantly CD4 T cell responses

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3. Neoantigen Prediction Tools
NeoSELECT™

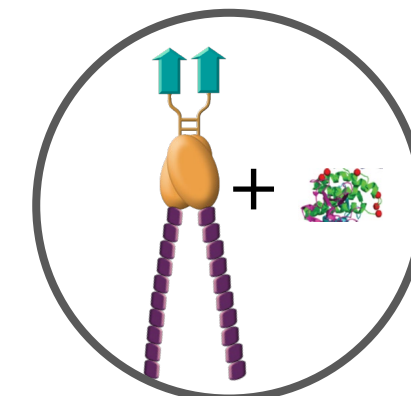
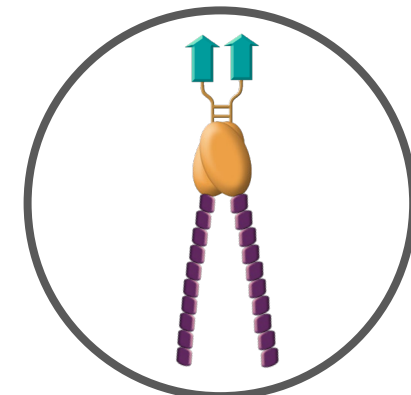
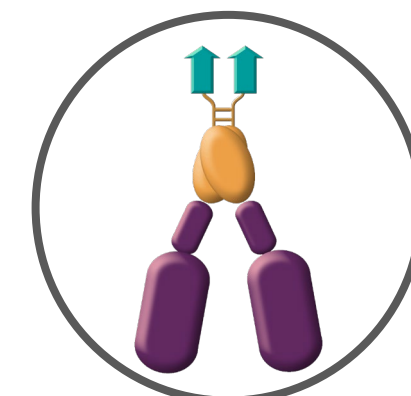


4. Vaccibody's Clinical Trial Experience
and Future Plans



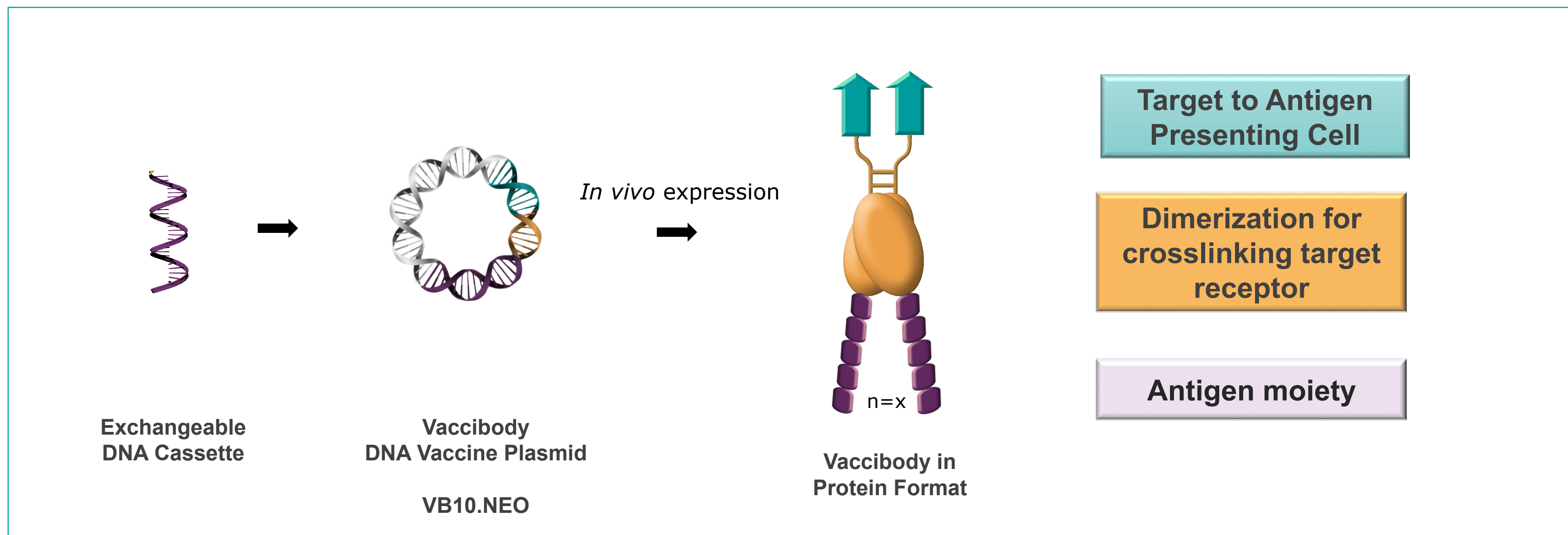
Vaccibody Product Pipeline

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

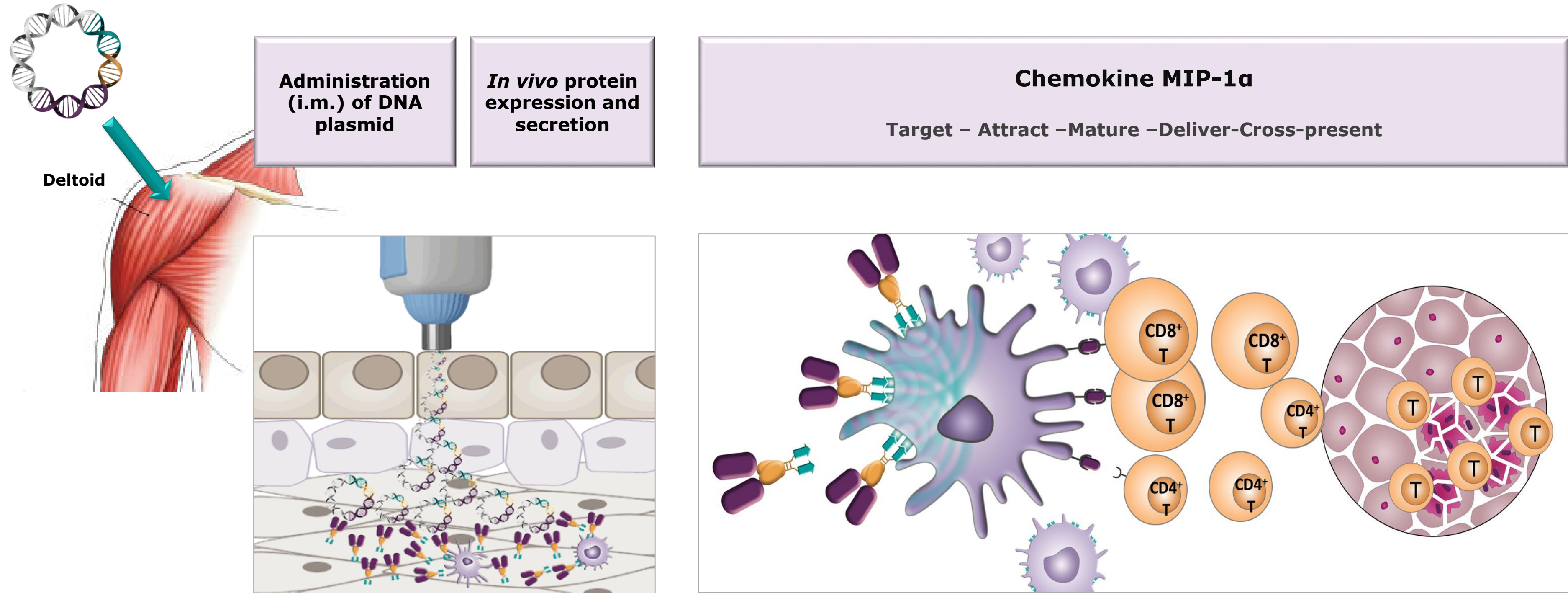


Vaccibody – Proprietary Vaccine Technology Platform

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



Mechanism of Action – Intrinsic Adjuvant



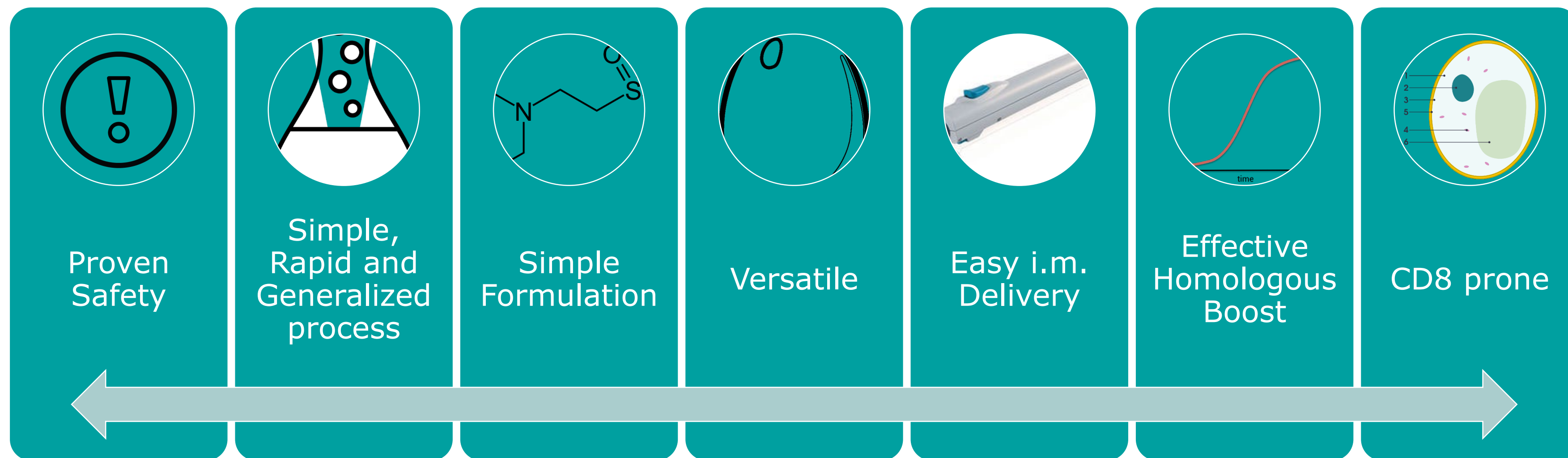
Patient Friendly, simple Vaccine Delivery

PharmaJet®



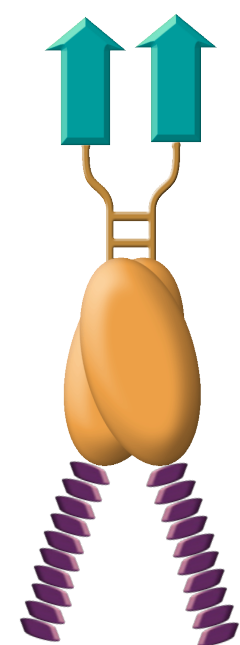
- ✓ **Needle free injection**
- ✓ **Small, handy, easy to use**
- ✓ **Minimal pain compared to electroporation**
- ✓ **Cost effective**
- ✓ **Applicable for multiple immunizations**
- ✓ **High patient compliance**

Naked DNA plasmid as IMP

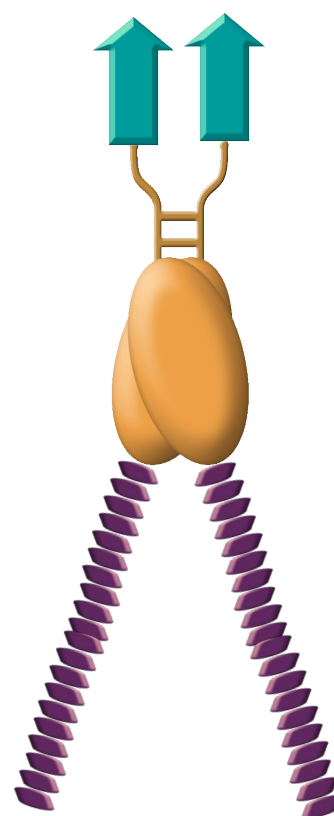


DNA plasmid is an ideal platform for bringing individualized neoantigen vaccines to the market as a viable product

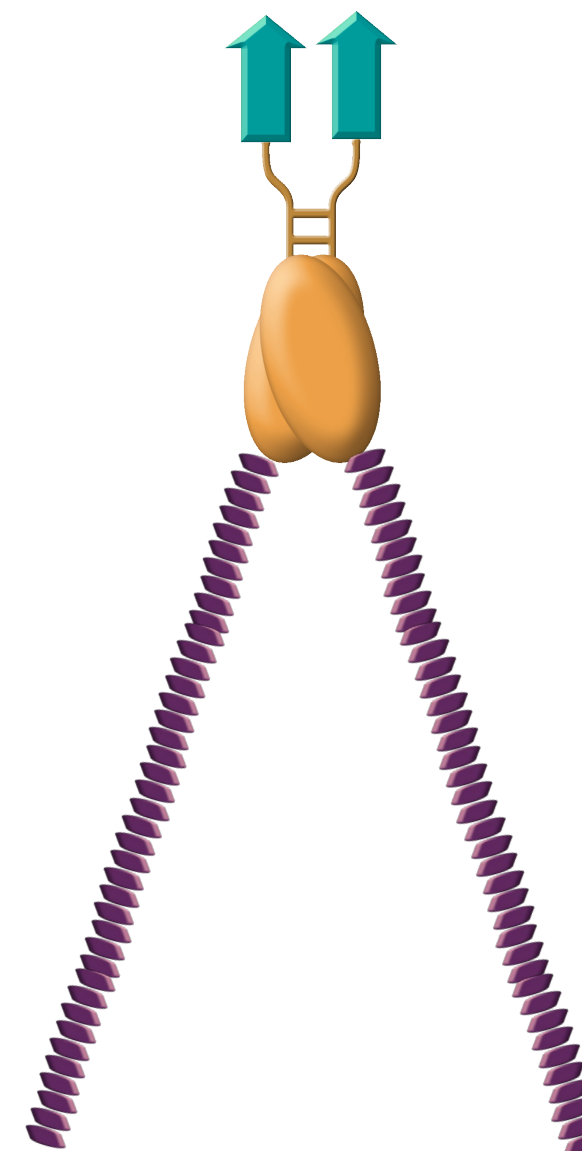
VB10.NEO – A Robust Vaccine Format



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

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

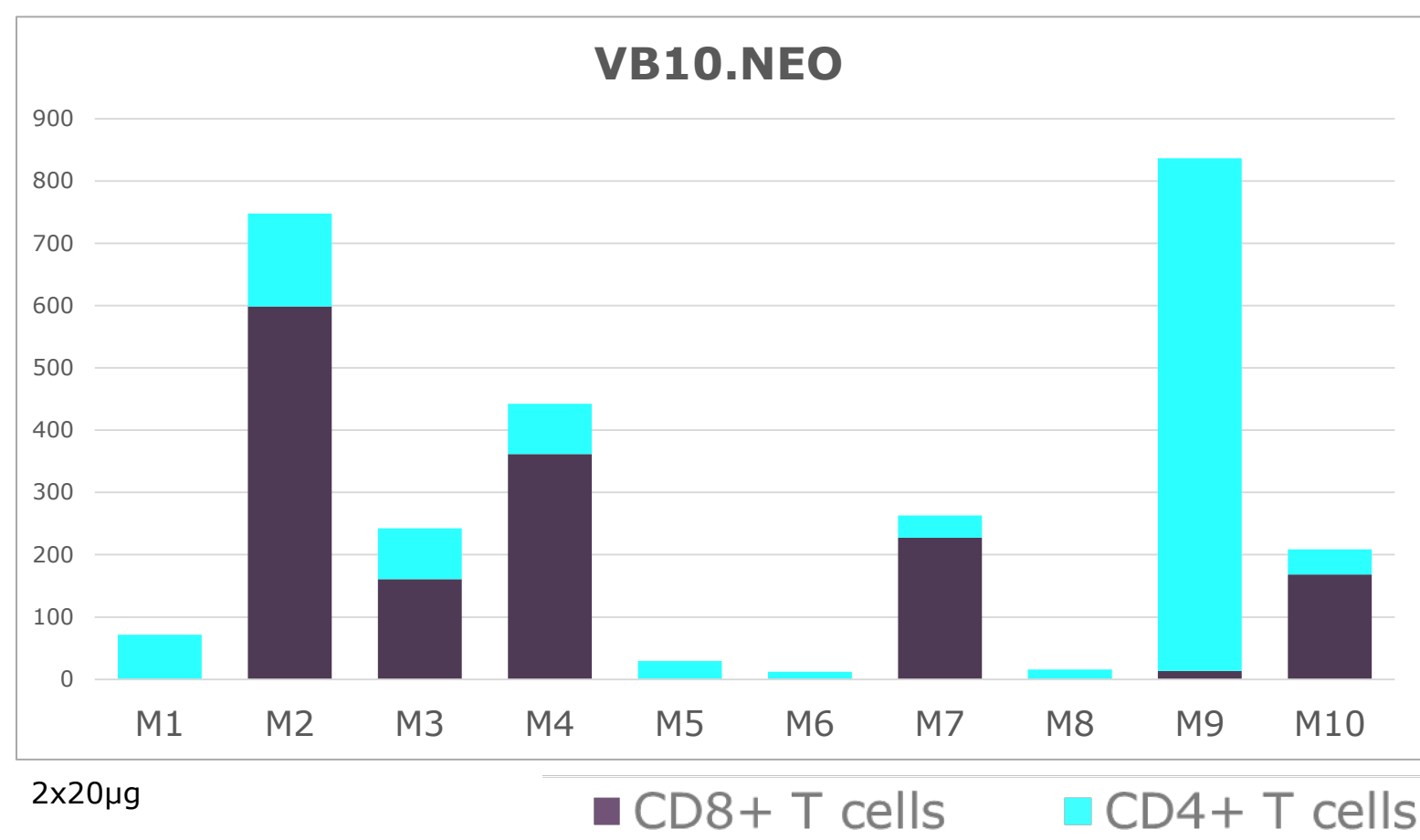
		Pep 1	Pep 2	Pep 3	Pep 4	Pep 5	Pep 6	Pep 7	Pep 8	Pep 9	Pep10
Peptide*	CD4	Light Blue	White	Light Blue	White	Light Blue	Light Blue	White	Light Blue	Light Blue	White
	CD8	White	Dark Blue	White	White	White	White	White	White	White	White
RNA*	CD4	Light Blue	White	Light Blue	Light Blue	White	White	Light Blue	Light Blue	Light Blue	White
	CD8	White	Dark Blue	White	White	White	White	White	White	White	Dark Blue
VB10.NEO	CD4	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue
	CD8	White	Dark Blue	Dark Blue	Dark Blue	White	White	Dark Blue	White	Dark Blue	Dark Blue

* Tested IFN- γ CD4 and CD8 T cell response against 10 identical neoepitopes from B16 melanoma

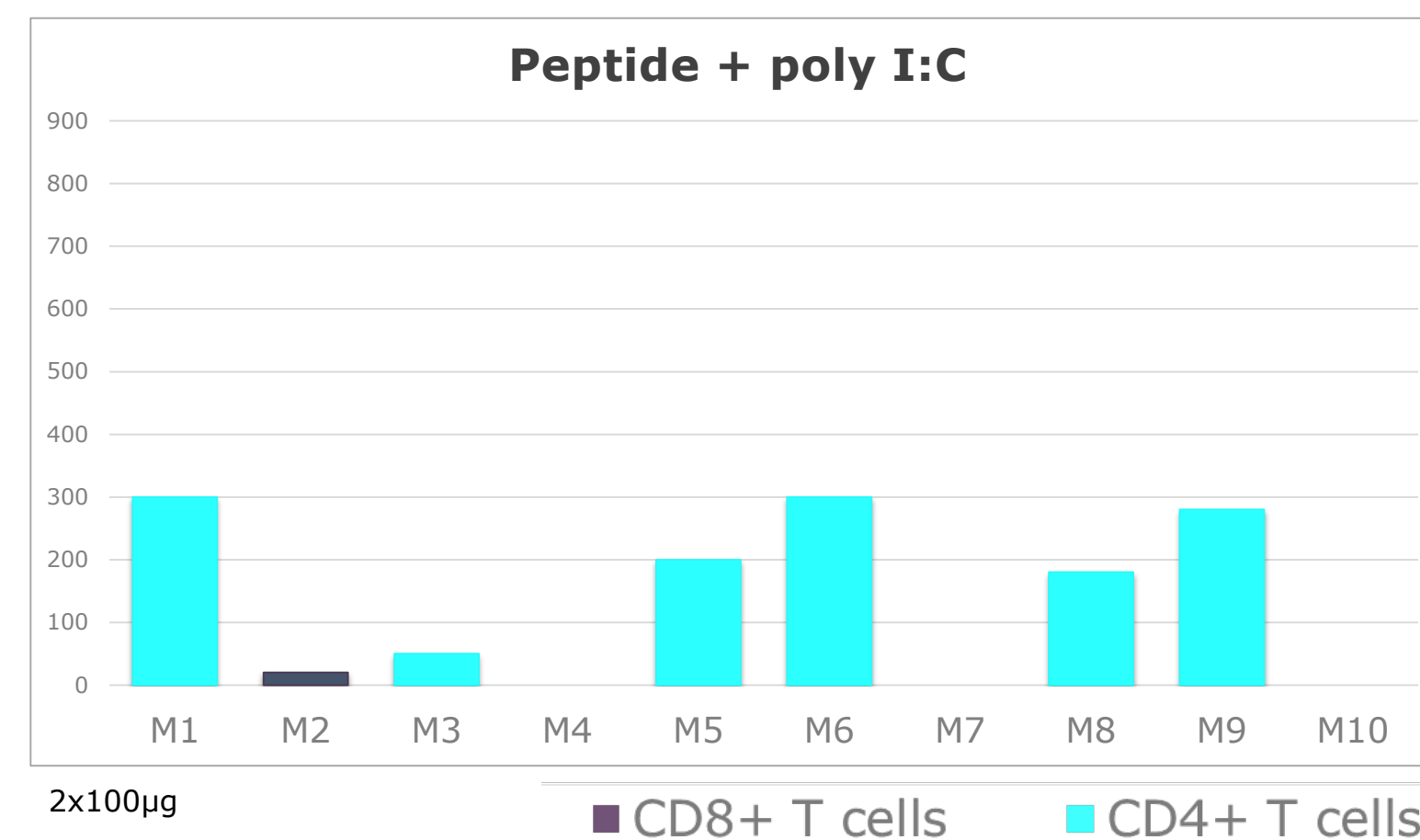
Peptide and RNA vaccines induces primarily CD4 T cell responses, while VB10.NEO induces strong, dominating CD8 responses to the identical neoepitope sequences

VB10.NEO leads to a unique CD8 dominated neoepitope response

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**

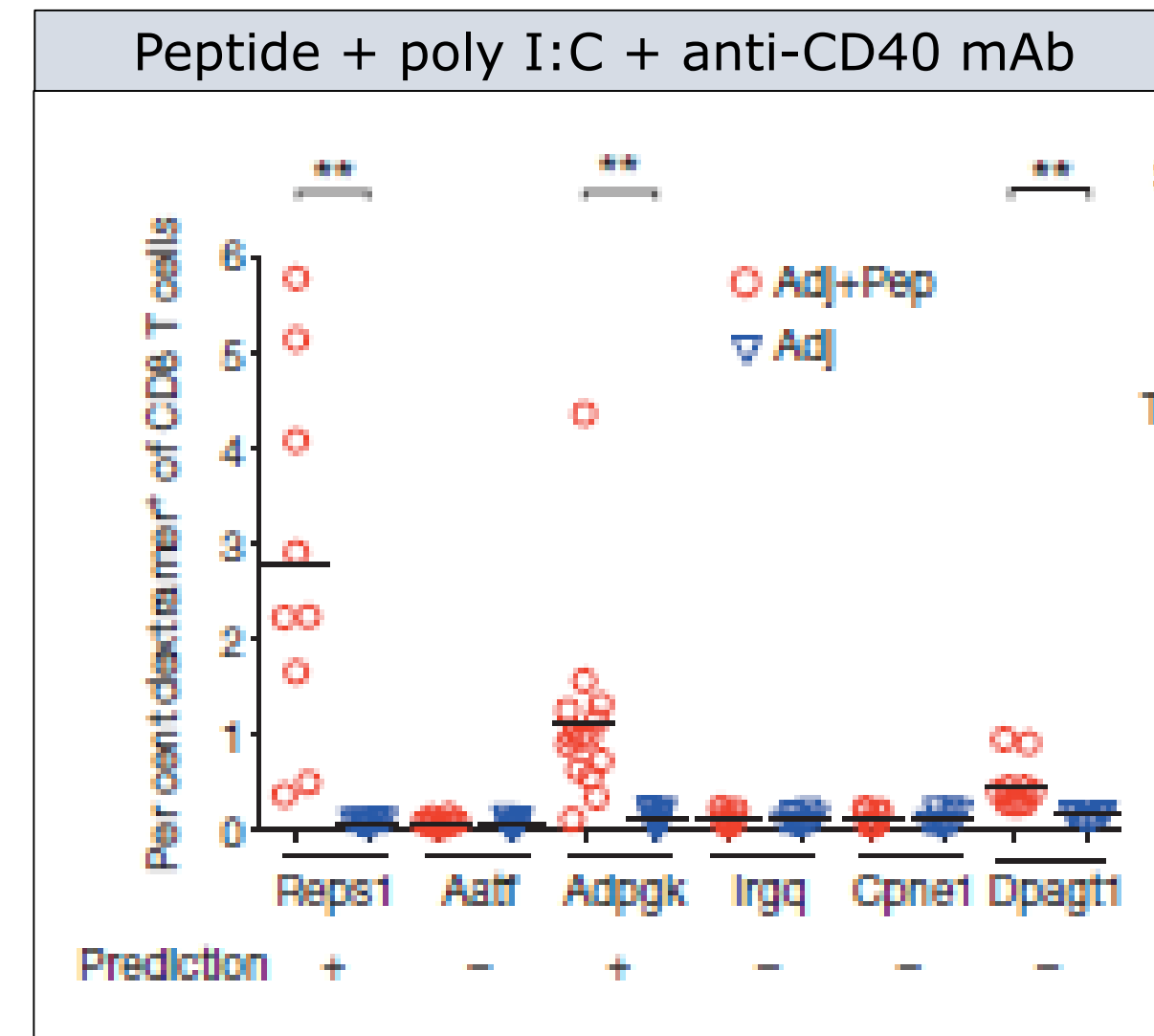
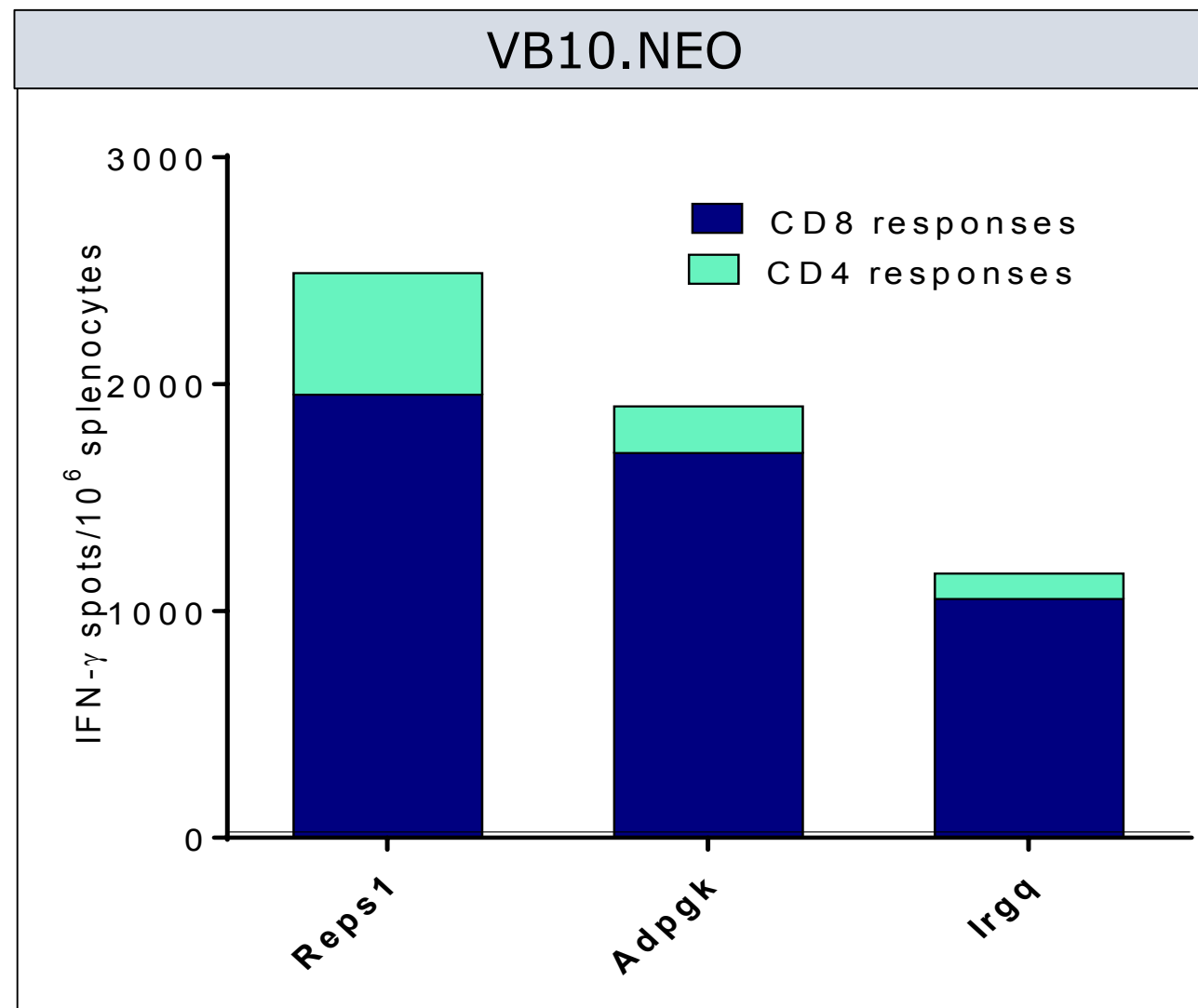


VB10.NEO induces strong, dominantly CD8+ T cell response to identical neoepitopes that induces **no or weak** immune response if delivered as peptide vaccine

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

MC38 colon carcinoma

Yadav et al., 2014



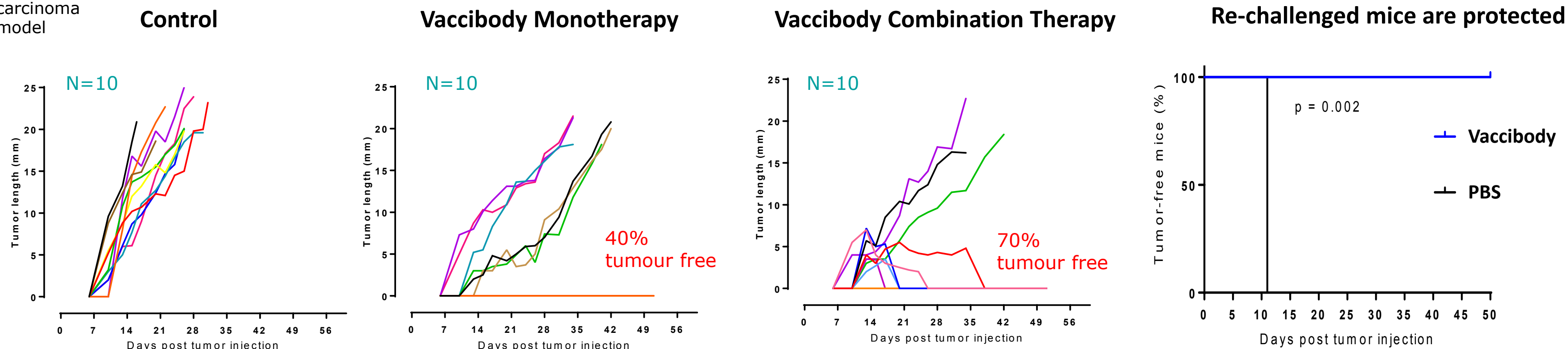
-VB10.NEO induces a strong CD8 T cell response, combined with a CD4 T cell response to all peptides tested for MC38 colon carcinoma.

-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

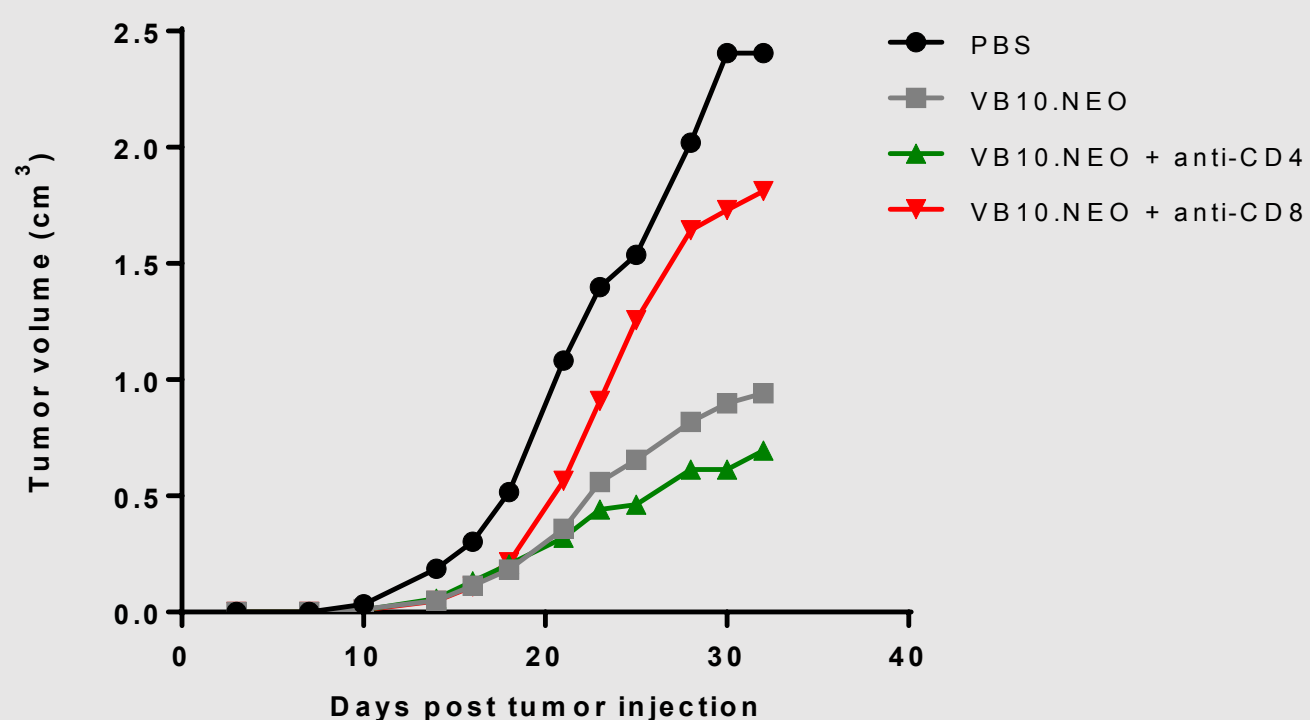
CT26 colon carcinoma model



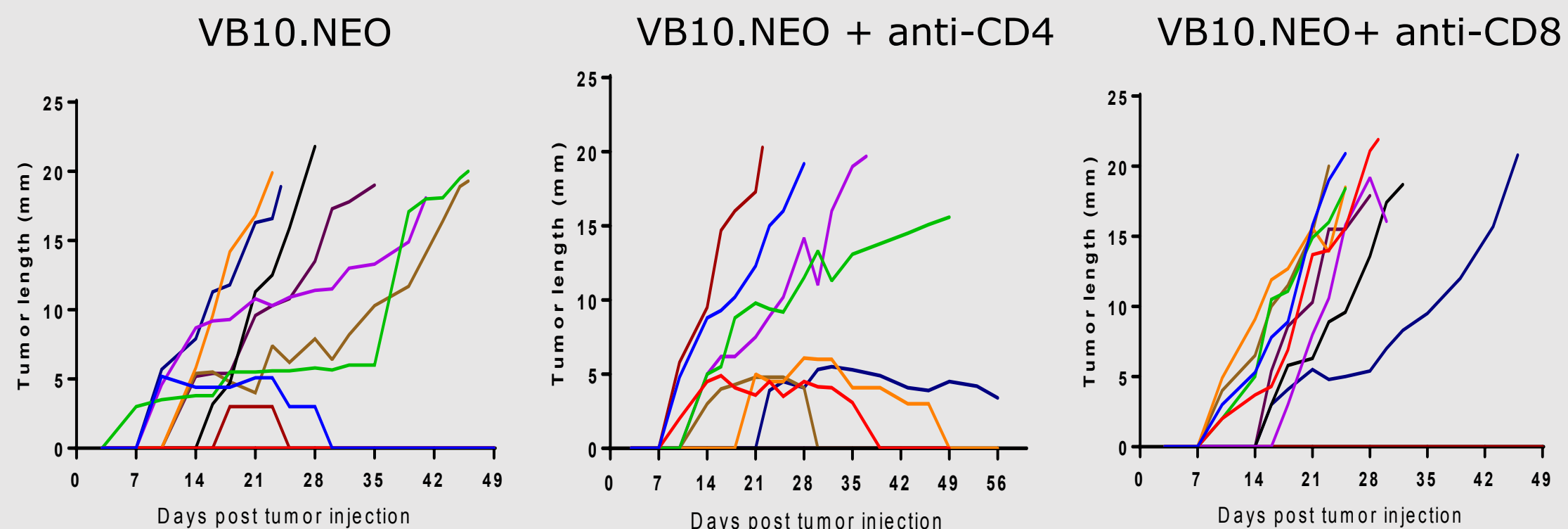
- Vaccibody vaccination induces strong CD8+ T cell responses and **tumor protection as Monotherapy**
- Combination with anti-PD-1 immunotherapy induced enhanced anti-tumour responses in mice involving **complete tumour regression** of large, established tumours
- **Long-term memory responses** ensure 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



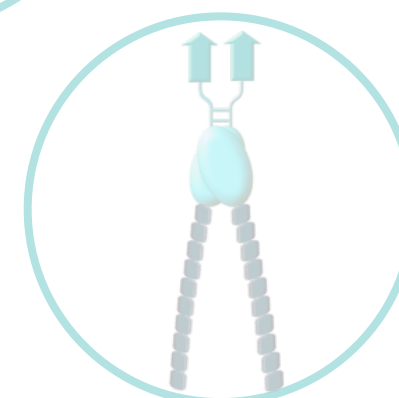
Depletion of CD8 T cells prohibit tumour protection in VB10.NEO vaccinated mice, indicating a crucial role of neoepitope-specific CD8 T cells for anti-tumour efficacy

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2. Vaccibody's Cancer Vaccine Strategy
Why the perfect fit for individualised Vaccines?



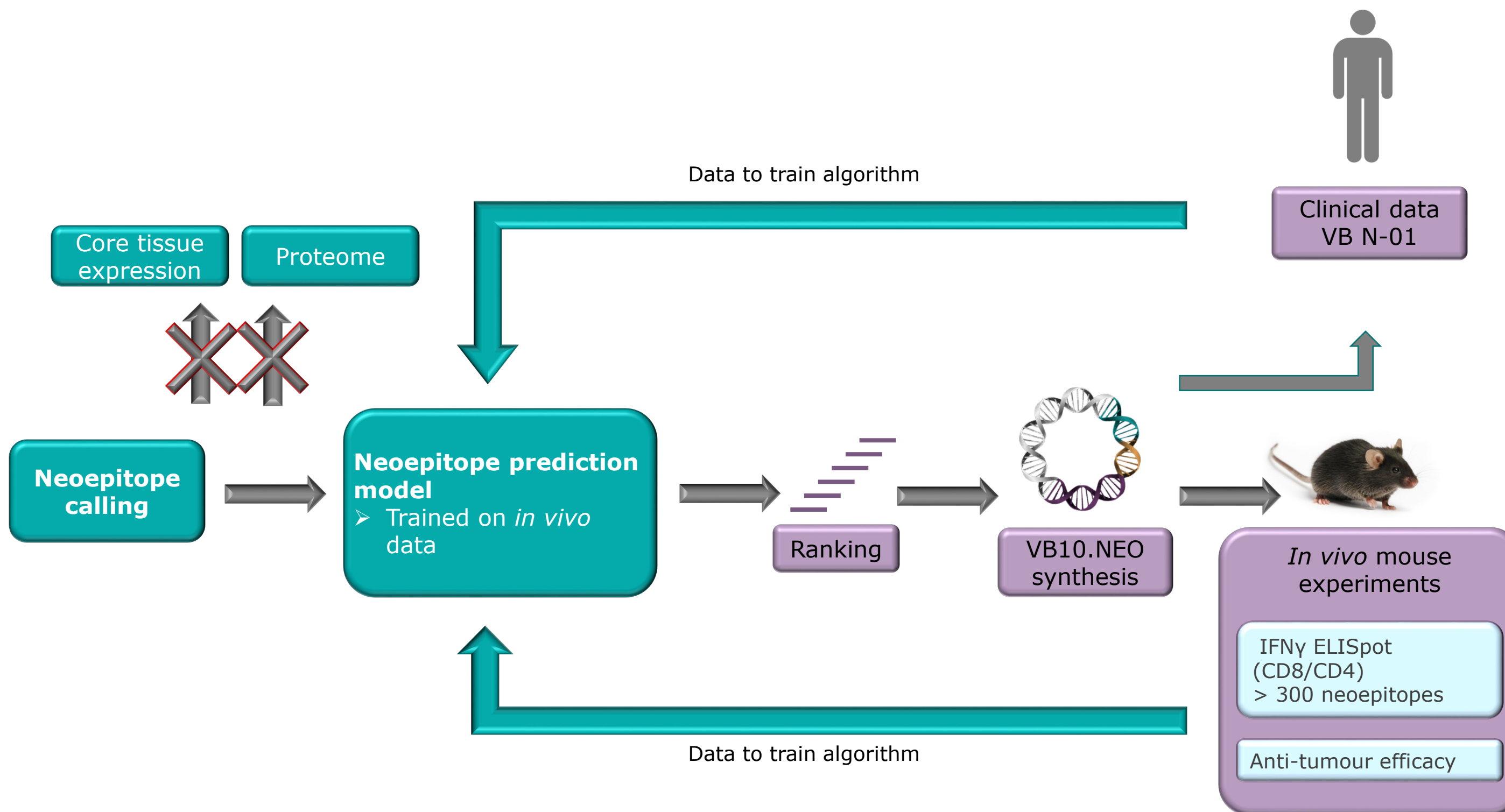
3. Neoantigen Prediction Tools
NeoSELECT™



4. Vaccibody's Clinical Trial Experience
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Developing VB10.NEO specific Neoepitope Selection

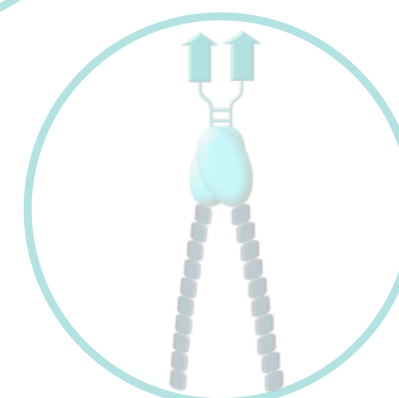


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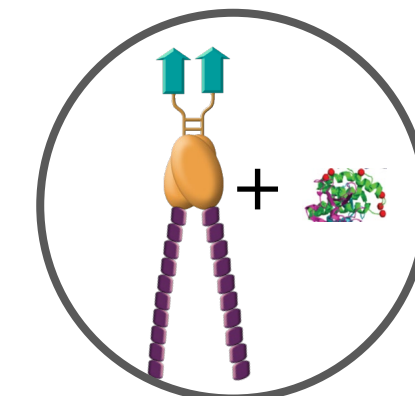
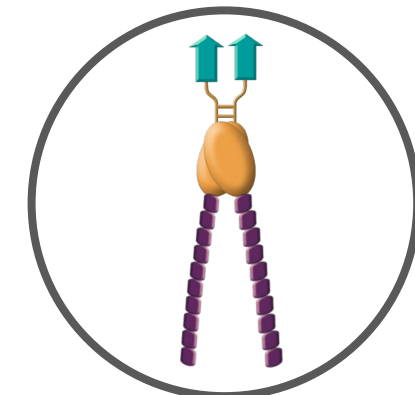
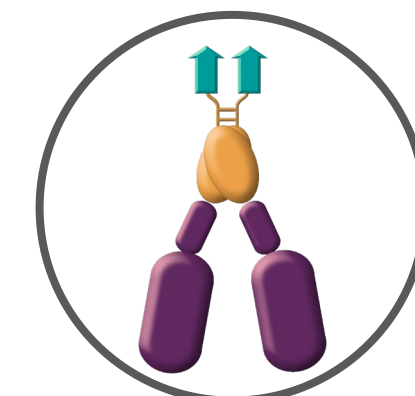


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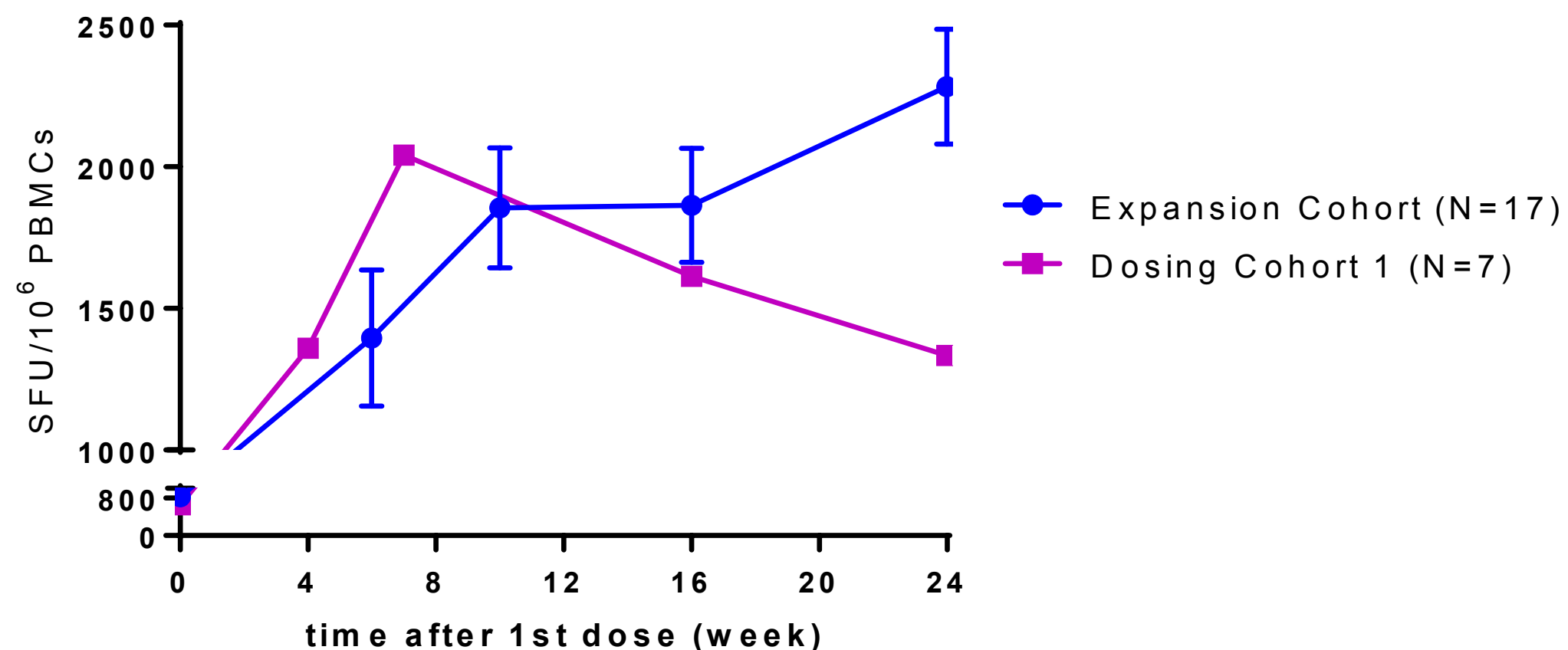


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MELANOMA LUNG (NSCLC) BLADDER RENAL HEAD AND NECK	VB N-01 (VB10.NEO)				
HEAD AND NECK	VB10.NEO + NKTR-214		NEKTAR®		



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

Clinical Trial VB N-01

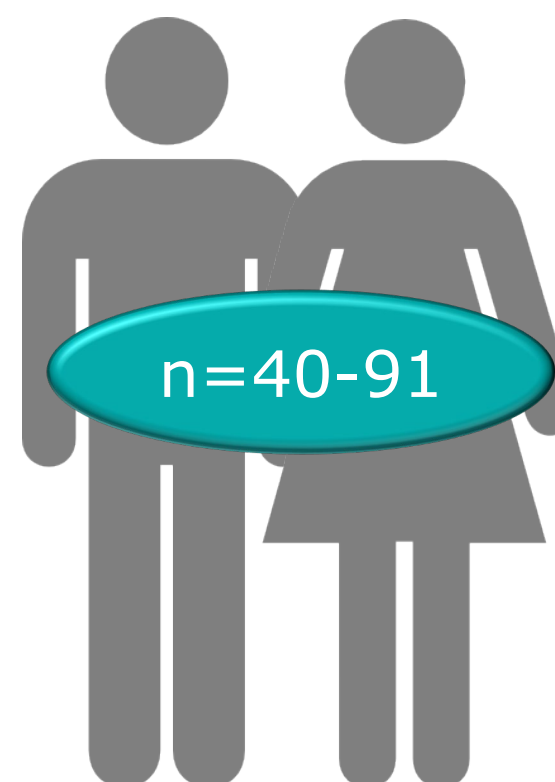
VB N-01: An open labelled first human dose phase 1/2a study to evaluate safety, feasibility and efficacy of multiple dosing with individualised VB10.NEO immunotherapy in patients with locally advanced or metastatic melanoma, NSCLC, clear renal cell carcinoma, urothelial cancer or squamous cell carcinoma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

FPI April 2018



VB10.NEO

VB N-01
→



n=40-91

Melanoma

NSCLC

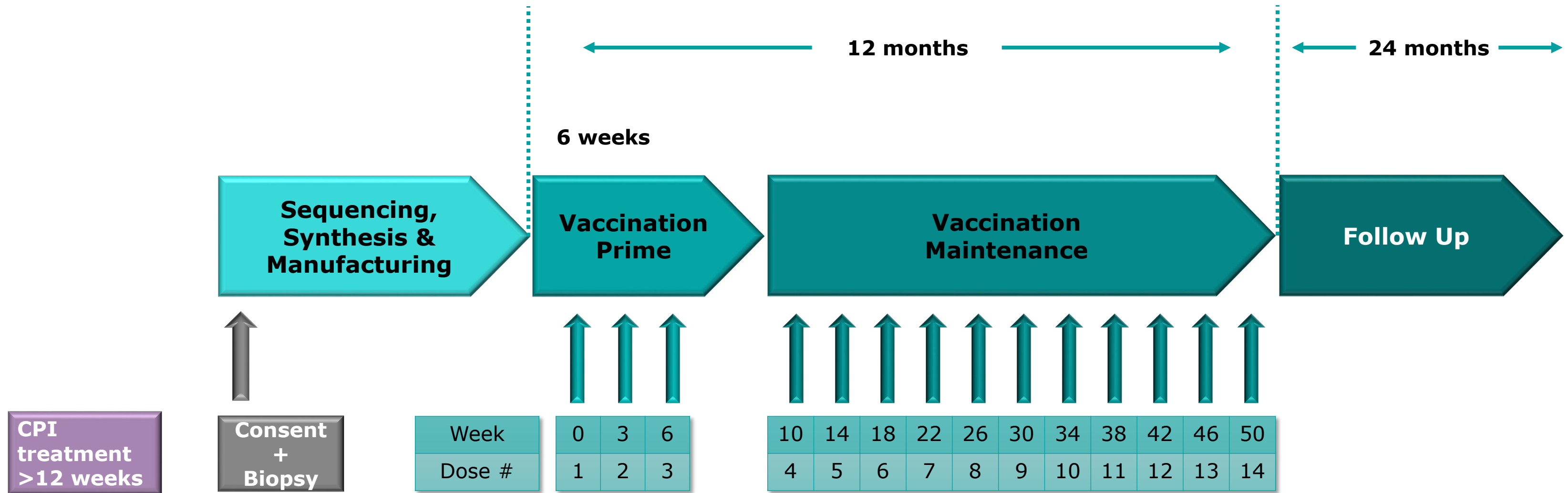
Clear Renal Cell Carcinoma

Urothelial Cancer

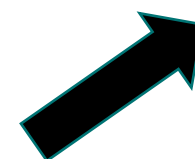
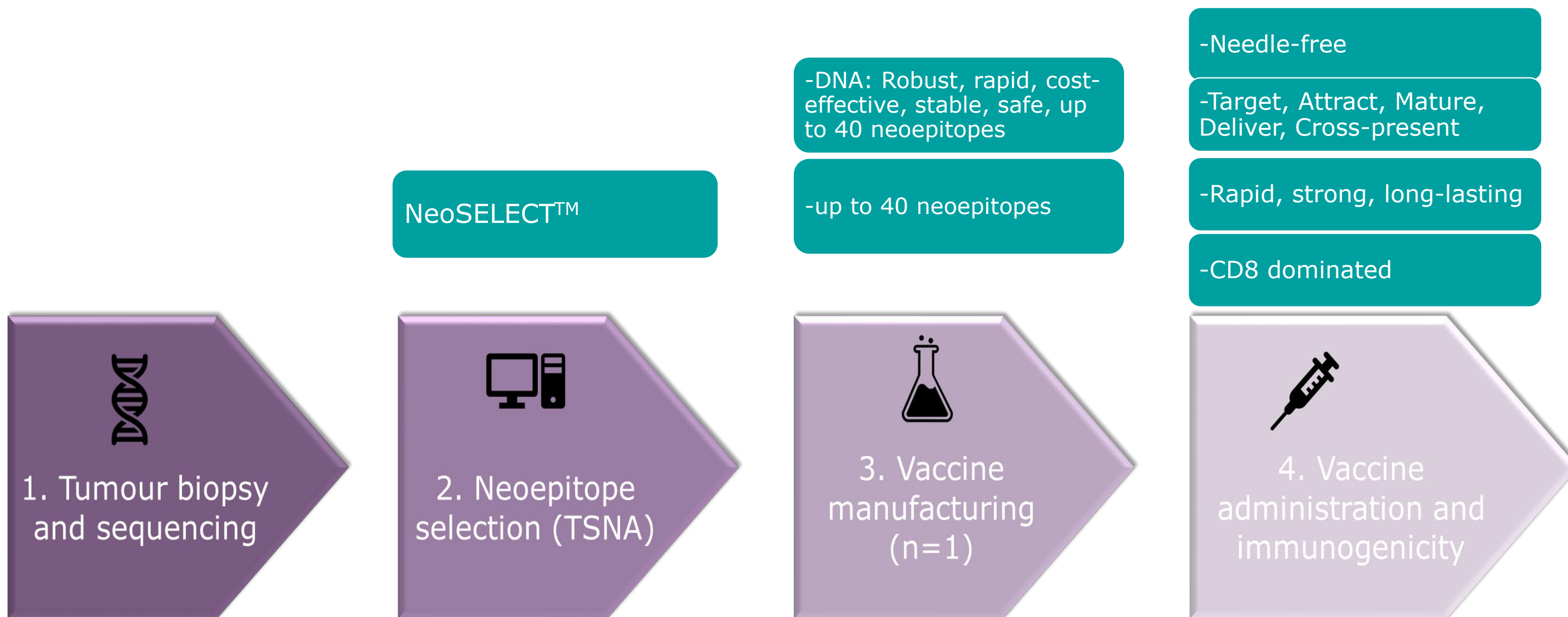
Squamous Cell Carcinoma
of the Head and Neck

- Approved CPI as SOC
- Moderate to high mutational load

Study Design and Treatment Schedule VB N-01



Vaccibody's Solution to Personalised Cancer Treatment



Vaccibody provide a Rapid, Cost-effective and Efficacious solution

vaccibody

www.vaccibody.com