nykode therapeutics

Optimizing RNA/DNA-Based Vaccine Design by Identifying Key Characteristics to Ensure Success of the Therapy

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Forward-looking statement

This announcement and any materials distributed in connection with this presentation may contain certain forward-looking statements. By their nature, forward-looking statements involve risk and uncertainty because they reflect the company's current expectations and assumptions as to future events and circumstances that may not prove accurate.

A number of material factors could cause actual results and developments to differ materially from those expressed or implied by these forward-looking statements.

Global leader in antigen presenting cell (APC)-targeted immunotherapy technology

nykode therapeutics

NYKODE THERAPEUTICS

Differentiated immunotherapies targeting antigens to Antigen-Presenting Cell (APC) to direct tailor-made immune responses with focus on oncology and autoimmune diseases

APC-targeted Oncology Platform validated and de-risked through strong durability and survival data

- Focused strategy to rapidly progress lead asset VB10.16 towards patients and markets in cervical cancer and head & neck cancer. Potential fast to market opportunity in advanced cervical cancer.
- Significant further commercial upside in early stage/adjuvant settings supported by Nykode data generated to date
- mRNA vaccine having demonstrated preclinical differentiation vs. existing 'antigen-alone' approaches

Autoimmune disease constitute a potential new therapeutic area in high-unmet need indications (e.g., MS, T1D)

Strategic partnerships with top tier US biopharma companies[1]

Genentech
A Member of the Roche Group
Up to ~$715M

REGENERON
Up to ~$925M

Well-capitalized with a cash position of $162.6m at December 31, 2023
Completed private placement of $45m in October, 2023 with primarily new international specialist investors

1. Note: Genentech has an exclusive license to VB10.NEO. Collaboration and license to 5 programs with Regeneron.

Rich and diversified pipeline

	Asset	Indication	Rights	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Catalyst
Oncology								
Off-the-shelf	VB10.16	HPV16+ cervical cancer	nykode [1]				C-02, C-04	Finalize enrolment Pt 1 (Q4 2024)
		HPV16+ head and neck cancer	nykode [2]			C-03		Dose level recommendation (H2 2024)
		HPV16+ locally advanced cervical cancer	nykode [3]				C-05	Protocol in development
	Regeneron programs	Undisclosed	nykode REGENERON [4]					Selection of lead candidate
	NYK011	Colorectal: pre-cancerous polyps to cancer	nykode					Update (H2 2024)
Individua-lized	VB10.NEO	Melanoma, lung, bladder, renal, head and neck cancer; locally advanced and metastatic tumors	nykode Genentech [5]				N-01	
		Incurable locally advanced and metastatic tumors	nykode Genentech [5]			N-02		
Infectious Disease								
Regeneron programs		Undisclosed	nykode REGENERON					
Autoimmune								
Internal		Undisclosed	nykode					Update (H1 2024)

1. Wholly-owned by Nykode. Potentially registrational. Roche supplies atezolizumab; 2. Wholly-owned by Nykode. Merck (MSD) supplies pembrolizumab; 3. Wholly-owned by Nykode. 4. Collaboration with Regeneron; 5. Genentech has an exclusive license to VB10.NEO.

VB10.NEO Individualized cancer immunotherapy

Modular vaccine technology allows APC-targeting to direct immune responses

DNA plasmid encoding Nykode's Vaccibody™ vaccine

Targeting unit to attract and bind APCs

Ability to tailor the targeting unit enables induction of different immune response profiles to specific diseases[1]

Dimerization unit for crosslinking targeted receptors on the surface of the APC

To facilitate strong bivalent binding

Antigenic unit presents globular antigens or set of T cell epitopes

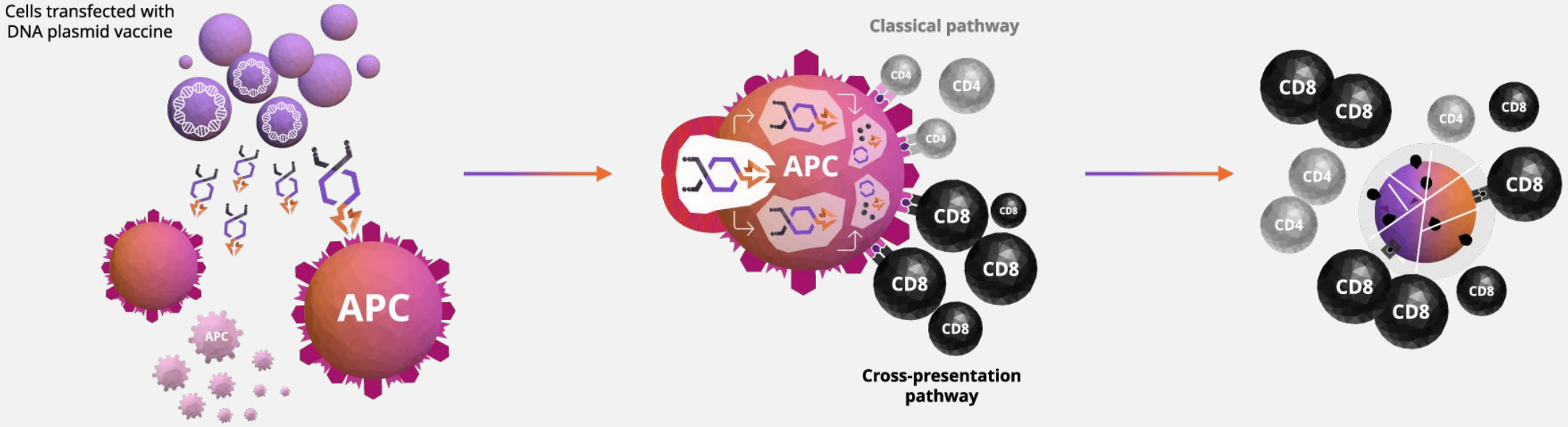
Antigens of choice from cancer, viruses, bacteria, parasites or autoimmune disease

Nykode's immunotherapy candidates may be delivered through DNA, mRNA, viral vectors or as recombinant proteins

Note: [1] Targeting unit can consist of natural ligands, including cytokines/chemokines; bacterial proteins; antibody fragments

Nykode's cancer vaccine platform induces a rapid, robust and long-lasting CD8 T cell response against cancer cells

MECHANISM OF ACTION – T CELL INDUCTION



1 Cells encode and secrete Vaccibody proteins, which attract a high concentration of APCs.

2 The APCs process and present the vaccine antigens to T cells and effectively activate CD8 killer T cells via cross-presentation.

3 The T cells attack cancer cells or pathogen-infected cells expressing the antigens.

Nykode's individualized cancer vaccine is designed to target a broad range of tumours

Vaccine design

- APC-targeted vaccine technology leverages targeting unit to enhance CD8+ response
- Induces immune response in hard-to-treat patients with low TMB

Sequencing of biopsy tissue

- Proprietary neoantigen selection algorithm optimizes predicted immune response profile
- Strong & broad antigen-specific response, with ~53% immunogenic neoepitopes per patient

Manufacture one vaccine per patient

- pDNA fast and robust manufacturing with high success rate and cost-effective manufacturing
- Rapid turnaround time from biopsy to vaccination

Clinical site

- Broad applicability across tumor types, including CPI-refractory and 'cold' tumors
- Safe and well-tolerated in combination with CPI

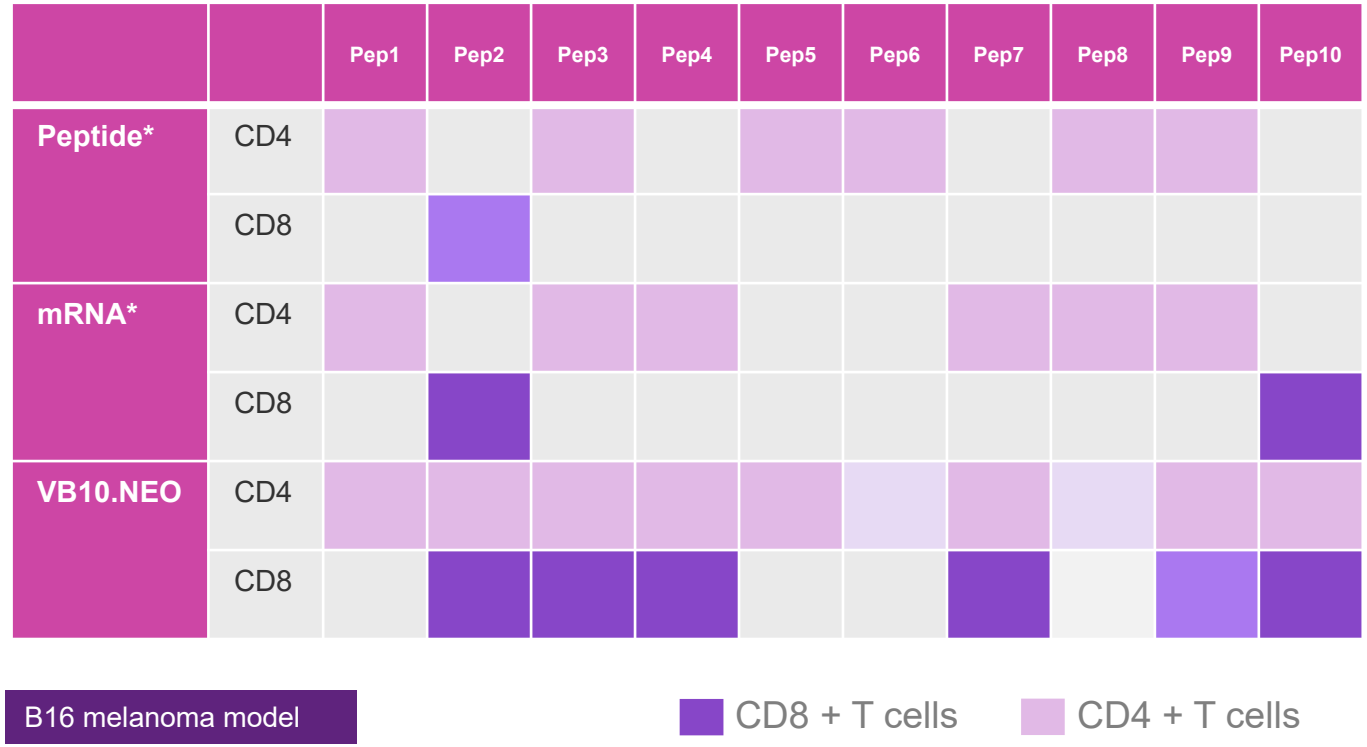
Key clinical results

- 2 clinical trials in more than 10 indications in recurrent / metastatic setting
- Broad and durable T cell responses in clinic, with neoantigen-specific T-cell clones sustained over 1 year
- Polyfunctional T-cell response predominated by CD8+ T-cells

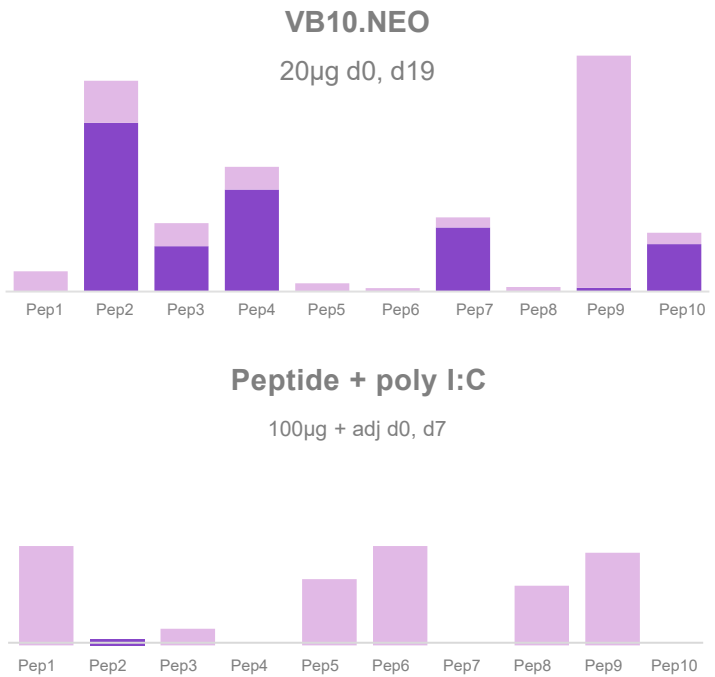
*Exclusively out-licensed to Roche and Genentech (2020)

Controlled cross-presentation by specific APC receptor targeting induces broader & stronger CD8 responses than non-targeted technologies such as mRNA- and peptide vaccines

Comparison with peptide and RNA vaccination strategies shows broader CD8 and CD4 responses with Nykode's technology

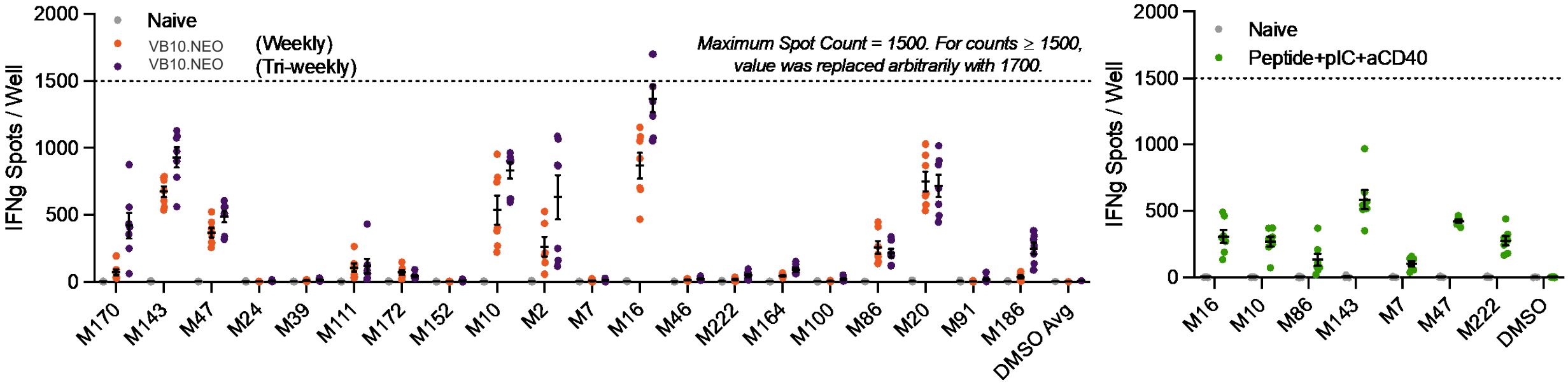


Addition of strong CD8 responses to epitopes non/weakly-immunogenic with other strategies



*Castle et al., 2012 and Kreiter et al., 2015

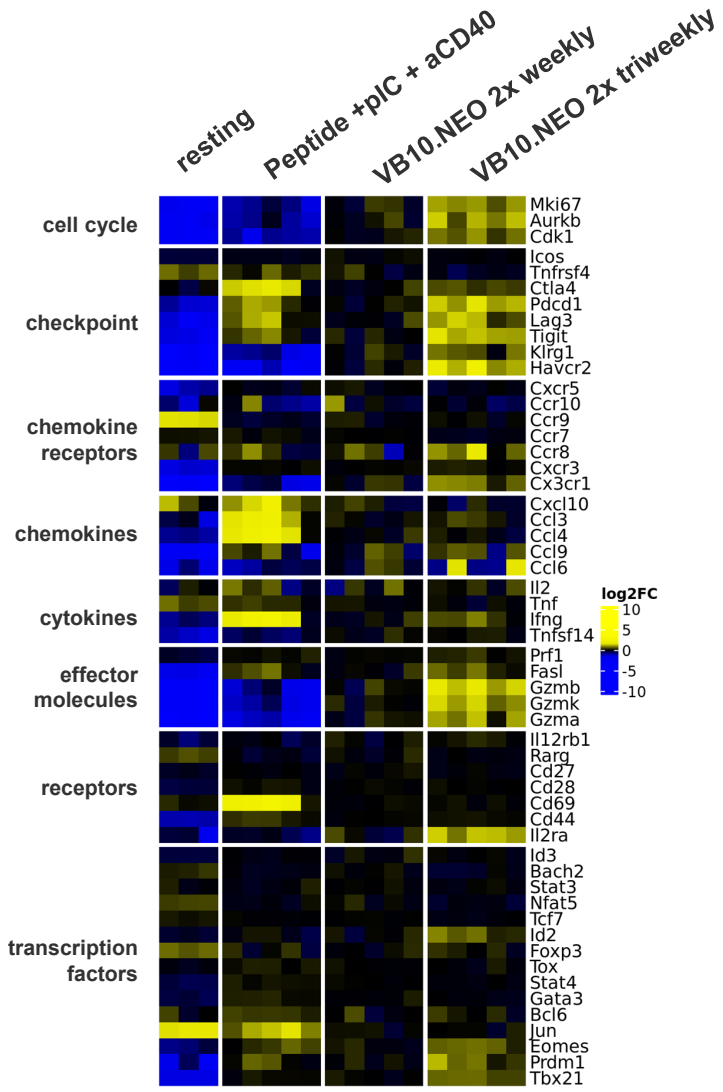
APC-targeted DNA vaccine induces a broader and stronger T cell response than peptide vaccines



The magnitude of the T cell responses are optimal with triweekly vaccination interval

Genentech
A Member of the Roche Group

APC targeted vaccine induce potentiated CD8 T cell phenotypes



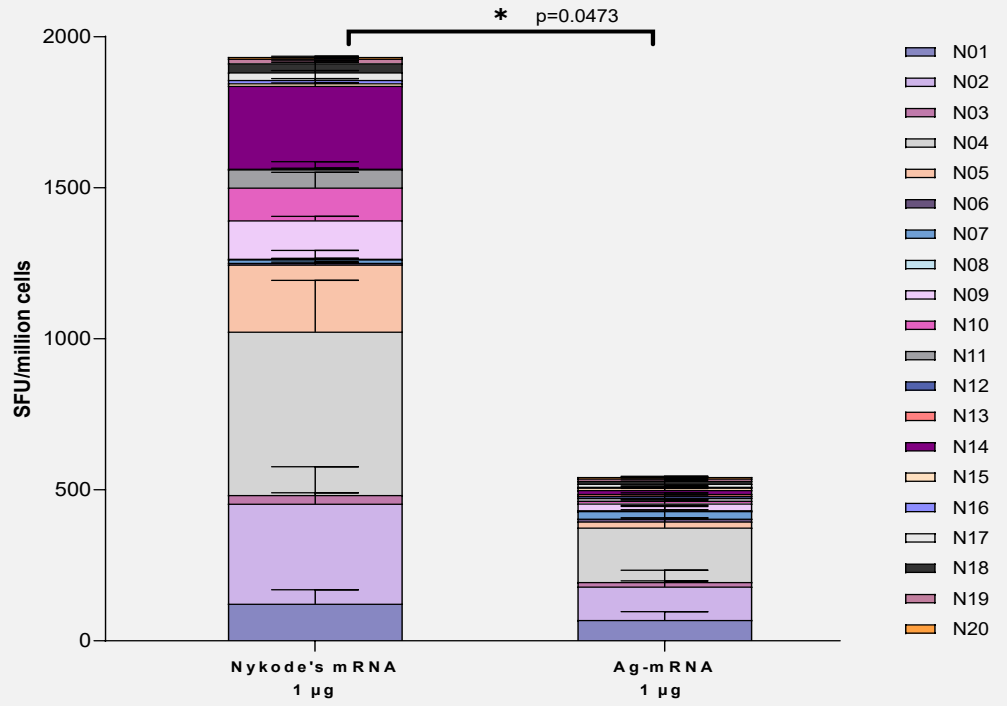
- Prominent increased expression of cell cycle, checkpoint and effector genes with VB10.NEO compared to peptide + adjuvant vaccines
- CD8 T cell transcription factor profile consistent with higher differentiation towards effector/effector memory phenotypes
- Tri-weekly dosing regimen is optimal inducing increased expression of activation and effector genes
- Pathway enrichment suggest that tri-weekly regimen potentially enhances immune responses, cell differentiation, proliferation, cell signaling and metabolic processes, promoting a stronger and more effective immune response

Genentech
A Member of the Roche Group

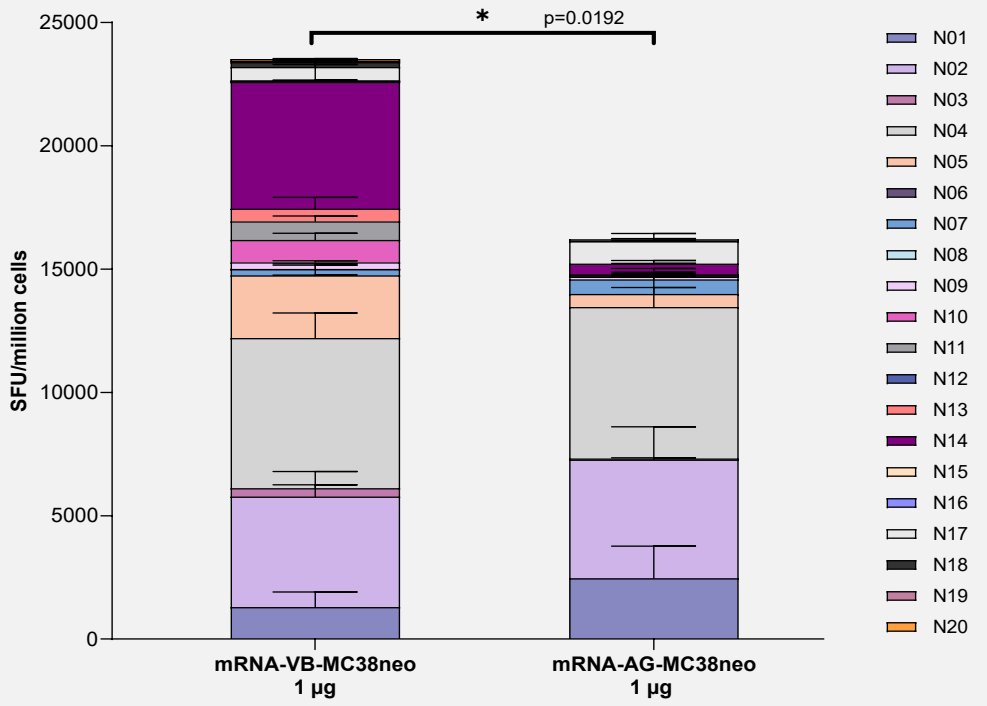
Nykode's APC-targeted technology offers similar improvement also as mRNA based vaccines

Stronger T cell responses to a wider variety of MC38 T cell epitopes

Prime vaccination only (D14)



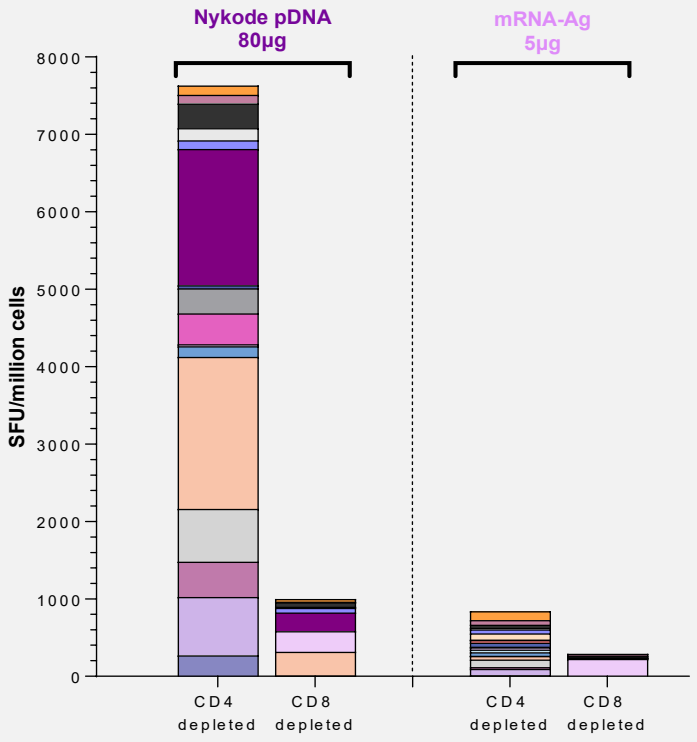
Prime + boost vaccination (D28)



The strong responses by Nykode's APC-targeted technology is primarily driven by broad CD8 T cell specificity

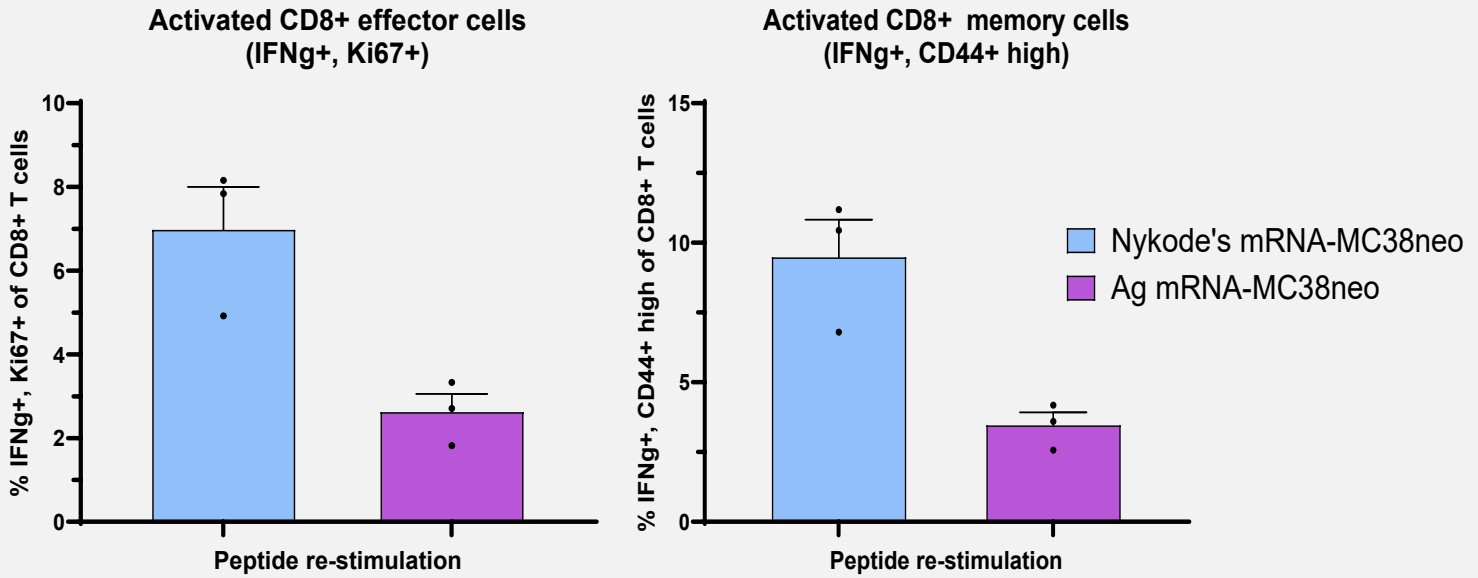
The strong responses by Nykode's vaccine are primarily CD8 driven and includes both effector and memory subtypes

Nykode pDNA vs Ag mRNA



d14

Nykode mRNA vs Ag mRNA



d28

VB10.NEO programs

Safety clearance of 9 mg dose with no safety concerns and no dose limiting toxicities observed

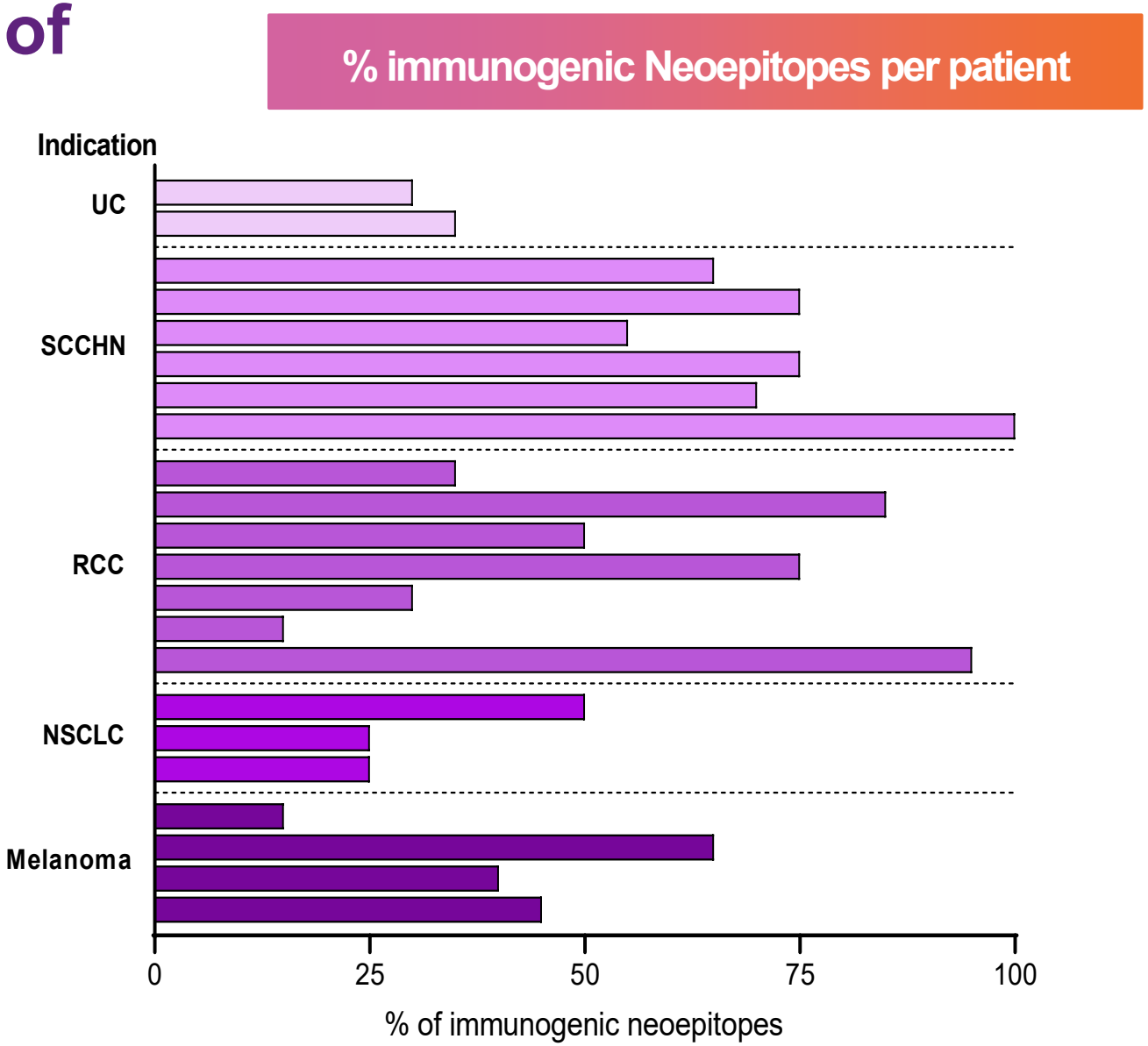
	N-01	N-02
Indication	r/m Melanoma, non-small cell lung cancer (NSCLC), clear renal cell carcinoma, urothelial cancer or squamous cell carcinoma of the head and neck (SCCHN)	r/m cancer, covering more than ten indications
Dose	3 mg dose in combination with a CPI	3-9 mg dose escalation, in combination with atezolizumab
Phase	1/2a	1b
Status	Finalized	Enrolling
Partnered	Genentech *A Member of the Roche Group*	

Note: Genentech has an exclusive license to VB10.NEO.

T cell responses to majority of selected neoepitopes

All patients across five indications showed a response to at least one neoepitope

On average, 53% of selected neoepitopes were immunogenic, ranging from 3 to all 20 neoepitopes in the VB10.NEO vaccine demonstrating a broad response

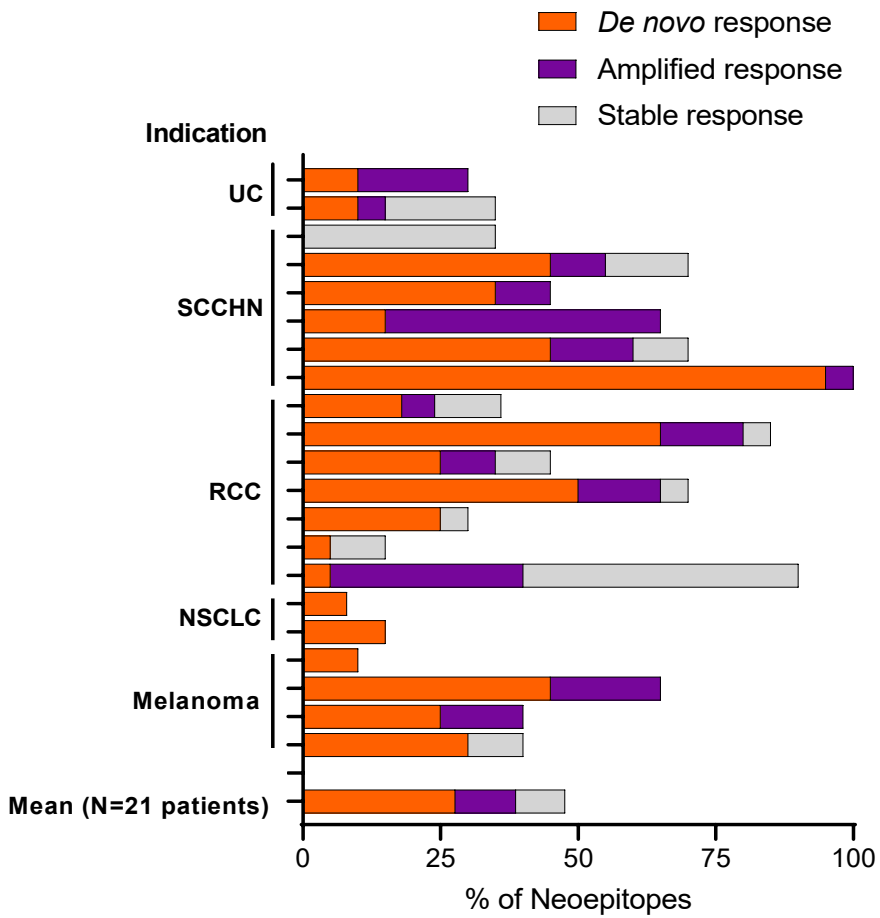


VB10.NEO amplifies pre-existing T-cell responses and induces multiple novel T-cell specificities

Expansion of both pre-existing and novel T-cell responses in most patients (at least one time point post vaccination)

- 20/21 (95%) *de novo* expanded
- 14/21 amplification of pre-existing

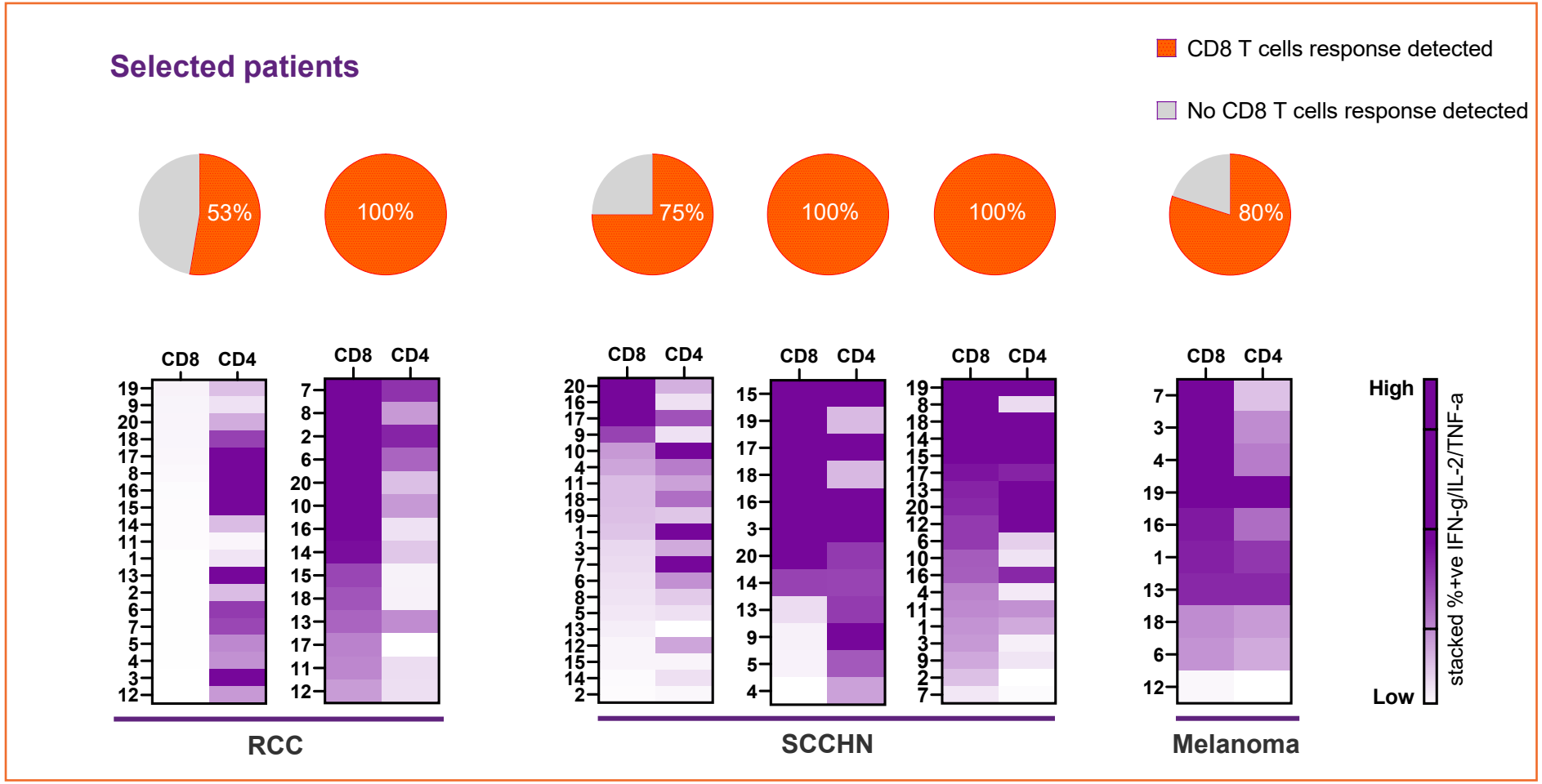
Expansion of pre-existing and induction of novel T cells



Analysis reported for patients with available PBMC, data missing for 1 or more neoepitopes for 1 patient (N=21)

Preliminary immune phenotyping shows that the majority of neoepitopes activates CD8 T cells

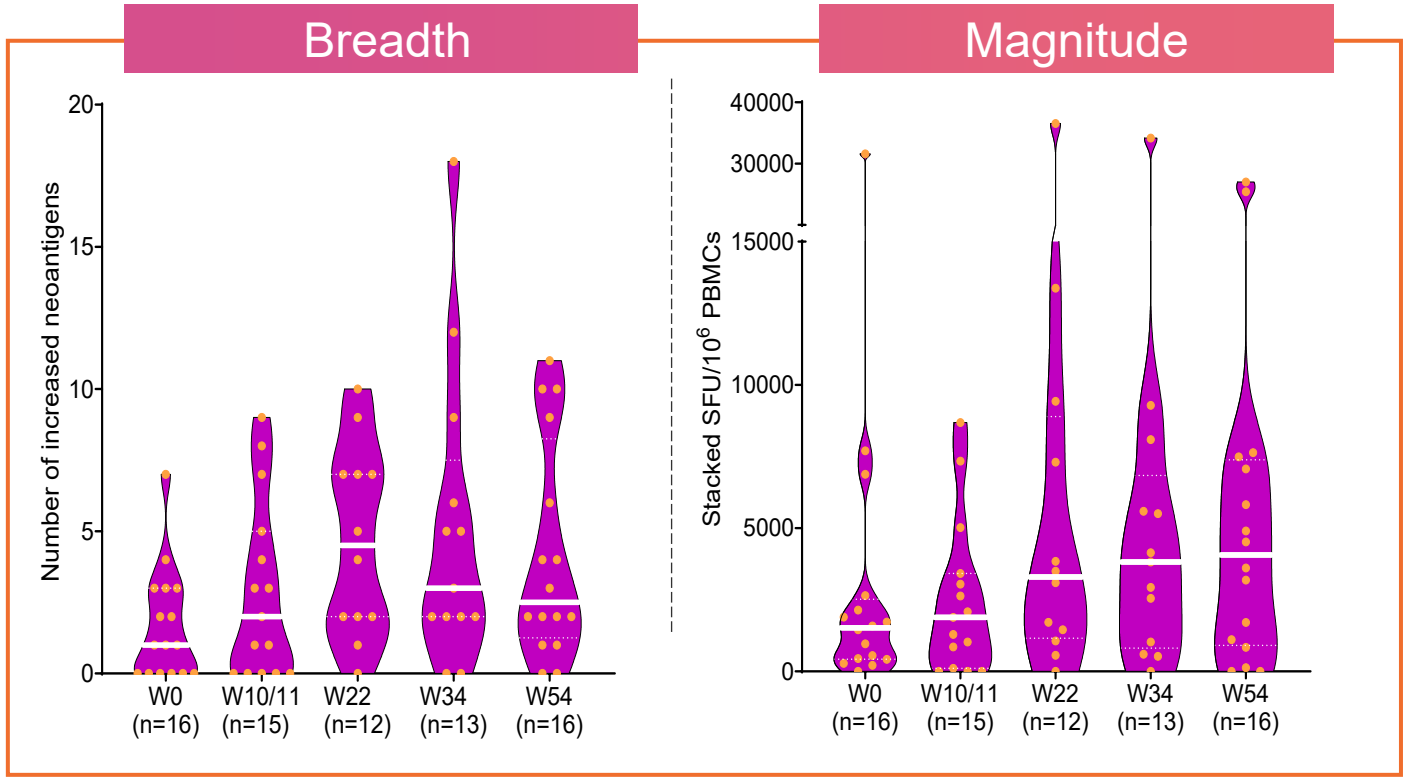
- T cell responses are characterized by both CD8 and CD4 T cells
- The majority of tested neoepitopes activated functional CD8 T cells in all subjects analyzed



CD8 response defined as ≥ 0.2% above DMSO background.
Phenotyping was performed by IVS ICS using PBMC from week 22 for 6 subjects. Number indicate neoepitope in VB10.NEO

Multiple vaccinations boost the breadth and magnitude of functional T cell responses

Patients completing 1-Year of treatment



Increase in the **breadth** and **magnitude** of functional T cell responses observed over time.

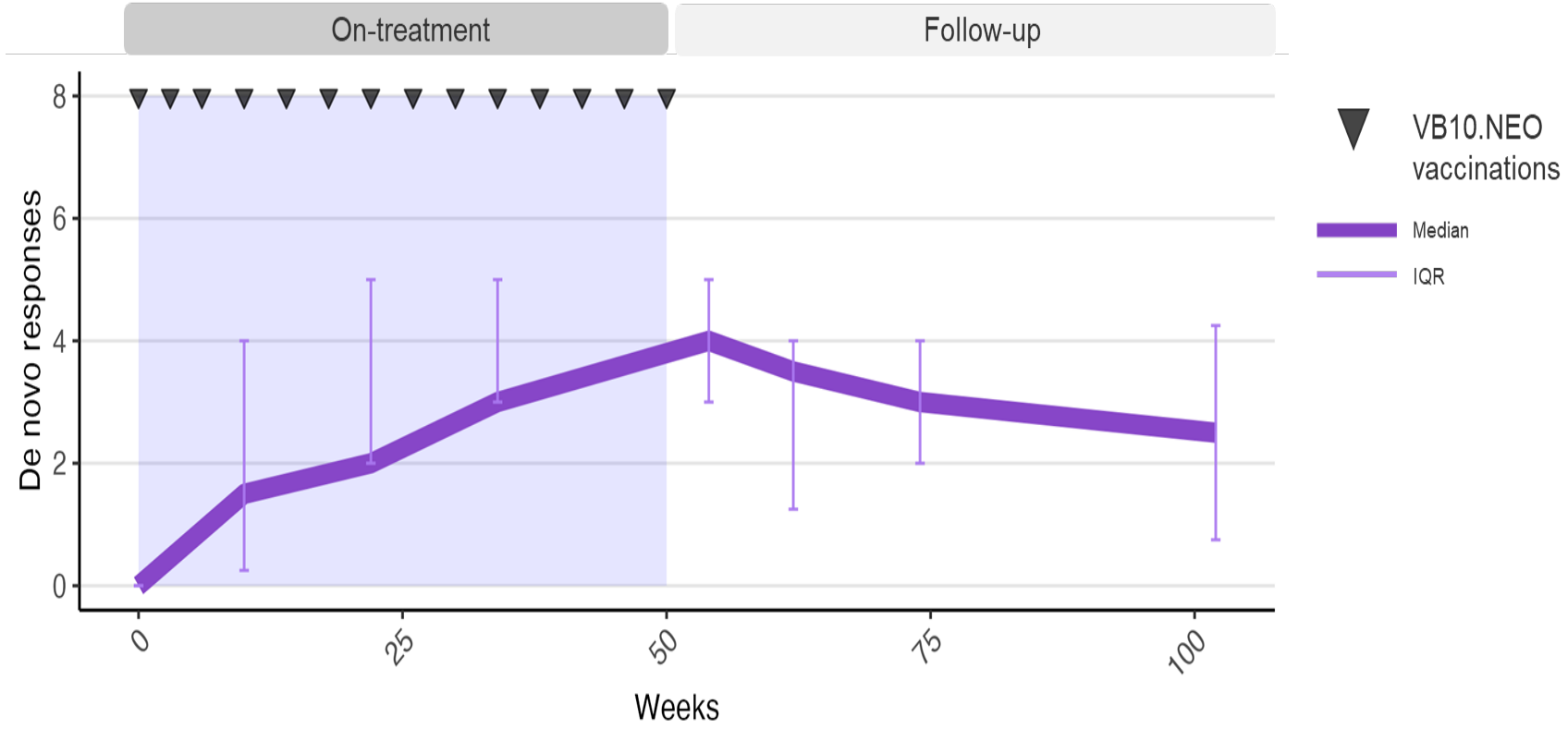
Breadth: Number of vaccine-induced NeoAg (*de novo* or amplified)

Magnitude: Stacked IFN-γ response of all immunogenic NeoAg

Patients completed and having PBMC collected up to 1-year treatment are included (N=16). Median is shown as horizontal lines.

Vaccine-specific T cells remain functional and immunogenic up to 1-year after last vaccination

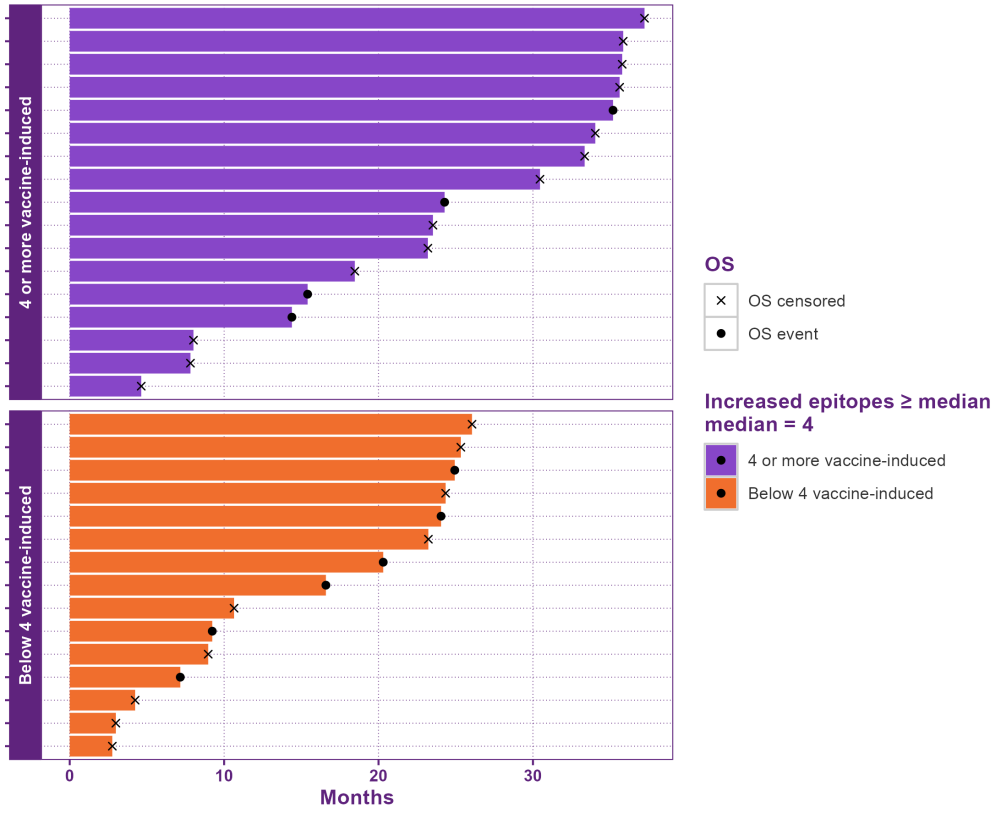
VB10.NEO induces a favorable and long-lasting T cell memory phenotype



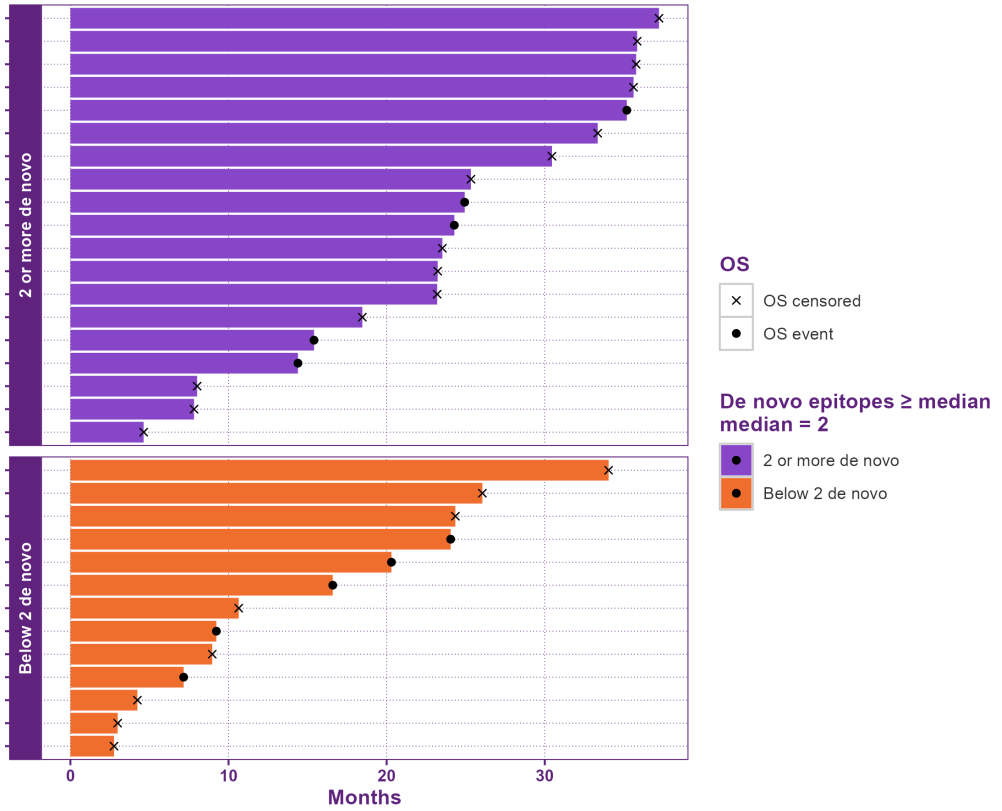
N=10 patients with on-treatment (OT) and follow-up (FU) samples. IQR: Interquantile range. OT data: actual *de novo* responses at weeks 10/11, 22, 34, 54. FU data: The latest positive timepoint defined the persistence of response (i.e. neoantigens were called positive at earlier FU timepoints if positive at later FU timepoint(s)).

T cell responses per patient

Total T cell responses



De novo T cell responses

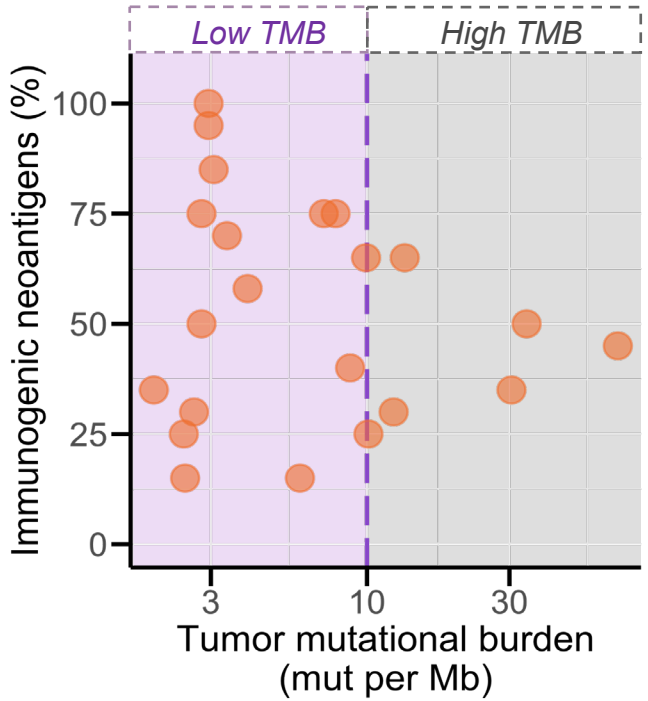


Patients grouped in lower and higher than median immune responses

Patients included are overlapping between EFR and FAS (N=32).

VB10.NEO induces T cell responses in hard-to-treat low-TMB patients

Immune reactivity towards VB10.NEO



VB10.NEO demonstrate a high immune reactivity in a hard-to-treat population of low-TMB patients (<10 mut/Mb).

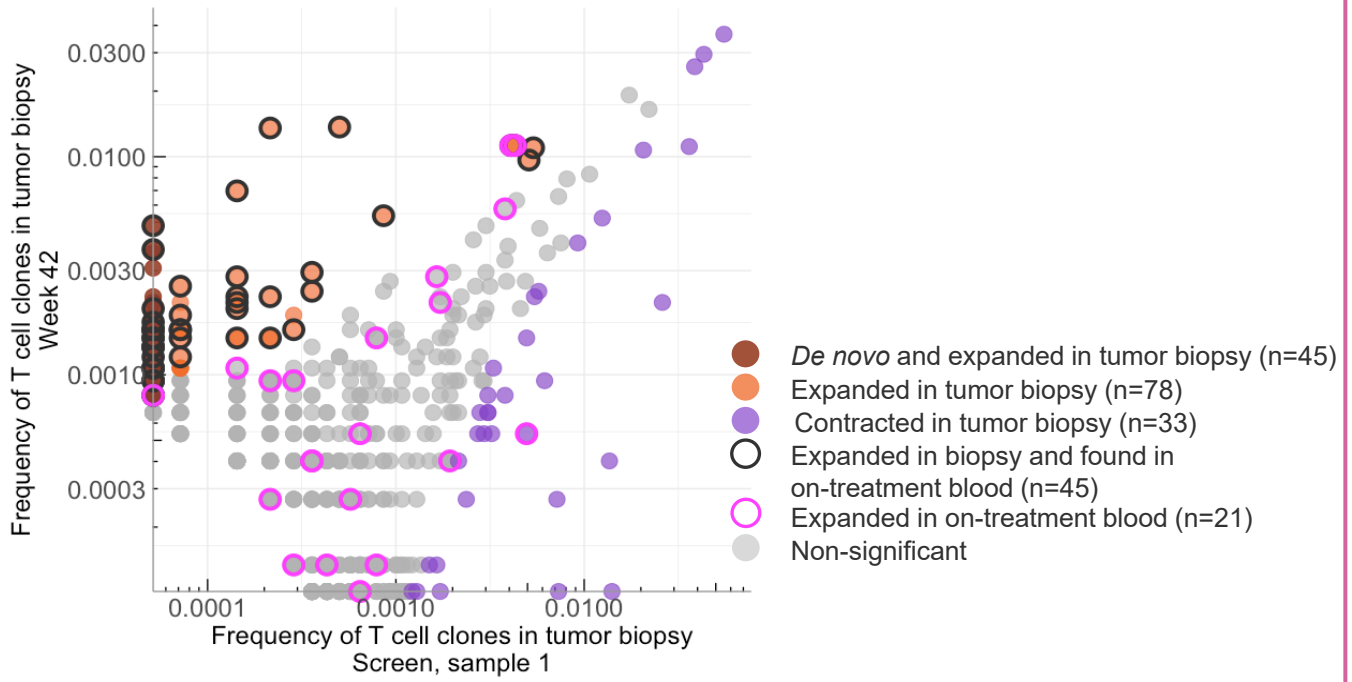
T cell clonotypes were expanded in tumor tissue after vaccination and were also found in blood

T cell clones expanded in the tumor also found in on-treatment PBMC

T cell clones found in the tumor expanded in post-vaccination PBMC

Indicates that vaccine-induced neoantigen-specific T cells in the periphery are able to infiltrate tumors

Expansion of novel T cell clones in on-treatment tumor samples



Data from 4 patients revealed expansion of T cell clones in the tumor when comparing baseline with on-treatment biopsies taken from the same tumor site (range 7-152 clones)

VB10.NEO Key Differentiators

Solid manufacturing chain

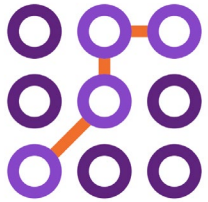
- ✓ 100% successful vaccine production
- ✓ Robust supply chain

Safety

- ✓ Safety profile similar to checkpoint inhibitor monotherapy
- ✓ No increase in immune-related adverse events

NeoSELECT

- ✓ High fraction of immunogenic neoantigens
- ✓ Strong ability to select neoantigens across different tumor entities



Immune response

- ✓ Induces broad and strong T cell responses
- ✓ Long-lived and persistent immune responses

Strong partnership

- ✓ Validated technology
- ✓ Unique targeting module

Competitive player

- ✓ Well-tolerated across trials and in different combinations
- ✓ Within the validated field of personalized vaccines

Key Conclusions

VB10.NEO is able to induce a broad and CD8 dominating T cell response both as pDNA and mRNA vaccines

VB10.NEO induces a T cell profile profile consistent with higher differentiation towards effector/effector memory phenotypes

Dosing regiment (Tri-weekly versus weekly) dosing is important for obtaining the strongest and most effective immune response

VB10.NEO was generally well tolerated in patients with various pre-treated and advanced cancers

Assessment of neoantigen-specific T cell reactivity demonstrated VB10.NEO-induced broad and long-lasting T cell responses, and the majority of tested neoantigens activated polyfunctional CD8 T cells

T cell responses were elicited in both TMB high and low patients indicating selection of high quality neoepitopes in a broad range of cancer indications

Acknowledgement

We would like to thank the patients, their families as well as investigators for their participation in the trial

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UNLOCKING THE FUTURE OF MEDICINE

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