



Nykode's individualized cancer vaccine approach across DNA and mRNA

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Personalized Cancer Vaccine Summit

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



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



Broad pipeline de-risked through strong durability and survival data

- ◆ Lead asset VB10.16 focused on high-unmet need indications, including locally advanced cervical cancer and r/m head and neck cancer



Strategic multiprogram collaboration in oncology and infectious diseases with Regeneron¹

REGENERON

















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




Well-capitalized with a cash position of \$124.6m at September 30, 2024

1. Collaboration and license to 5 programs with Regeneron.

Broad pipeline targeting early to late-stage cancer treatment

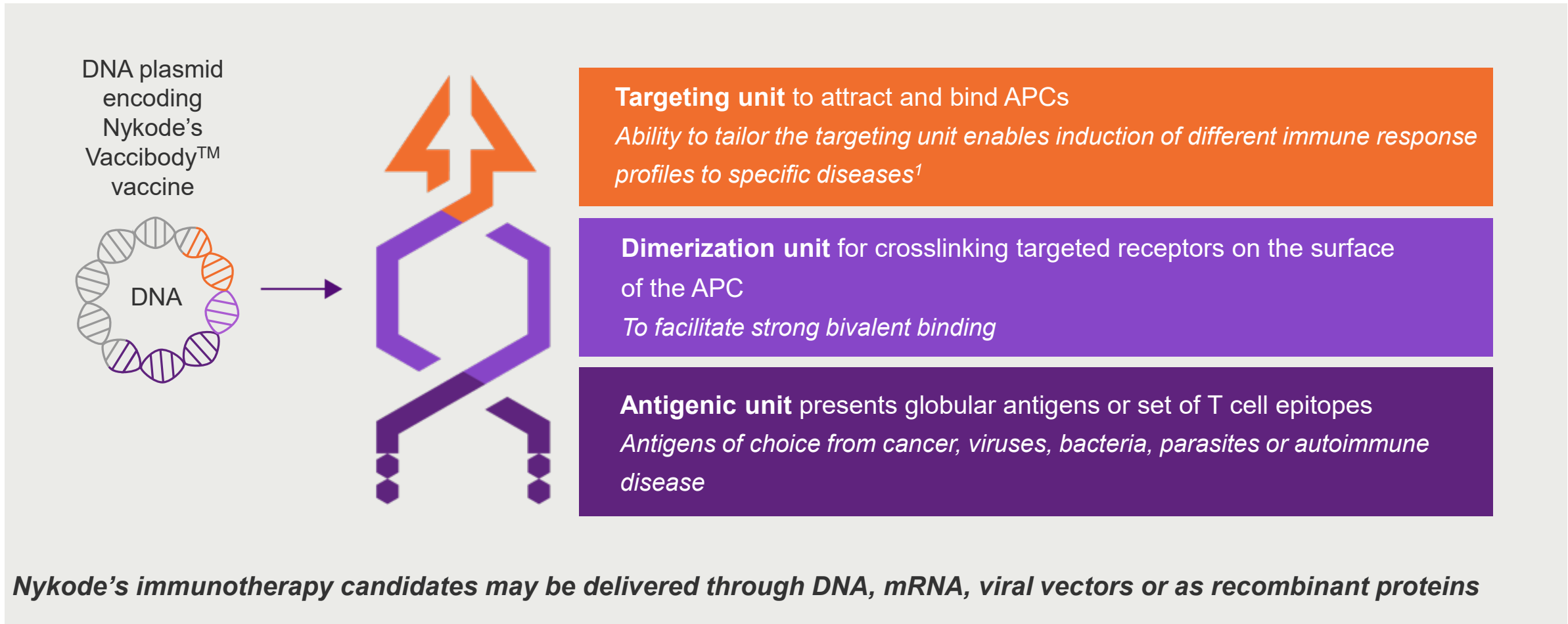
	Asset	Indication	Rights	Preclinical	Phase 1	Phase 2	Phase 3
Oncology							
Off-the-shelf	VB10.16	HPV16+ cervical cancer	 ¹				C-02
		HPV16+ head and neck cancer	 ²				C-03
	Regeneron programs	Undisclosed	  ³				
Individualized	VB10.NEO	Incurable locally advanced and metastatic tumors	 ²				N-02
Infectious Disease							
	Regeneron programs	Undisclosed	  ³				
Autoimmune							
	Internal	Undisclosed					

1. Wholly-owned by Nykode. Roche supplies atezolizumab; 2. Wholly-owned by Nykode. Merck (MSD) supplies pembrolizumab; 3. Collaboration with Regeneron



VB10.NEO Individualized cancer immunotherapy

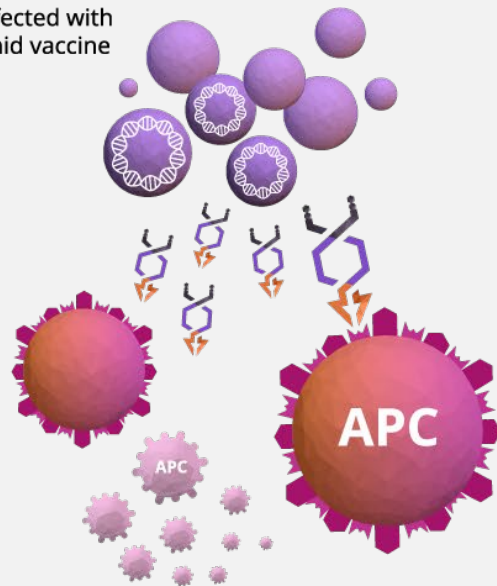
Modular vaccine technology allows APC-targeting to direct immune responses



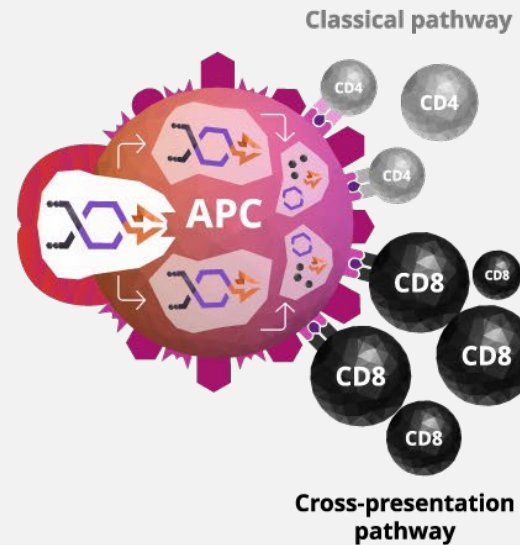
Nykode's cancer vaccine platform induces a rapid, robust and long-lasting CD8 T cell response against cancer cells

MECHANISM OF ACTION – T CELL INDUCTION

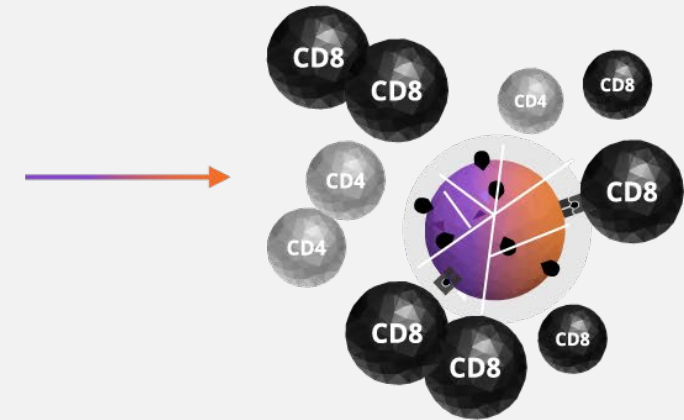
Cells transfected with DNA plasmid vaccine



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

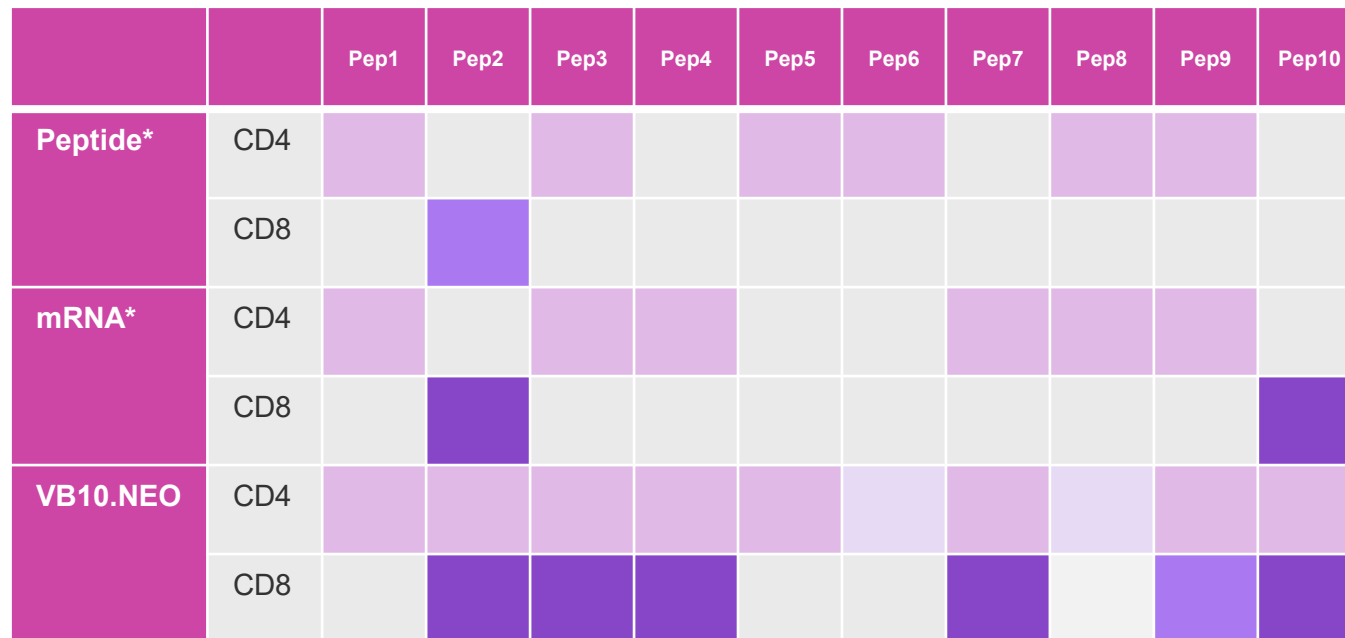
- ◆ 2 clinical trials in more than 10 indications in recurrent / metastatic setting
- ◆ Broad and durable T cell responses in clinic, with neoantigen-specific T-cell clones sustained over 1 year
- ◆ Polyfunctional T-cell response predominated by CD8+ T-cells
- ◆ Immune responses correlate with clinical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



VB10.NEO preclinical data with both DNA and mRNA

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

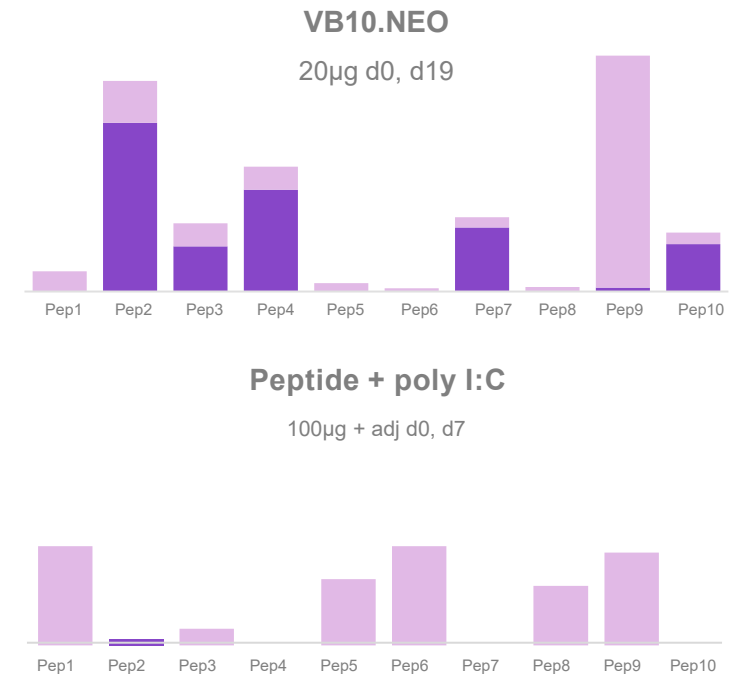
Comparison with peptide and RNA vaccination strategies shows broader CD8 and CD4 responses with Nykode's technology



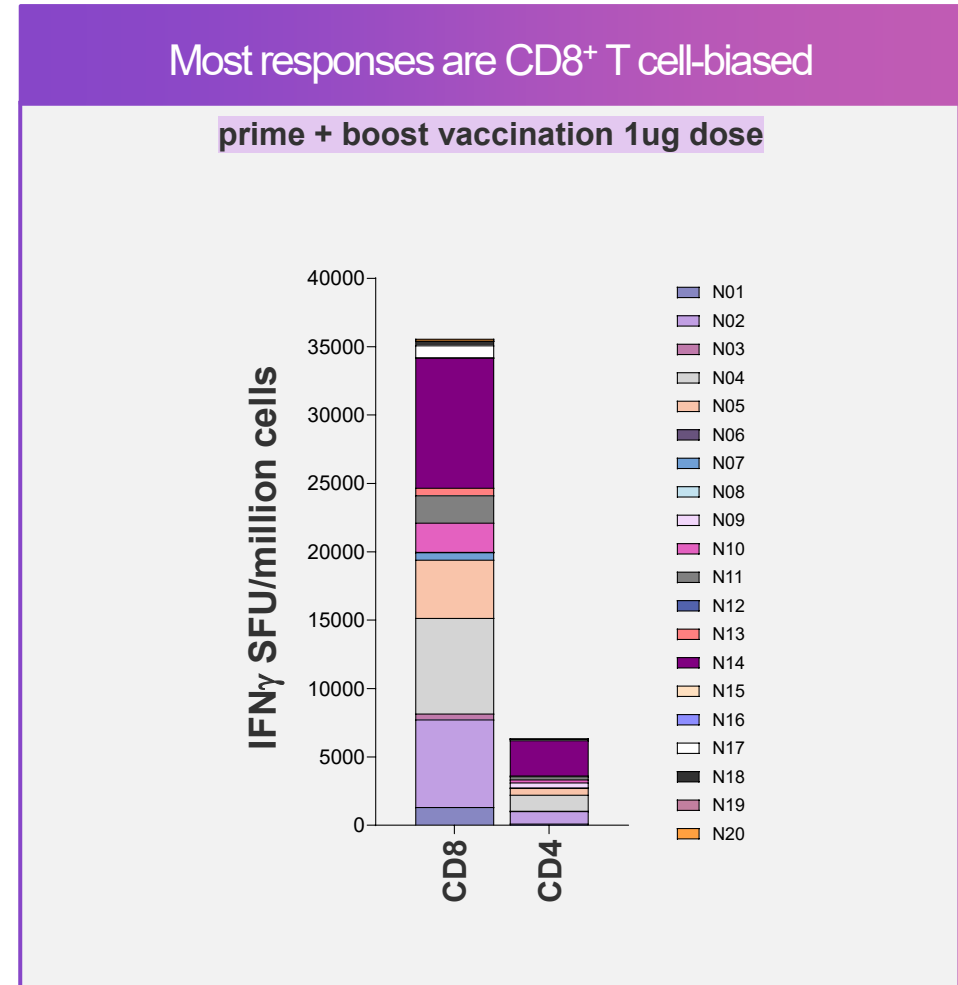
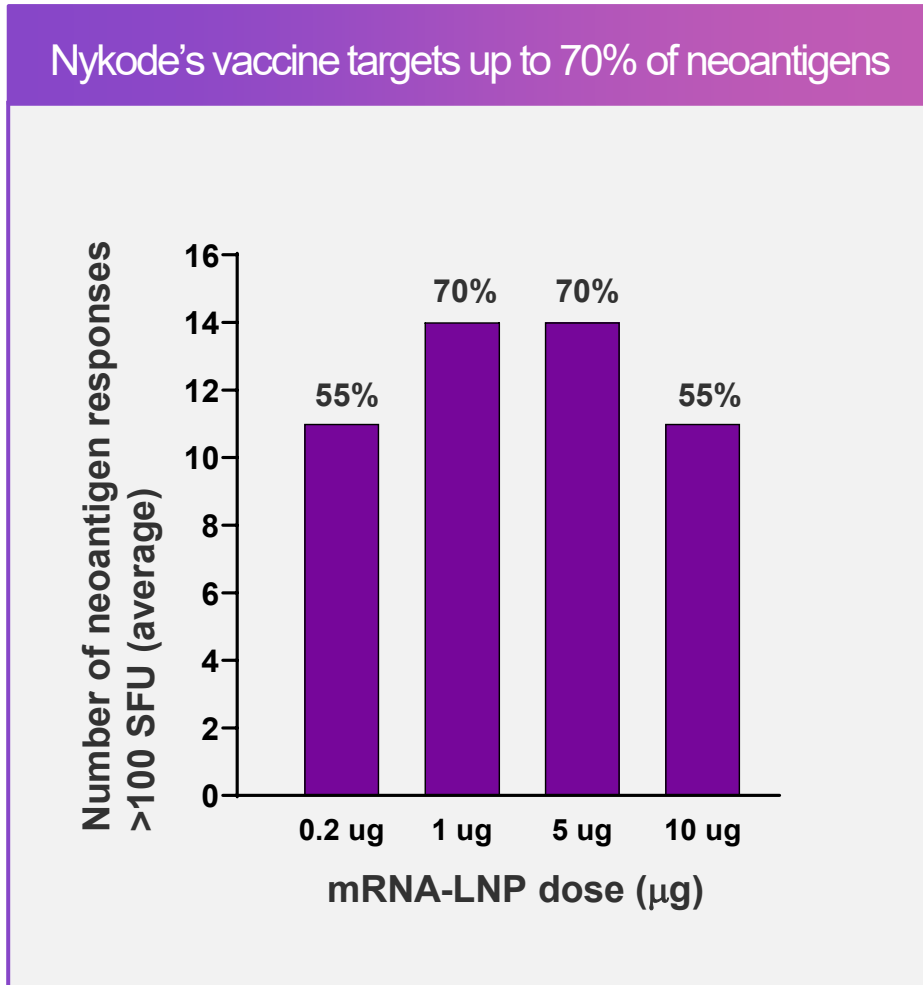
B16 melanoma model

Dark Purple CD8 + T cells Light Purple CD4 + T cells

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



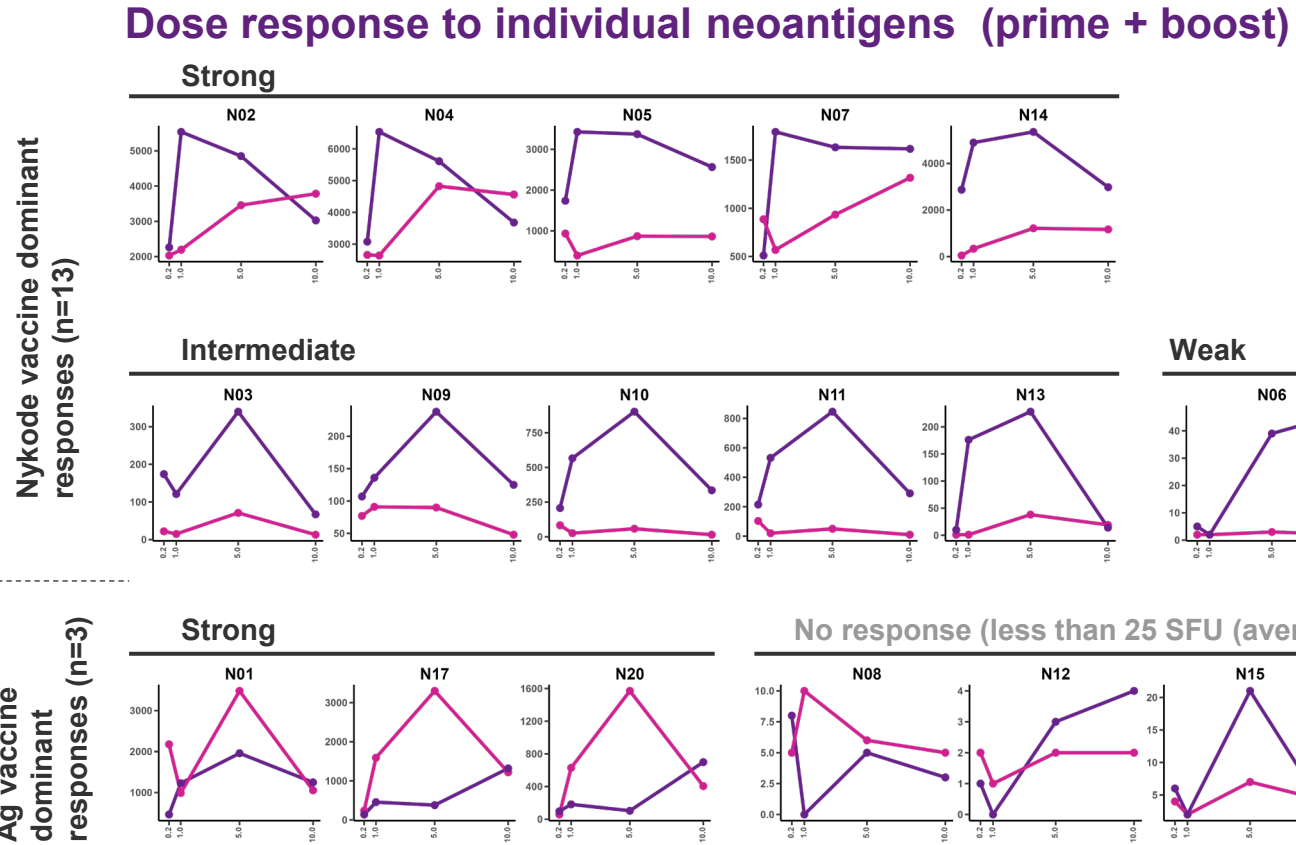
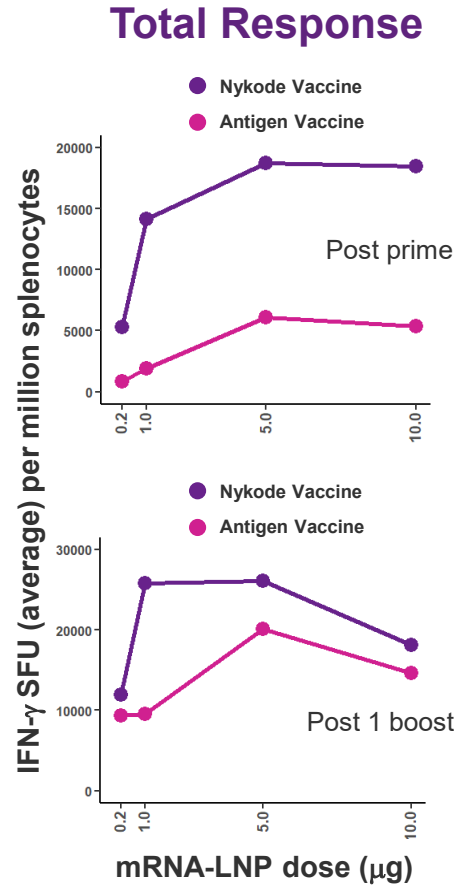
Nykode's neoantigen vaccine elicits broad T cell responses that are biased toward cytotoxic CD8+ T cells



MC38 colorectal model

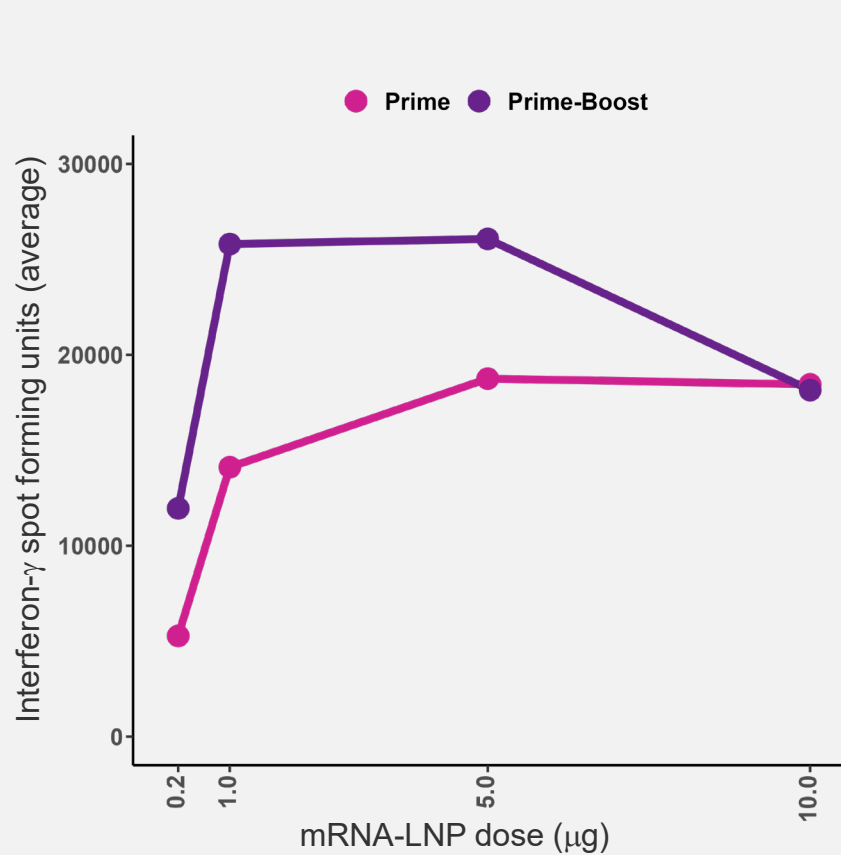
Superior dose-response kinetics of Nykode's neoantigen vaccine compared to a control neoantigen vaccine

Nykode's neoantigen vaccine elicits stronger T cell responses with a different dose-response for individual neoantigens

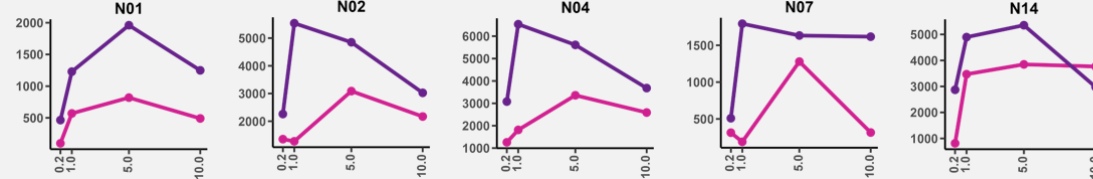


Nykode's neoantigen vaccine elicits strong and broad T cell responses after single (prime) or two (prime & boost) vaccinations

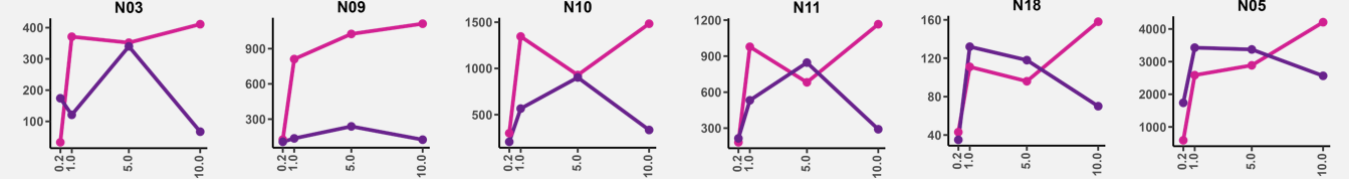
Nykode's neoantigen vaccine elicits strong & broad T cell responses across a range of mRNA-LNP doses



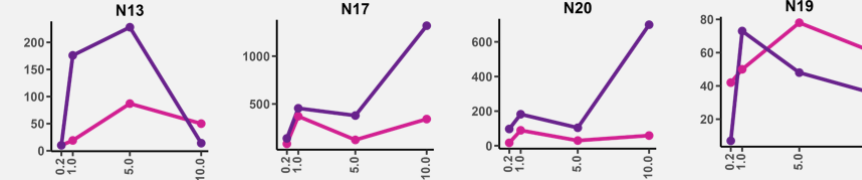
Strong responses with boost effect- peak at lower doses post prime



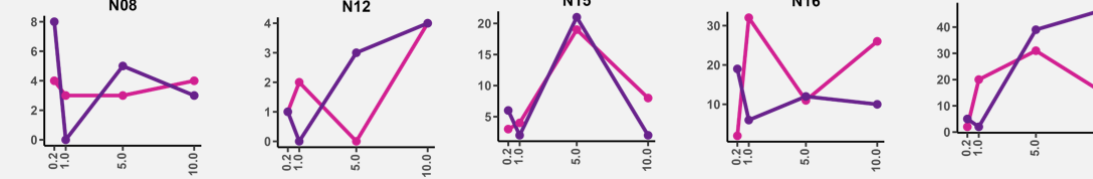
Intermediate responses with no to negative boost effect –peak at highest dose post prime



Weak or intermediate responses with boost effect- peaked at lower doses post prime



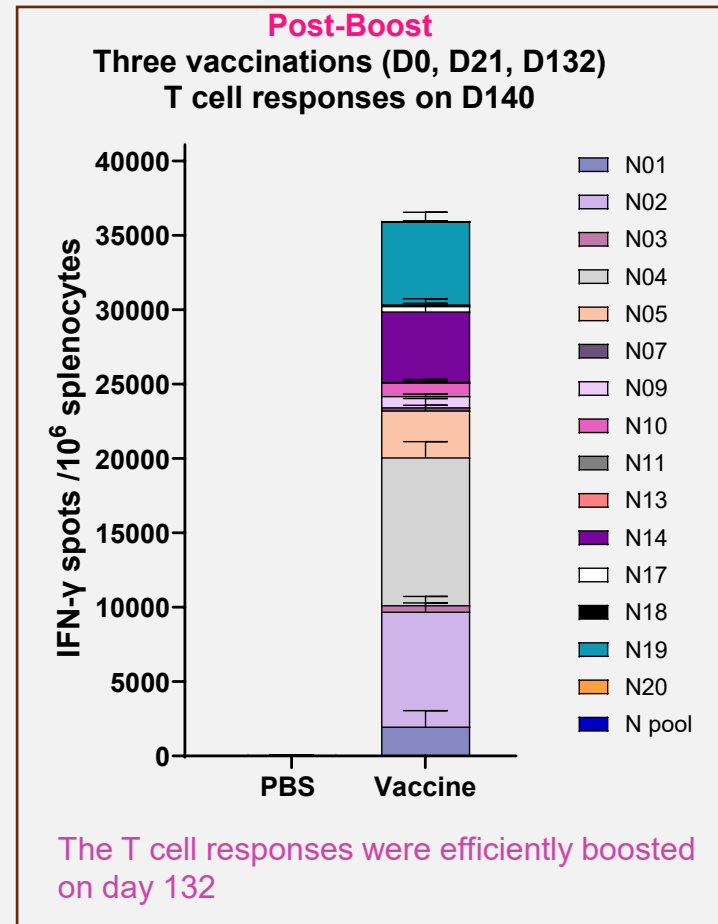
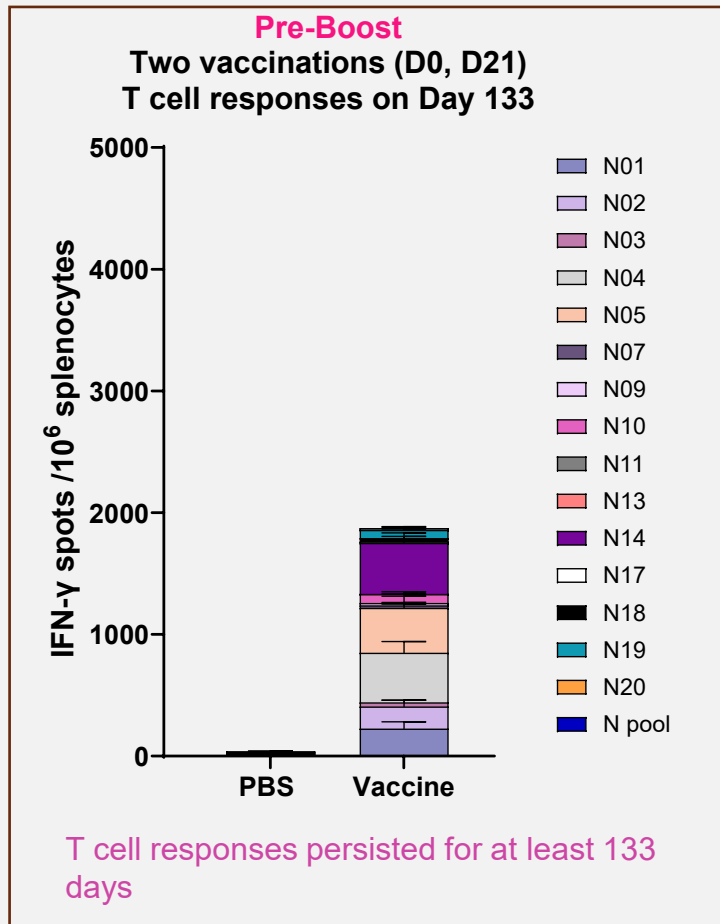
Weak to No response with no boost effect



C57BL/6 n=5 per group | Vaccination (1ug) on day 0 & 21 | IFNγ fluorospot on day 7 (prime) & 28 (prime + boost)

Nykode's neoantigen vaccine elicits durable responses

Nykode's neoantigen vaccine leads to durable immune responses that are efficiently boosted after more than 100 days



	Pre-Boost	Post-Boost	Increase
N01	227	1985	9x
N02	182	7721	43x
N03	34	445	13x
N04	407	9931	24x
N05	367	3148	9x
N07	22	232	11x
N09	18	740	41x
N10	73	914	13x
N11	1	1	None
N13	2	54	29x
N14	418	4725	11x
N17	13	367	29x
N18	28	104	4x
N19	66	5555	84x
N20	5	22	5x
N pool	12	19	None

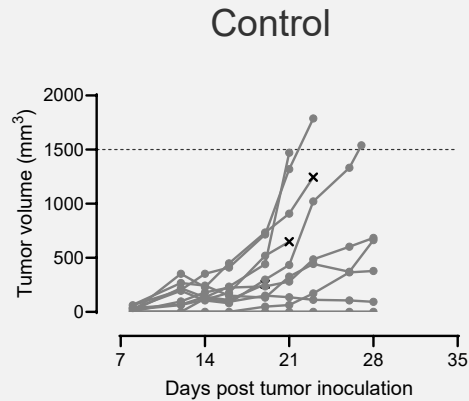
N pool = N06, N08, N12, N15, & N16 combined

- 14/20 (70%) boosted >2-fold
- Unlike post 2nd dose day 21, all strong and intermediate responding neoantigens were boosted post 3rd dose at day 133

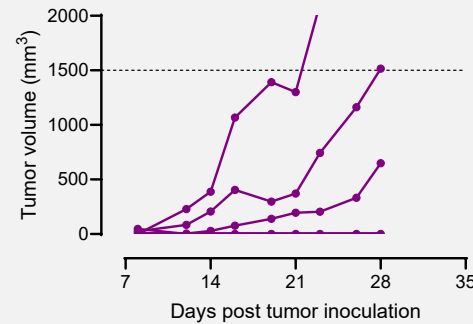
Durable responses are functional

Nykode's neoantigen vaccine elicits durable responses that protect from tumor challenge on day 90

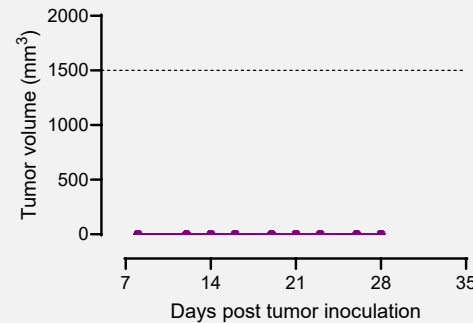
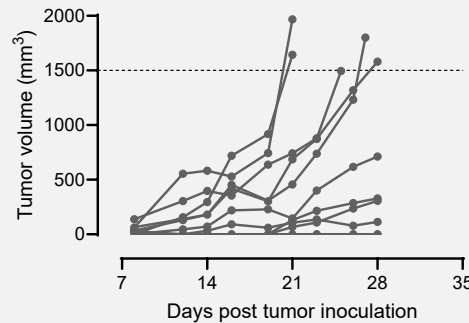
Single Vaccination
Day 0



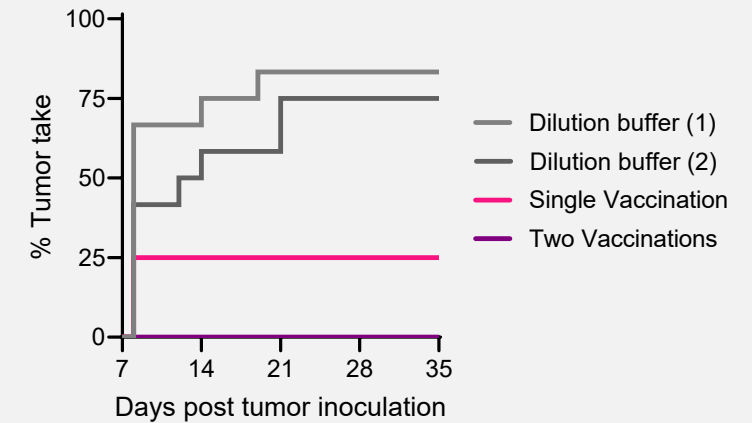
Nykode neoantigen vaccine



Two Vaccinations
Day 0, Day 21



Tumor development




- Two vaccinations completely prevents tumor development in all mice
- Single vaccination provides protection in 75% of mice (versus 25% in control groups)

A microscopic view of a cell culture, likely a fibroblast or epithelial cell line, showing a dense network of cells. The image is overlaid with a large, semi-transparent purple shape that contains the text. The background is a blurred, light-colored surface, possibly a petri dish or a slide.

VB10.NEO clinical data

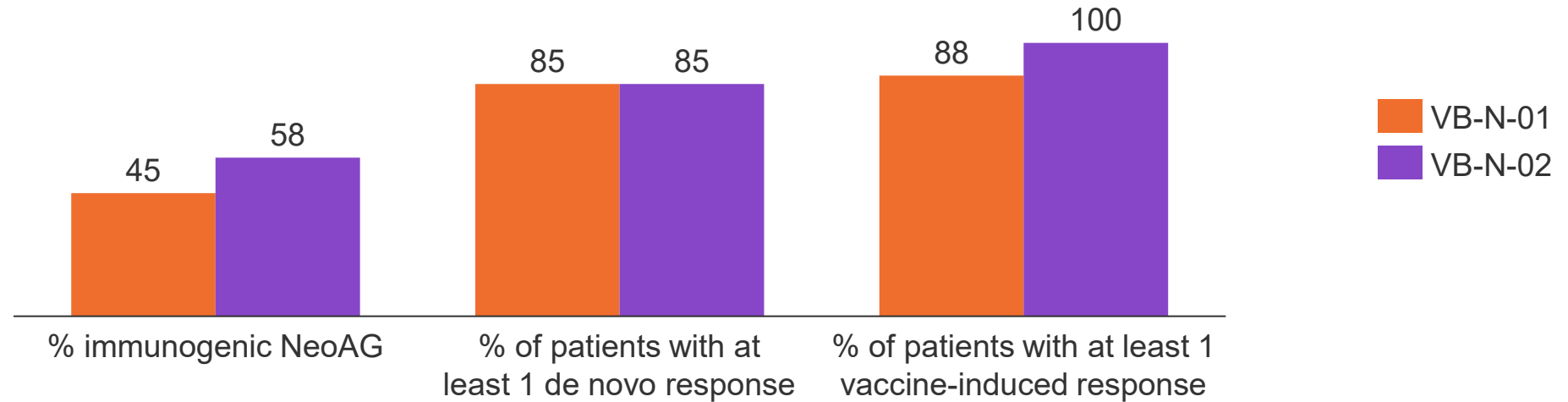
VB10.NEO programs

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	Enrolment concluded
Rights		

Preliminary data from VB- N-02 confirms VB10.NEO's potential

Preliminary immunogenicity data from the VB-N-02 trial¹ confirms earlier observations from the N-01 trial:



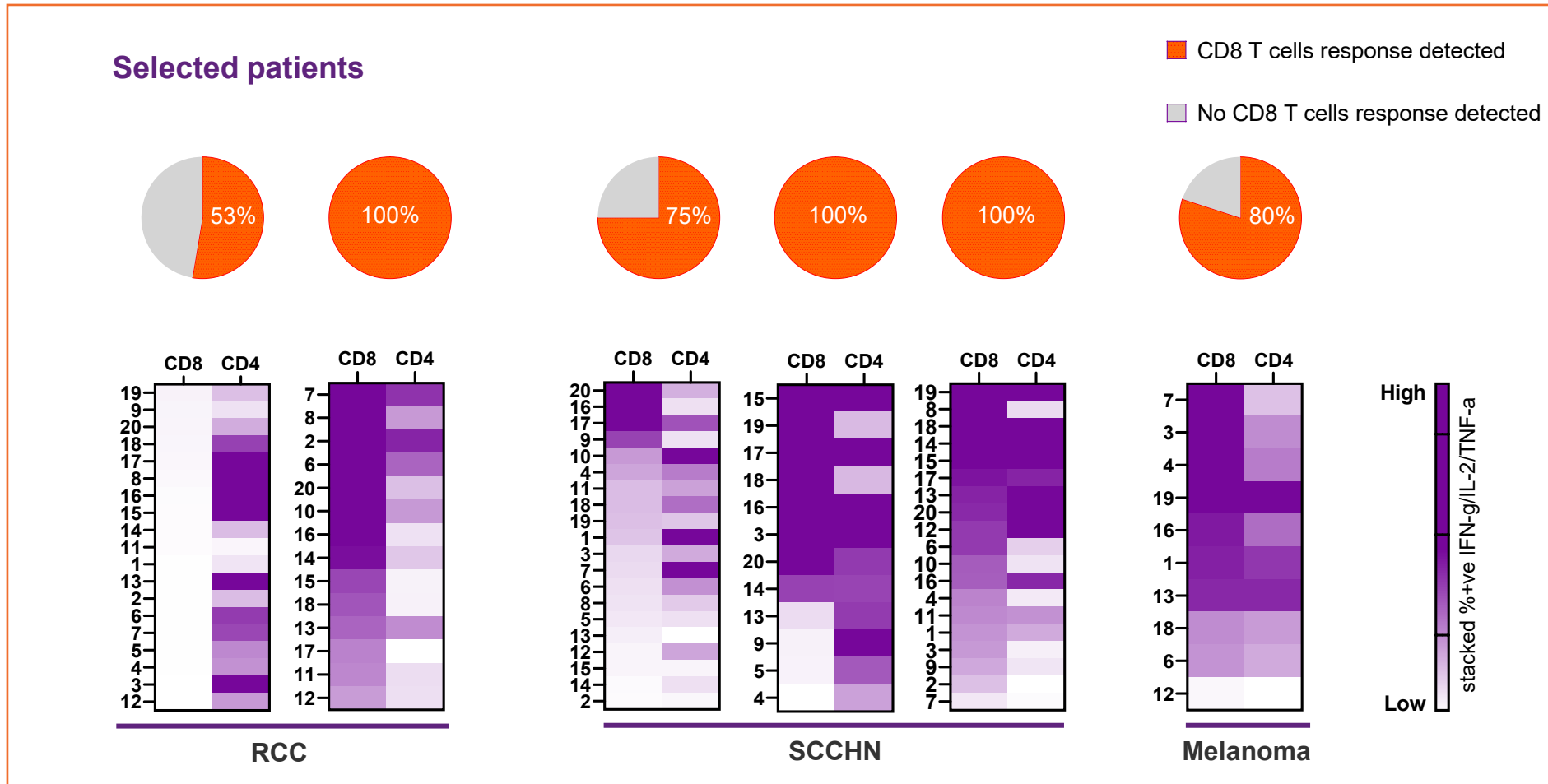
Additionally,

- A persistent expansion of T cell clones in the majority of evaluable patients measured by TCR sequencing. Persistently expanded clones emerged as early as after 2-4 vaccinations and showed durable frequencies
- The induction of persistent de novo T cell responses were confirmed by IVS ELISpot

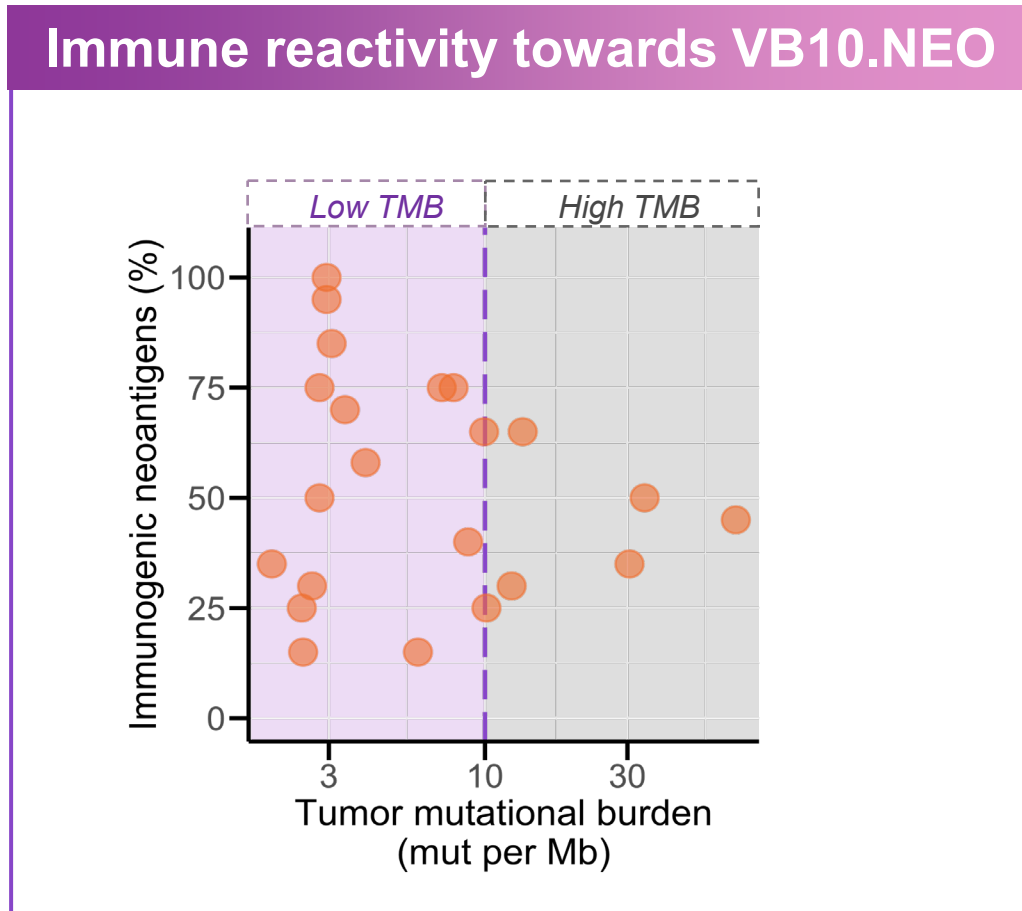
Based on the preliminary immunogenicity VB-N-02 data, Nykode remains confident in VB10.NEO's potential and is assessing the optimal path forward for the program, including exploring potential new partnerships

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

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



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



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

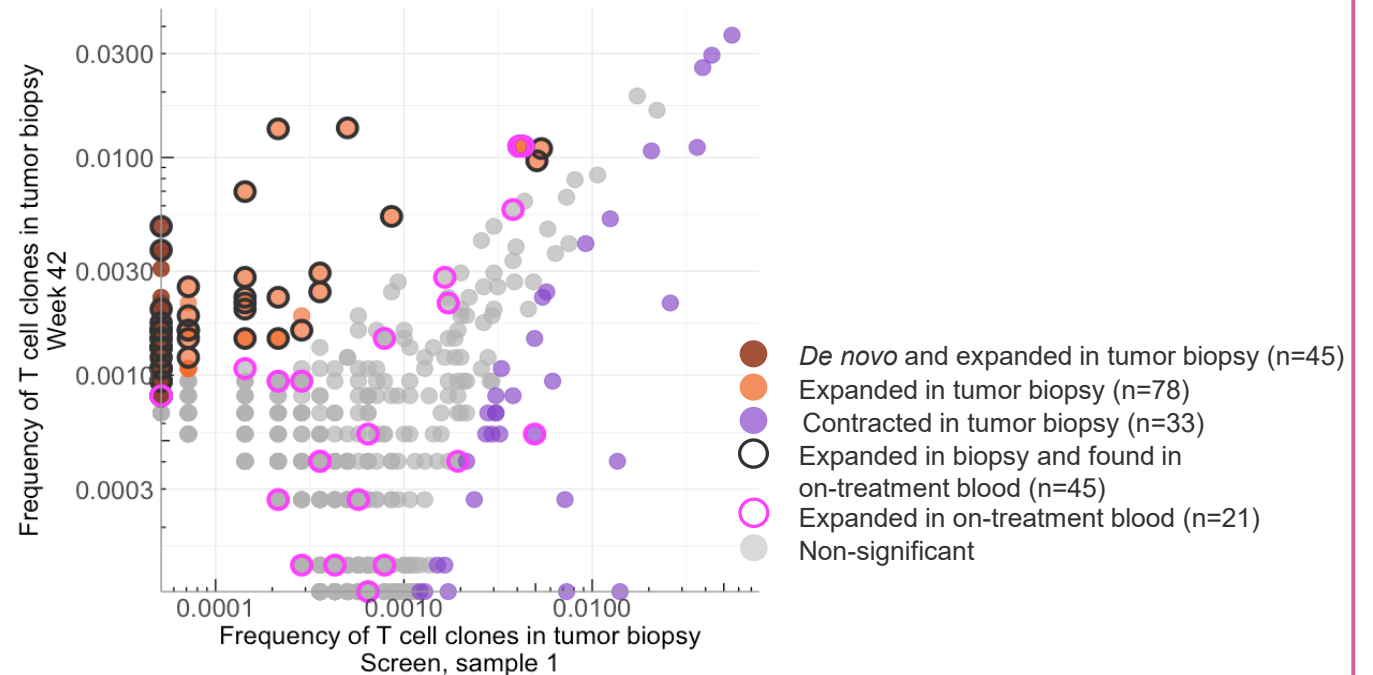
T cell clonotypes were expanded in tumor tissue after vaccination and were also found in blood

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

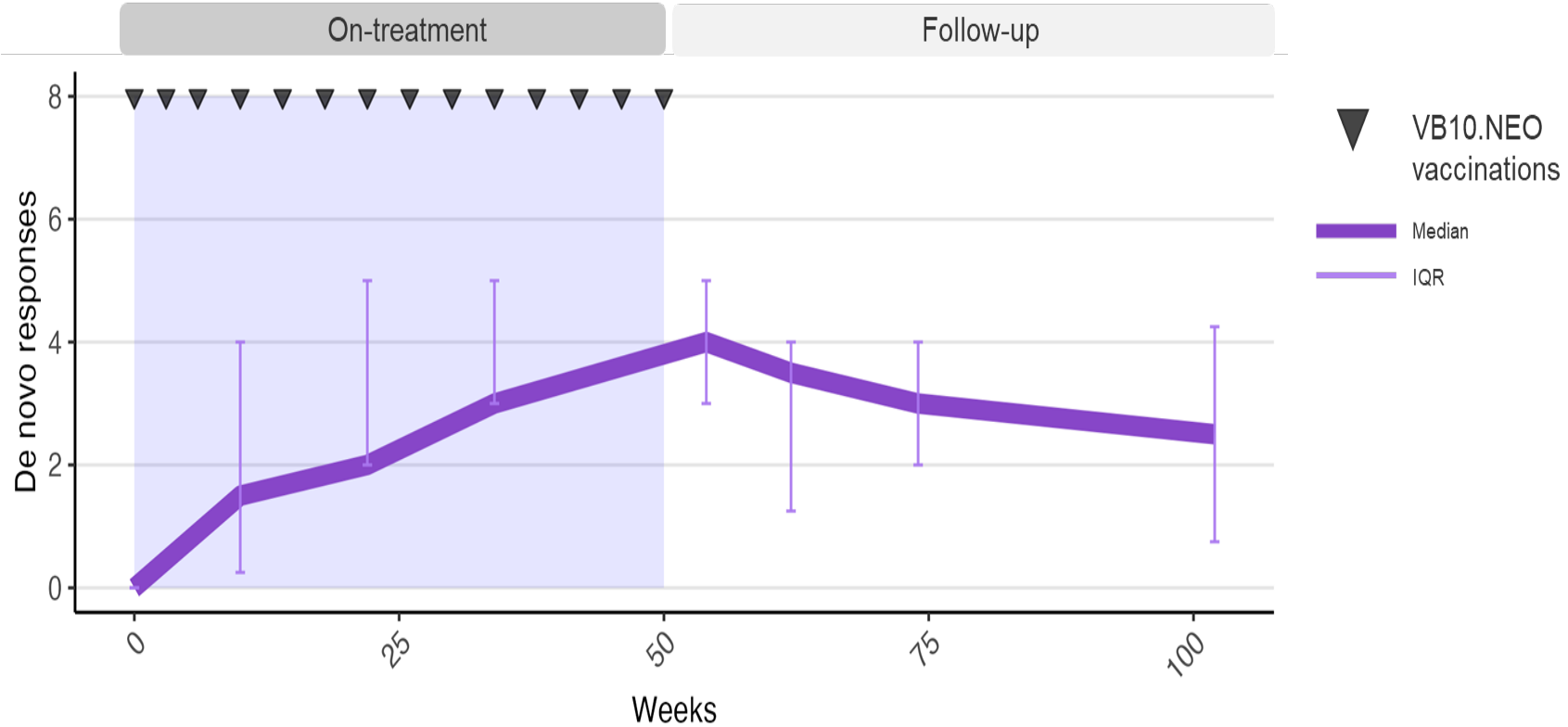
Indicates that vaccine-induced neoantigen-specific T cells in the periphery are able to infiltrate tumors

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



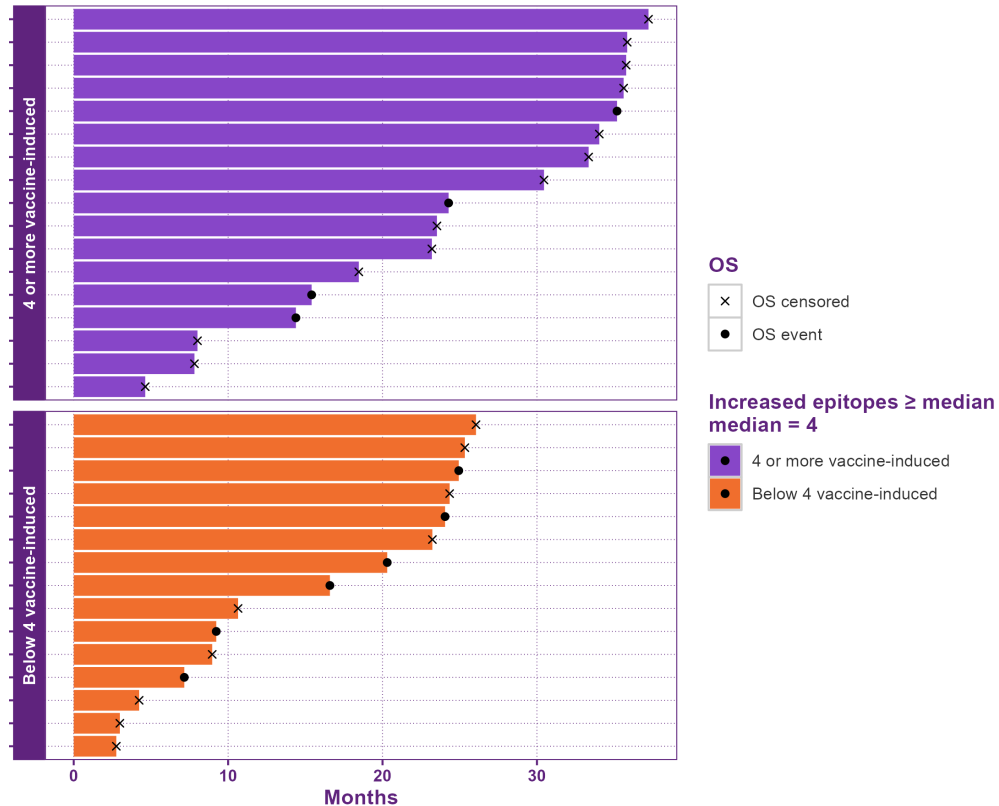
Vaccine-specific T cells remain functional and immunogenic up to 1-year after last vaccination

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

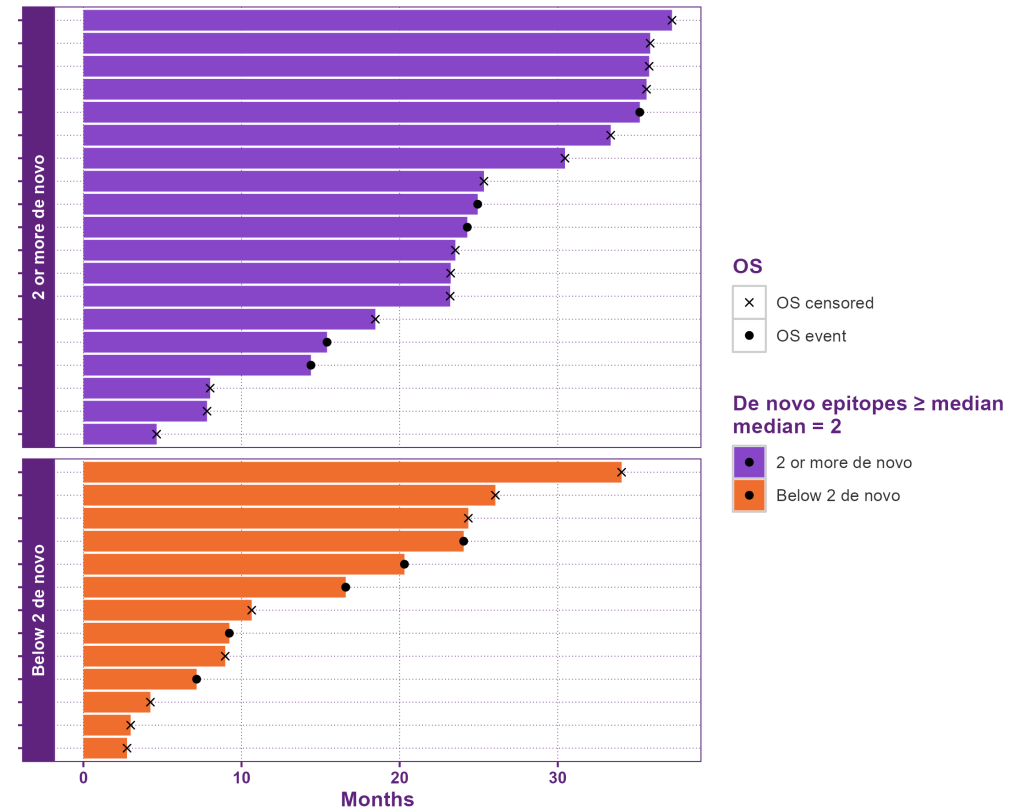


T cell responses per patient

Total T cell responses



De novo T cell responses



Patients grouped in lower and higher than median immune responses

Solid manufacturing chain

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



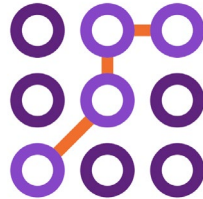
Safety

- ✓ 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



VB10.NEO Key Differentiators

Immune response

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



Competitive player

- ✓ Well-tolerated across trials and in different combinations
- ✓ Competitive COGS and TAT



Acknowledgement

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

UNLOCKING THE FUTURE OF MEDICINE

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