nykode therapeutics

Antigen presenting cell targeted vaccines

mRNA Cancer Vaccine Summit
October 12, 2023
Boston, MA

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

NYKODE THERAPEUTICS

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

Strategic partnerships with top tier US biopharma companies[1]

Genentech
A Member of the Roche Group

REGENERON

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

Autoimmune disease constitute a potential new therapeutic vertical

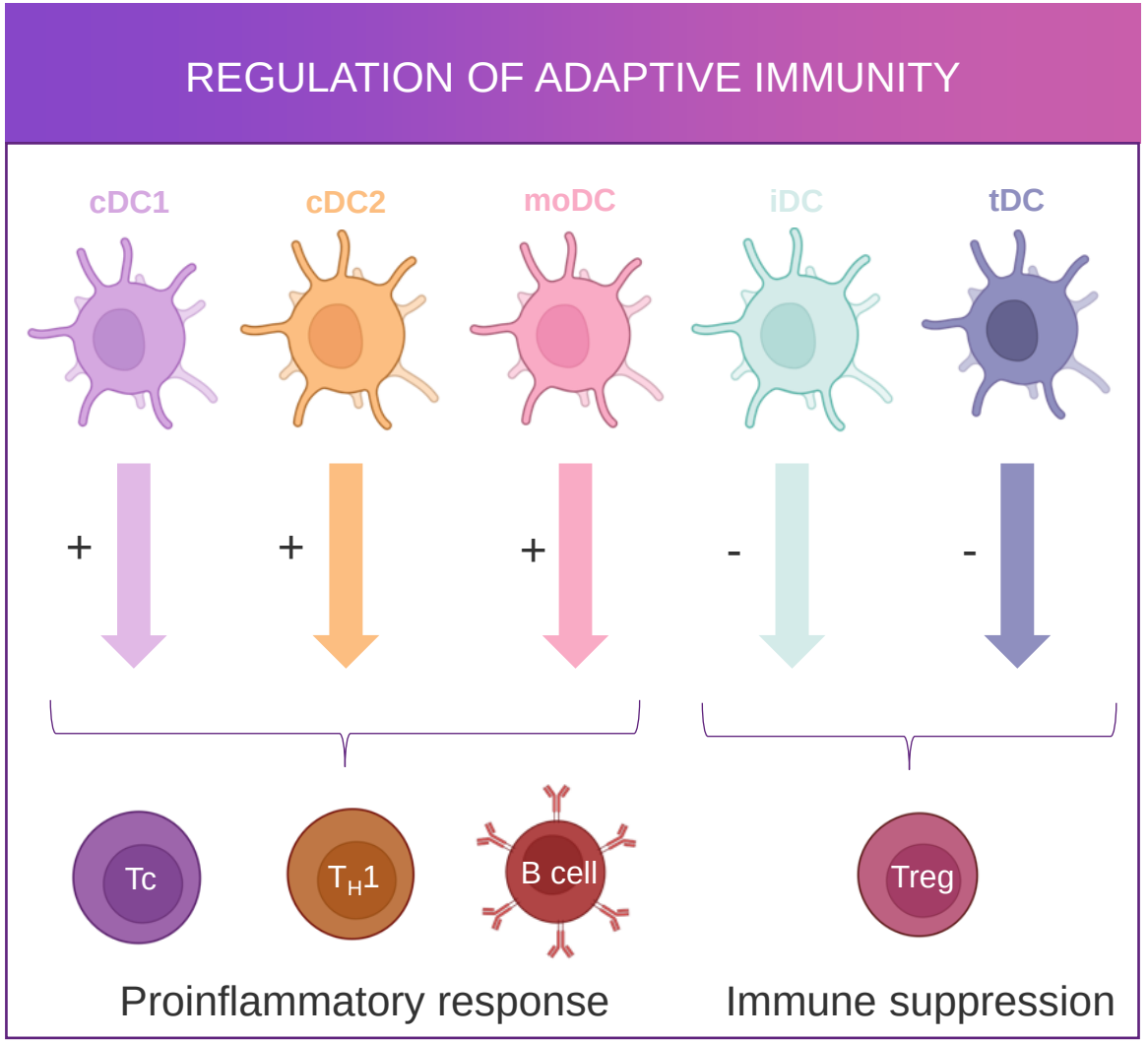
1. Note: Genentech has an exclusive license to VB10.NEO. Collaboration and license to 5 programs with Regeneron. Collaboration and license with Adaptive Biotechnologies on SARS-CoV-2 T cell vaccine. Roche supplies atezolizumab. Merck (MSD) supplies pembrolizumab

Rich and diversified pipeline

	Asset	Indication	Preclinical	Phase 1	Phase 2	Phase 3	
Oncology							
Off-the-shelf	VB10.16	HPV16+ cervical cancer					
	VB10.16	HPV16+ head and neck cancer					
	Regeneron programs	Undisclosed					REGENERON
	Internal	Undisclosed					
Individualized	VB10.NEO	Melanoma, lung, bladder, renal, head and neck cancer; locally advanced and metastatic tumors					Genentech A Member of the Roche Group
	VB10.NEO	Locally advanced and metastatic tumors					Genentech A Member of the Roche Group
Infectious Disease							
	Regeneron programs	Undisclosed					REGENERON
	Internal	Undisclosed					
Autoimmune							
	Internal	Undisclosed					

Antigen presenting cells - the portal to adaptive immunity

- Activation of the adaptive immune system is key to obtain effective and long-term immune responses
- APCs are the gatekeepers to adaptive immunity
- APCs come in different “flavors” with specialized immune functions
- Targeting antigens and epitopes directly to APCs is a highly effective way of triggering the desired adaptive immune responses



Modular vaccine technology allows APC-targeting to direct immune responses

DNA plasmid encoding Vaccibody

Module 1: Targeting unit to attract and bind APCs

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

Module 2: Dimerization unit for crosslinking targeted receptors on the surface of the APC

To facilitate strong bivalent binding

Module 3: Antigenic unit globular antigens or set of T cell epitopes

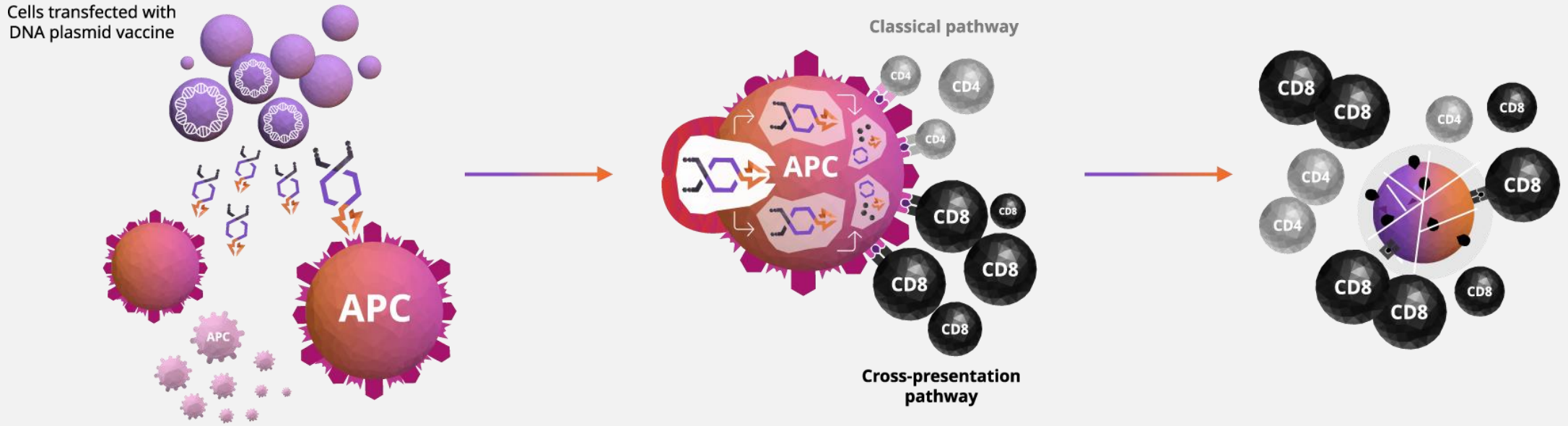
Antigens of choice from cancer, viruses, bacteria, parasites or autoimmune disease

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 vaccines induce 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.

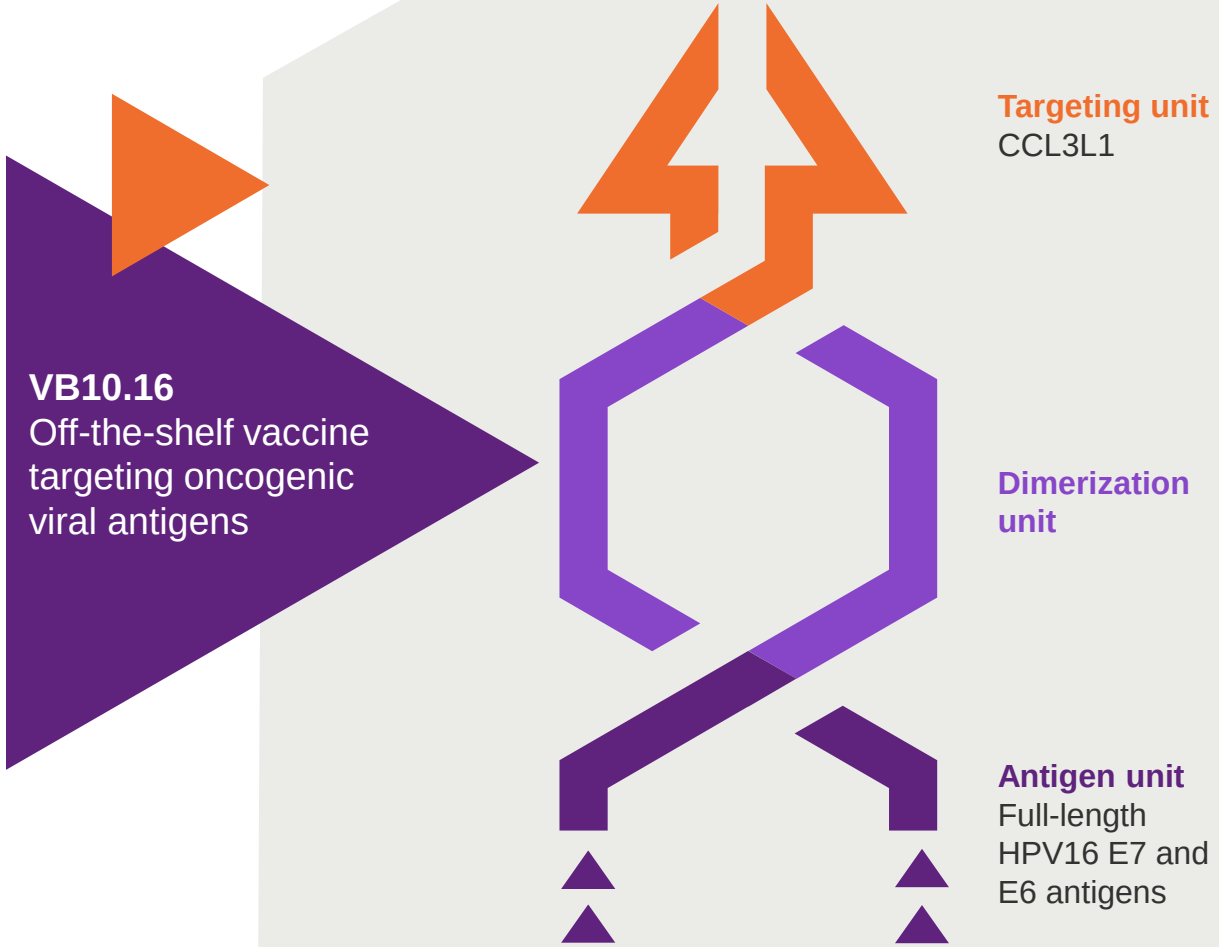
2 The APCs process and present the vaccine antigens to T cells and effectively activate CD8 killer T cells via cross-presentation.

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

VB10.16: therapeutic vaccine candidate for HPV16+ cancers

Off-the-shelf therapeutic cancer DNA vaccine against HPV16 induced malignancies

- HPV16 is the most prevalent oncogenic HPV strain
- Targeting the cancer-specific full-length HPV16 E7 and E6 antigens

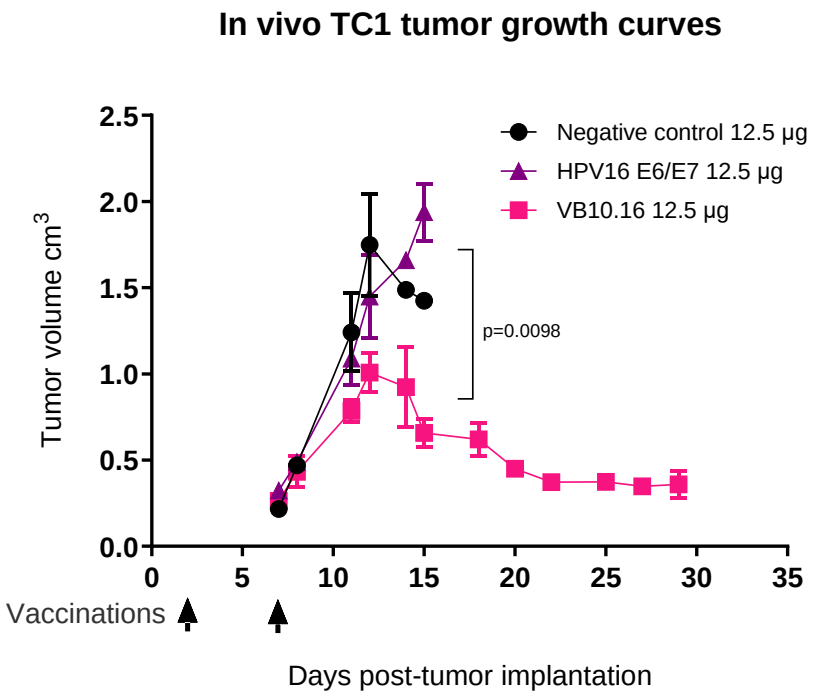


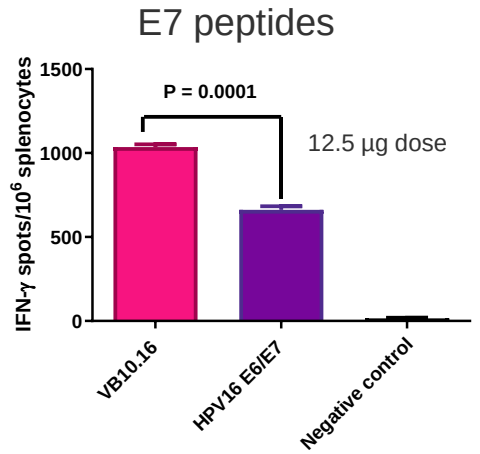
APC targeted HPV16 vaccine drives superior anti-tumor responses in an E6+E7 positive tumor model

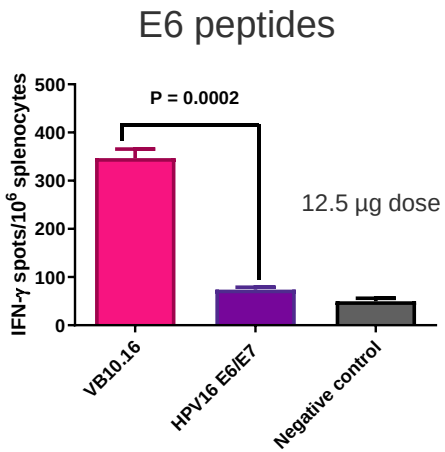
VB10.16 compared to non-targeted vaccine

- Induction of significantly stronger HPV16 specific IFN-γ T cell responses
- Strong anti-tumor efficacy with regression of large established tumors

E6+E7 POSITIVE TC1 TUMOR MODEL



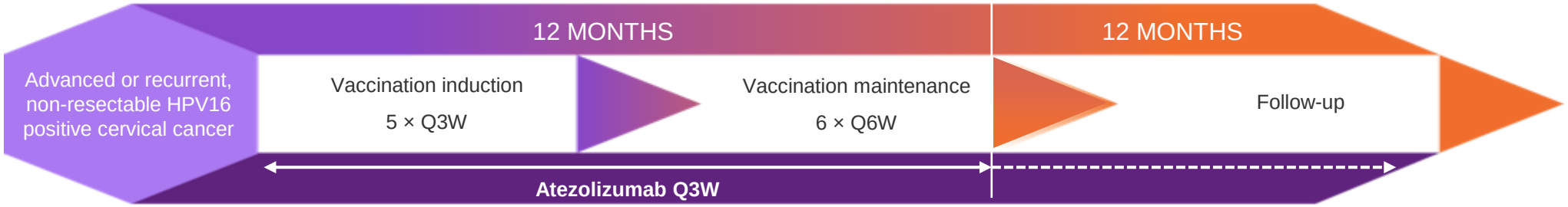




VB-C-02: VB10.16 plus atezolizumab (Tecentriq®) in advanced cervical cancer

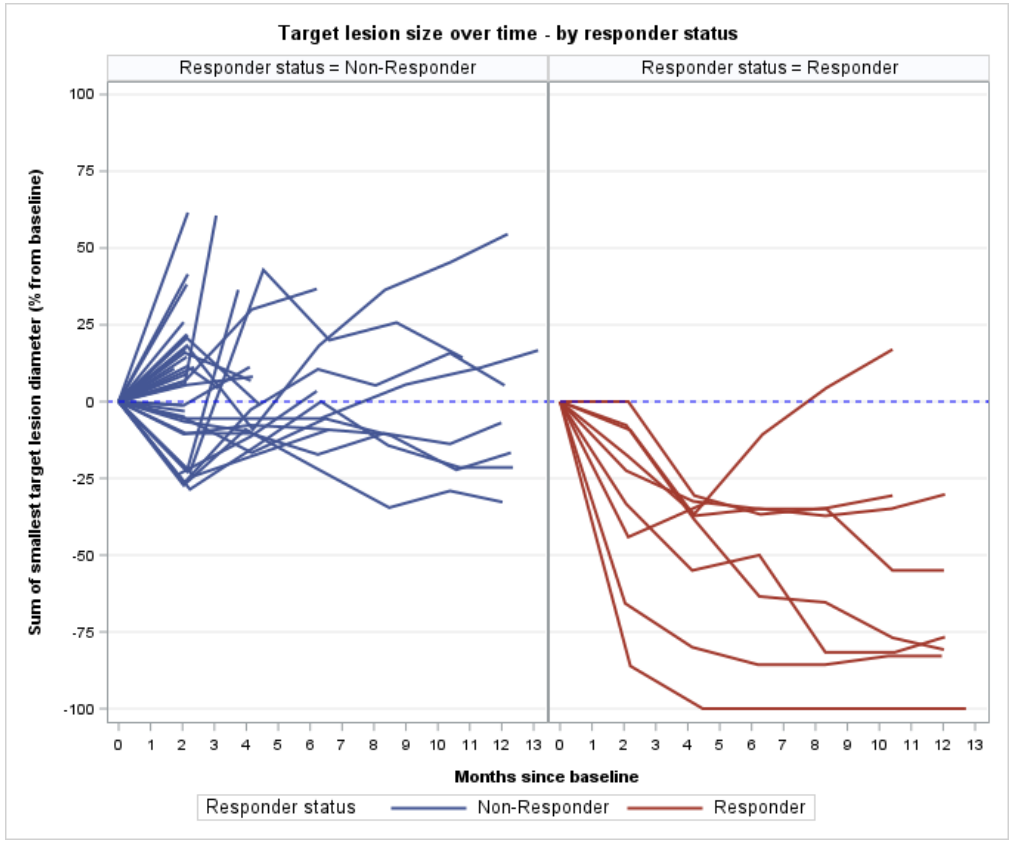
A Multi-Centre, Single Arm, Open-label Phase 2a Trial of the Combination of VB10.16 and atezolizumab in Patients with Advanced or Recurrent, Non-resectable HPV16 Positive Cervical Cancer (NCT04405349)

- **Objectives:** Safety/tolerability, immunogenicity and efficacy
- **Primary endpoints:** Incidence/severity of AEs, overall response rate (ORR) as per RECIST 1.1 by blinded independent central review (BICR)
- **Secondary endpoints:**
  - Duration of response (DOR)
  - Progression-free survival (PFS)
  - Overall survival (OS)
  - Evaluate immunogenicity of VB10.16 in combination with atezolizumab by analysing HPV16 E6/E7-specific cellular immune responses
- Conducted in Europe in 6 countries (Germany, Belgium, Bulgaria, Czech Republic, Poland and Norway)
- Fully enrolled with 52 patients
- Enrolled patients received treatment with 3 mg VB10.16 in combination with 1200 mg atezolizumab up to 48 weeks, with atezolizumab monotherapy dosed every 3 weeks, and a follow up period of up to 12 months

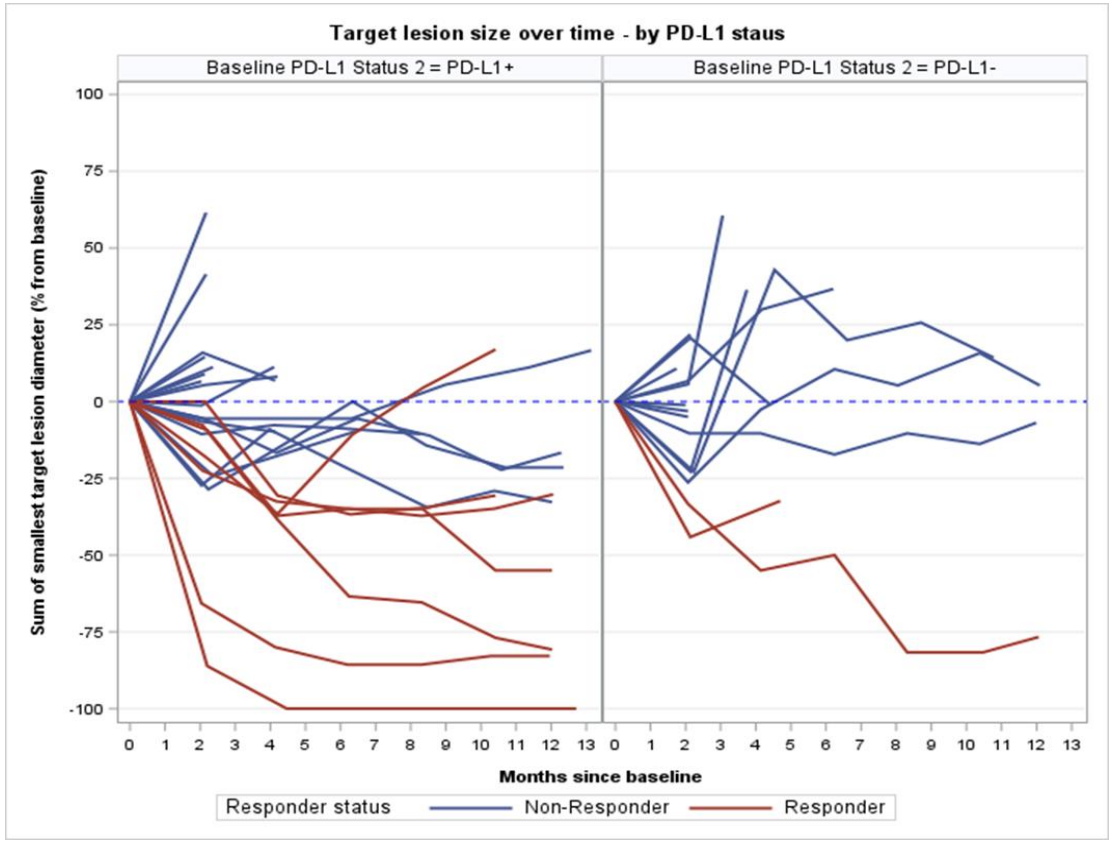


VB10.16 coupled with CPI led to durable responses

All (n = 47)



By PD-L1 status (n = 40)



Note: 7 out of 47 responders had PD-L1 unknown status, 40 out of 47 had known PD-L1 status

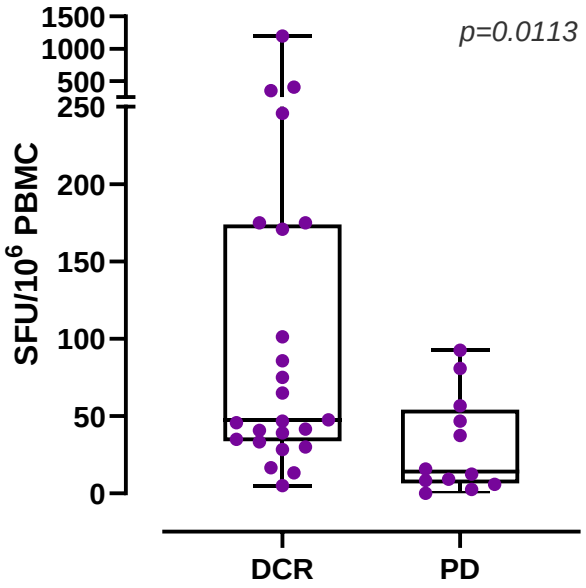
C-02 data supports patient population selection for potentially registrational study

- Clinical activity observed across all endpoints, with strongest results in PD-L1+ patients with 1 prior line of systemic therapy
- Duration of response data in PD-L1+ patients show potential for competitive positioning in this patient population

Endpoint	All	PD-L1+ and 1 prior line of SACT
ORR	19%	40%
CR	6%	13%
DCR	60%	80%
mDOR, months	17.1	17.1
mPFS, months	4.1	16.9
mOS, months	16.9	>25 N.R.

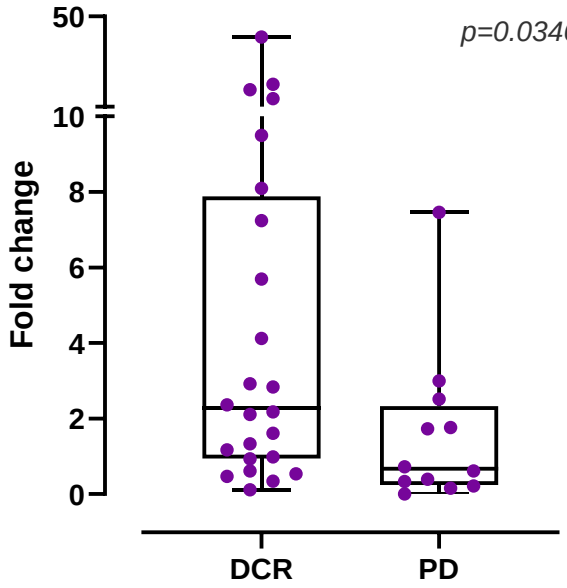
VB10.16 induced HPV16-specific T cell responses that are significantly correlated with clinical response

HIGHER PEAK T CELL RESPONSES IN PATIENTS WITH DISEASE CONTROL



Absolute count at peak visit post-treatment

HIGHER FOLD INCREASED T CELL RESPONSES IN PATIENTS WITH DISEASE CONTROL



Fold change, baseline to peak count post-treatment

Note: Ex vivo ELISpot analysing HPV16 E6 and E7 responses with background subtracted n = 36 (n = 24 DCR, n = 12 PD). Data not available for 11 subjects

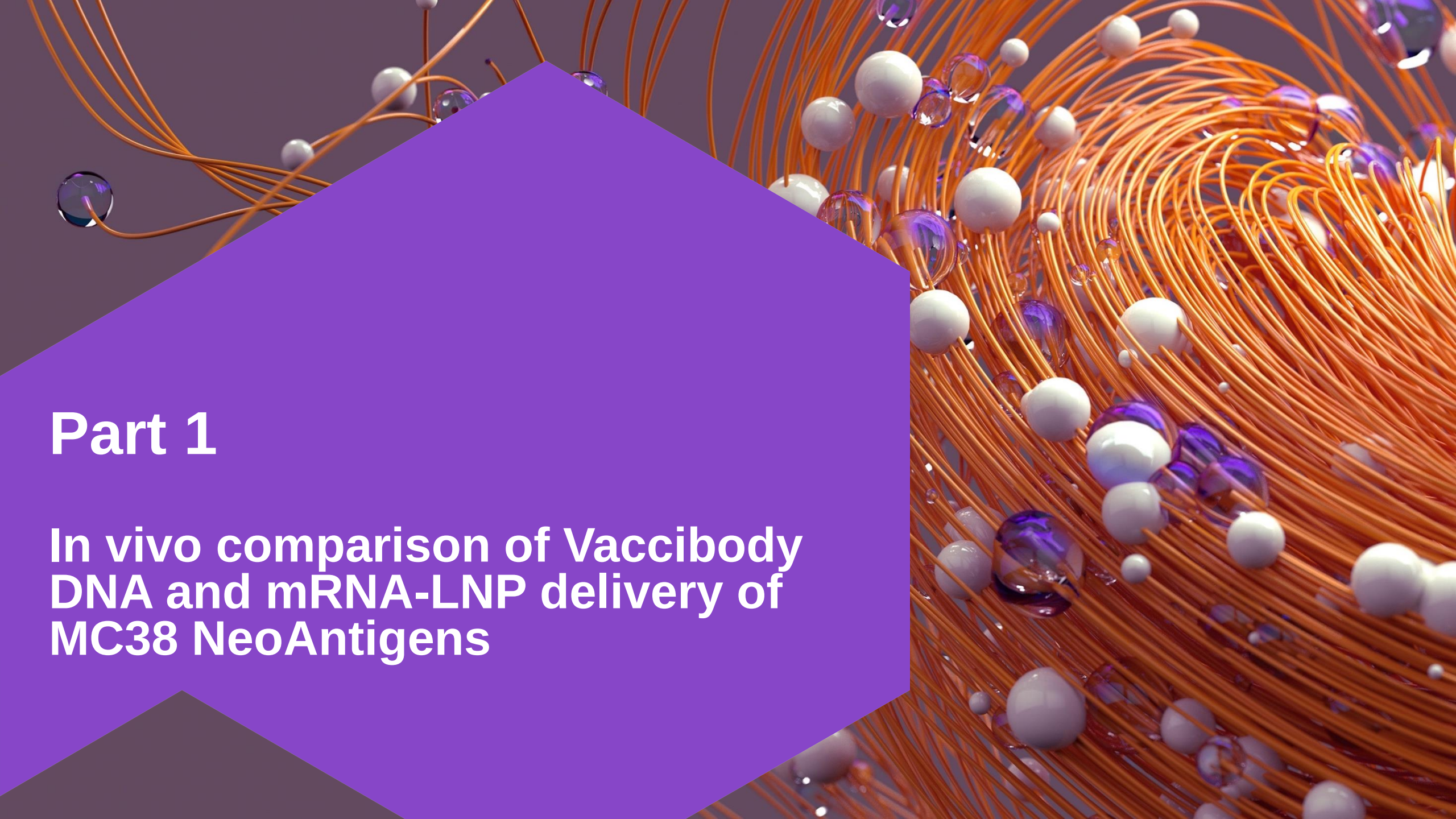
VB10.16 in combination with atezolizumab showed promising clinical profile with favorable tolerability in patients with advanced HPV16+ cervical cancer

- Clinically relevant endpoint mPFS was 4.1, 6.3 and 16.9 months for all, PD-L1+ and PD-L1+ with one prior treatment line, respectively
- Clinically relevant endpoint mOS was 16.9 months and not reached (> 25 months) for all patients and PD-L1+ patients, respectively
- VB10.16 plus atezolizumab demonstrated ORR 19% with median duration of response 17.1 months and DCR of 60%
- In the PD-L1+ and PD-L1+ plus one prior treatment line subgroups, overall response rates were **29%** and **40%**, respectively
- VB10.16 induced HPV-16 specific T cell responses that are significantly correlated with clinical response

Together these findings indicate a potentially differentiated and lasting anti-tumor response pattern of the combination treatment compared to checkpoint inhibitor monotherapy[1]

The subgroup analyses support the planned studies with VB10.16 in PD-L1+ patients who have received max 1 prior line of systemic anticancer treatment in the advanced disease setting

Note:[1]Chung et al. Efficacy and safety of pembrolizumab in previously treated advanced cervical cancer: Results from the phase II KEYNOTE-158 study. J Clin Oncol 2019; Tewari et al. Survival with cemiplimab in recurrent cervical cancer. N Engl J Med 2022; Tabernero et al. Phase II multicohort study of atezolizumab monotherapy in multiple advanced solid cancers. ESMO Open. 2022.



Part 1

In vivo comparison of Vaccibody DNA and mRNA-LNP delivery of MC38 NeoAntigens

mRNA and LNP platforms used in our preclinical studies

- In the clinical setting, we so far leveraged the benefits of needle free delivery of Vaccibodies by DNA to induce $CD8^+$ responses with high tolerability
- We are exploring other delivery modes guided by disease specific applications

mRNA

TriLink BIOTECHNOLOGIES part of Maravai LifeSciences

N1-Methyl-Pseudo-U modified
Capped (Cap 1) using CleanCap® AG
Polyadenylated (80A)

Lipid Nanoparticles (LNPs)

PRECISION NANOSYSTEMS

GenVoy-ILM based lipid formulation
intramuscular (i.m.) injection

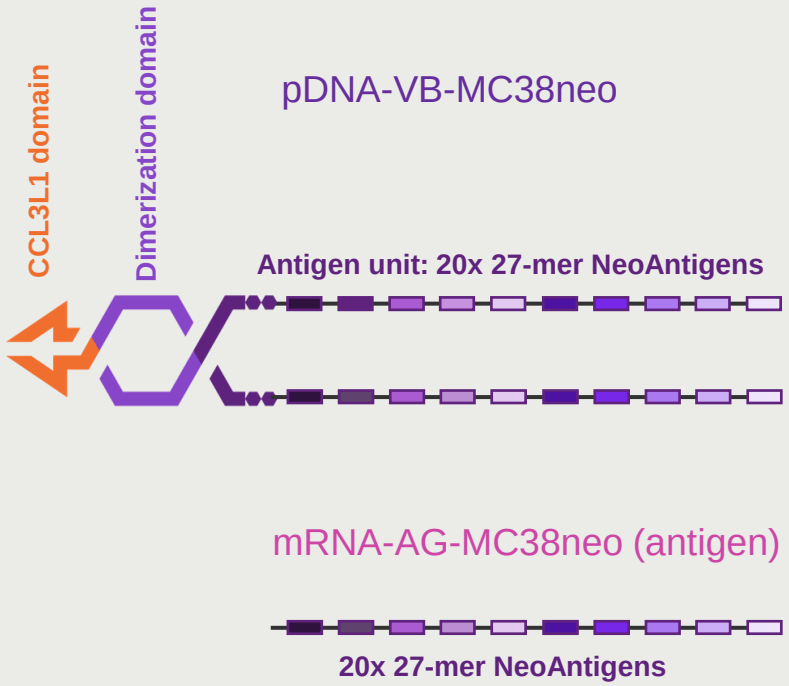
Target characteristics for mRNA/LNP formulation

- Particle size < 200 nm (preferably <100 nm)
- Polydispersity index < 0.2
- Encapsulation efficiency (%EE) > 70% (preferably > 80%)

Sample ID	Size (d.nm)	PDI	Zeta Potential (mV)	Encapsulation efficiency (%)	Final RNA concentration (mg/mL)
Example 1	110	0.16	-4	99	504
Example 2	115	0.16	-5	99	524

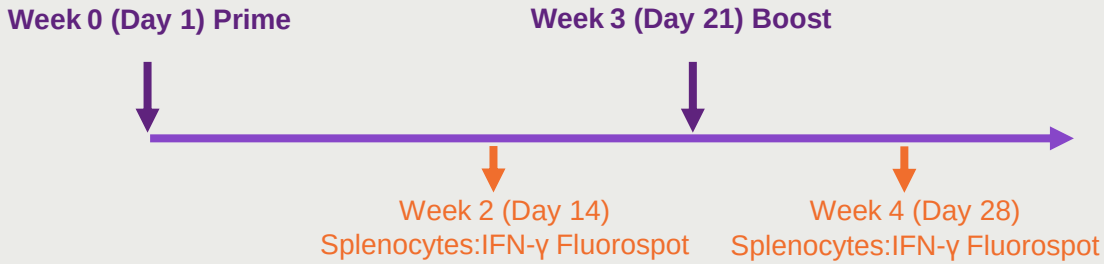
MC38 NeoAntigen vaccine: Vaccibody delivered as pDNA compared to antigen delivered as mRNA-LNP

Constructs used



Experimental setup

C57BL/6
n=5 per group

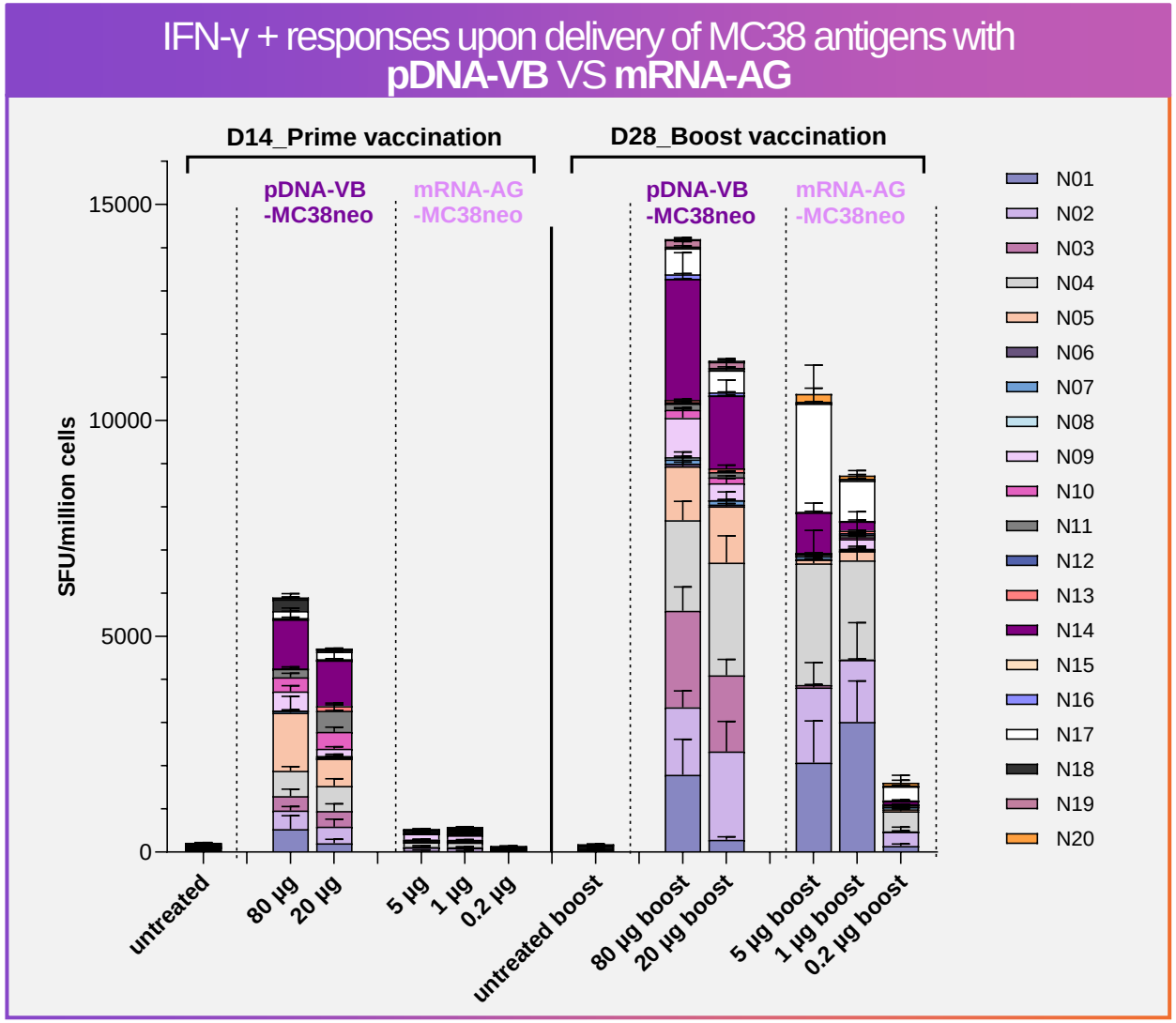


Five groups:

1. pDNA-VB-MC38neo (20, 80ug) intramuscular + electroporation
2. mRNA-AG-MC38neo (0.2, 1, 5ug) in LNP intramuscular

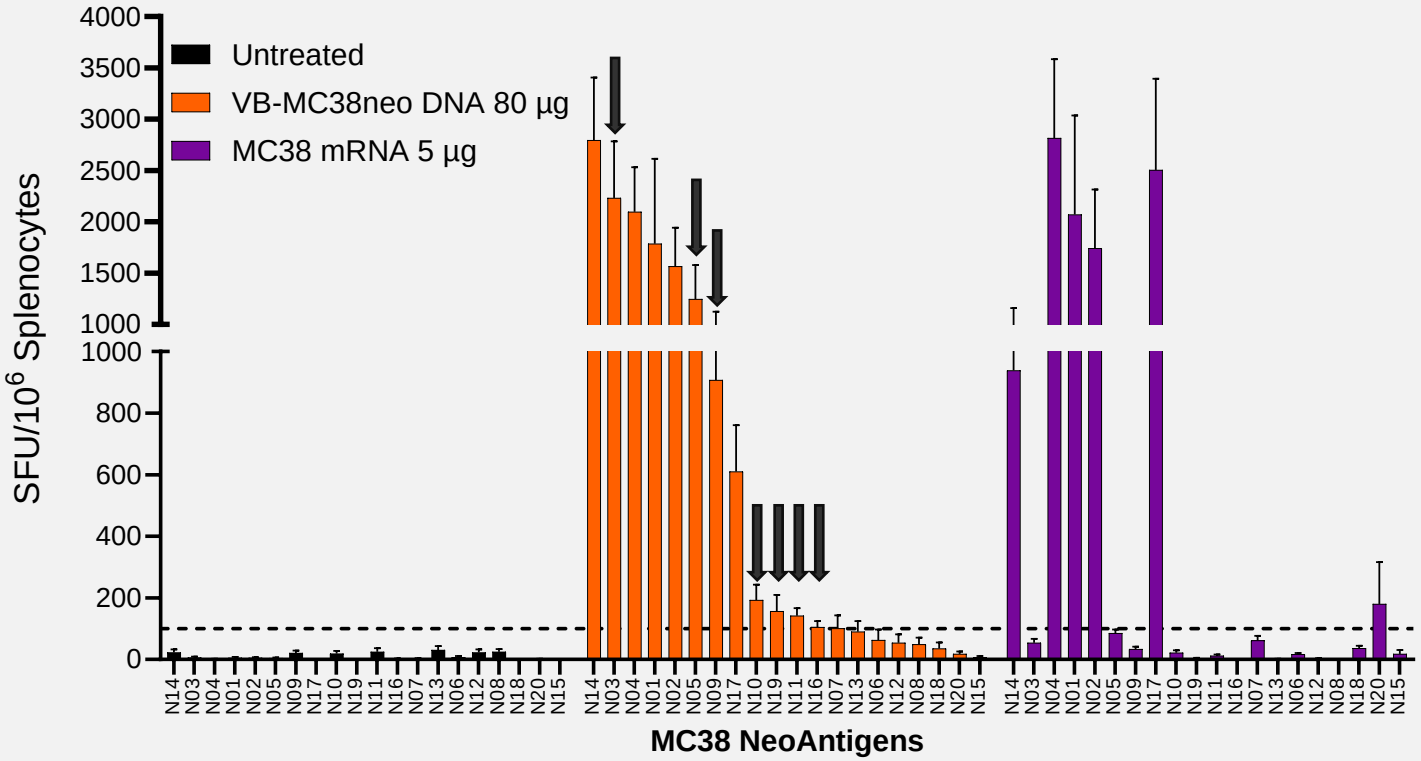
pDNA-VB and mRNA-AG drive strong MC38neo immunogenicity after prime+boost regimen

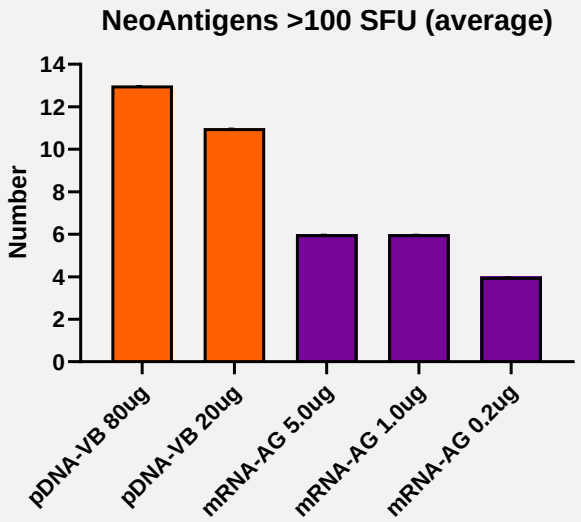
- pDNA-VB induces significantly stronger immune responses compared to mRNA-AG after a single immunization
- Similar magnitude of total T cell responses by DNA and mRNA immunization after boost
- pDNA-VB induces a broader T cell response compared to mRNA-AG



Vaccibodies delivered as pDNA generates broader T cell responses to MC38 NeoAntigens

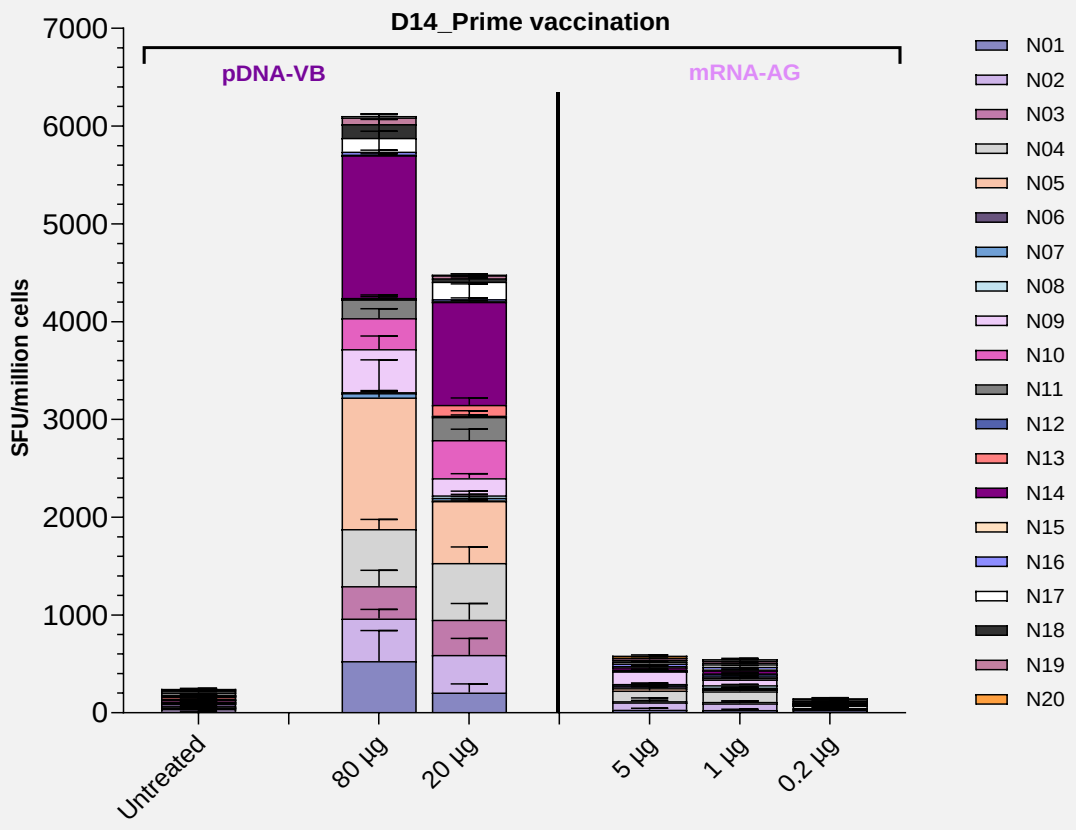
DNA-encoded vaccibody induced responses to a greater number of neoantigens

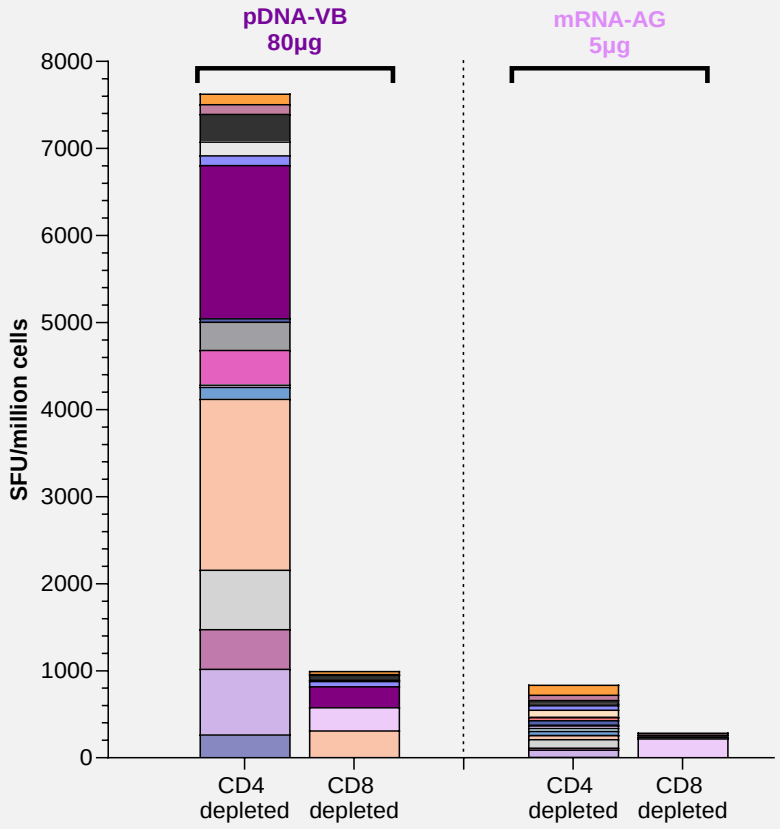




DNA vaccibody immunization generates strong CD8+ driven prime responses against multiple MC38 NeoAntigens

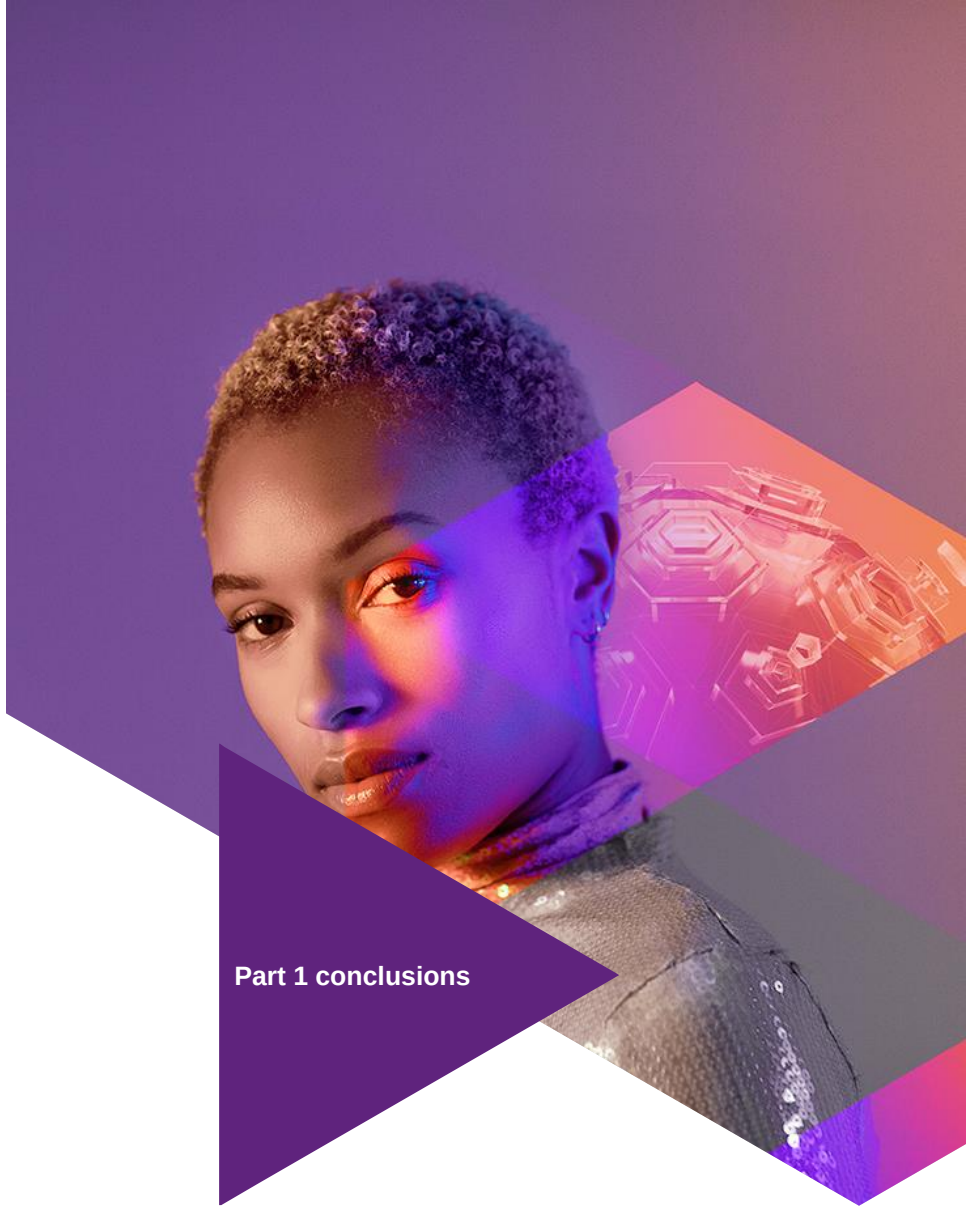
Strong prime responses seen with DNA-VB vaccination are CD8 driven





Conclusions Part 1

- DNA vaccination with Vaccibodies containing NeoAntigens result in broader T cell responses compared to mRNA-LNP delivery of the same NeoAntigens
- DNA vaccination with Vaccibodies containing NeoAntigens generates superior T cell responses following a single vaccination driven primarily by CD8 responses compared to mRNA delivery of the same epitopes
- Similar magnitude of total T cell responses by DNA and mRNA vaccination after boost

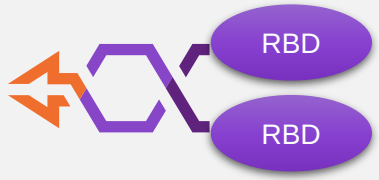


Part 2

Vaccibody delivery by mRNA in LNP

mRNA-LNP delivered Vaccibodies encoding viral structural antigens are intact and highly immunogenic

Design and In vitro characterization

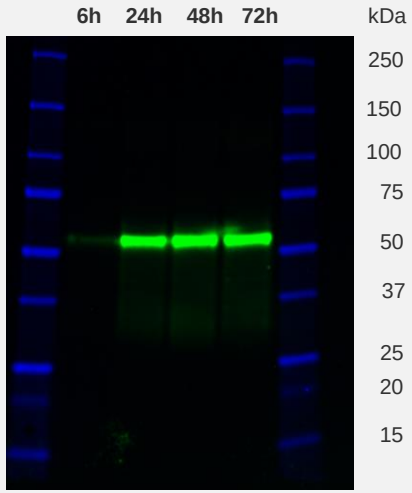


CCL3L1 domain

Antigen unit: SARS-CoV2-RBD

- Well expressed protein
- Correct MW
- Binds CCR5

mRNA-VB2060

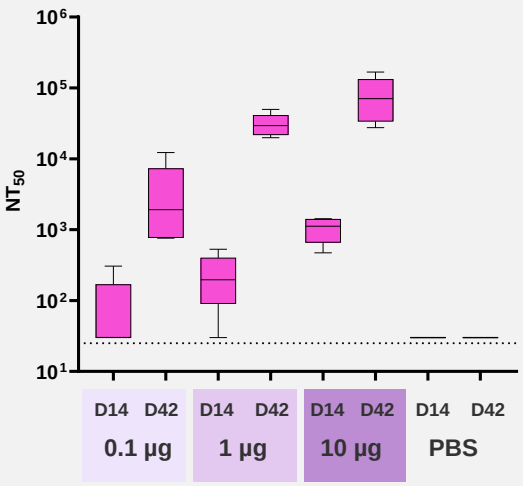


mRNA-LNP transfection

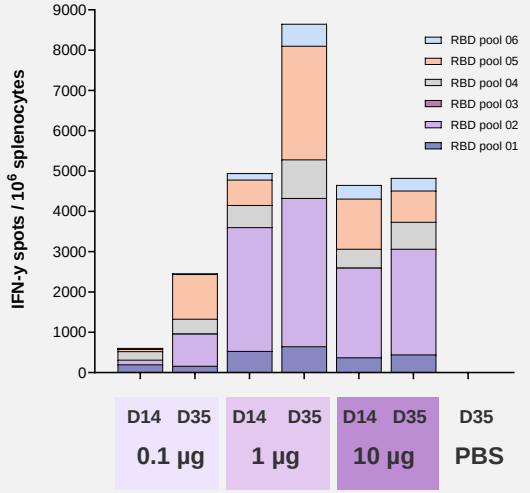
In vivo

mRNA-LNP Vaccibodies elicit dose-dependent strong antiviral antibody and T cell responses, and demonstrate boost effect

Neutralizing antibodies



T cell responses



mRNA-LNP delivered Vaccibodies encoding a NeoAntigen cassette are intact and highly immunogenic

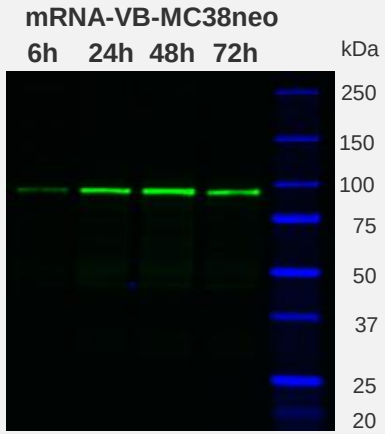
Design and in vitro characterization

mRNA-VB-MC38neo

CCL3L1 domain

Antigen unit: 20x 27-mer NeoAntigens

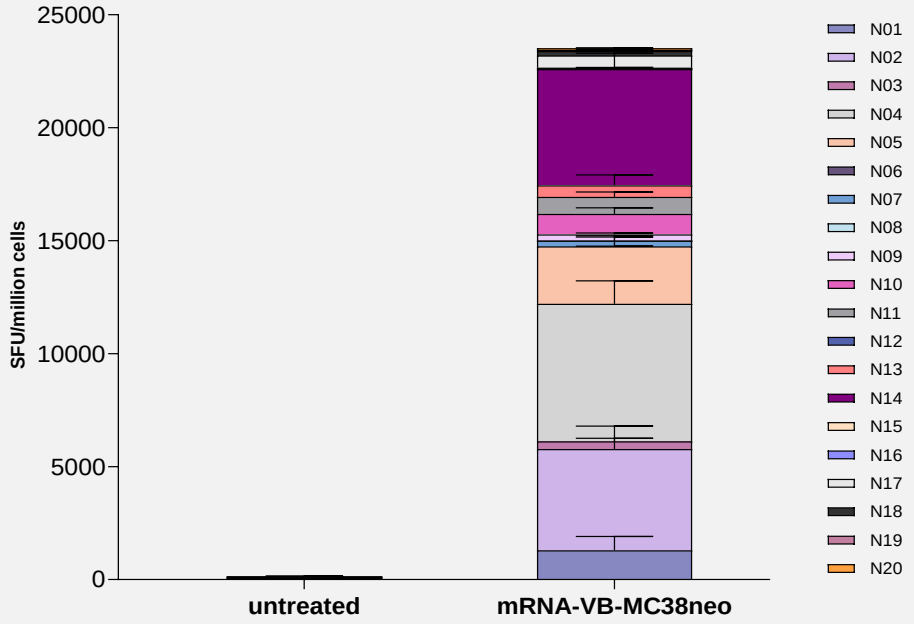
- Well expressed protein
- Correct MW



mRNA-LNP transfection

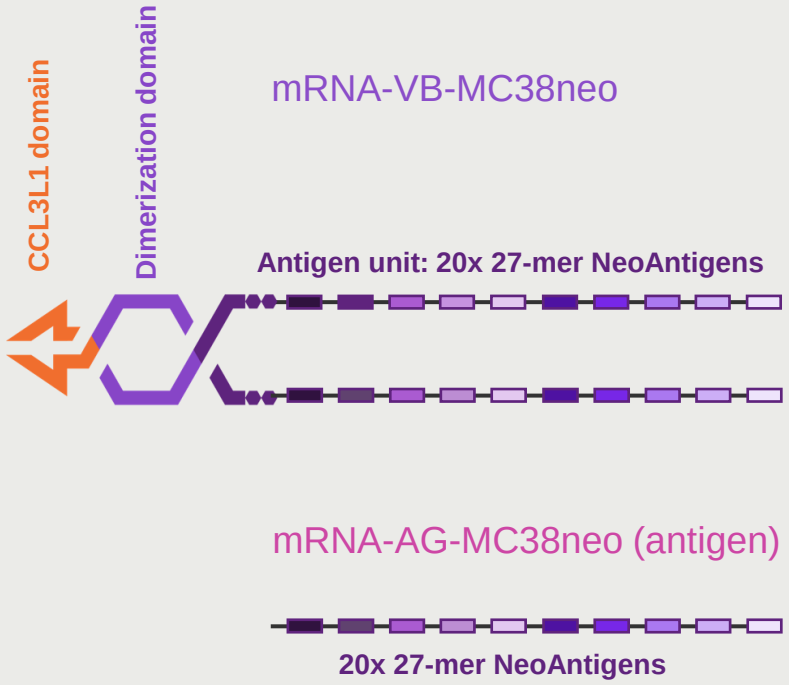
Strong and broad T cell responses

Vaccination with 1ug of the Vaccibody neoantigen vaccine resulted in a broad T cell response in IFN-γ Fluorospot assay (prime-boost regimen)



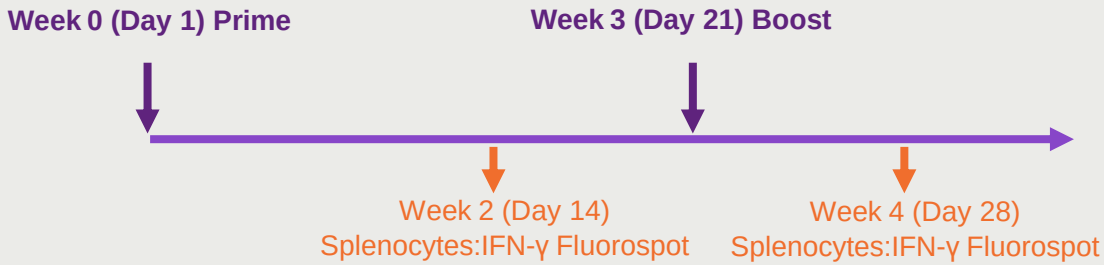
MC38 NeoAntigen vaccine: Vaccibody compared to antigen alone when both are delivered as mRNA-LNP

Constructs used



Experimental setup

C57BL/6
n=5 per group



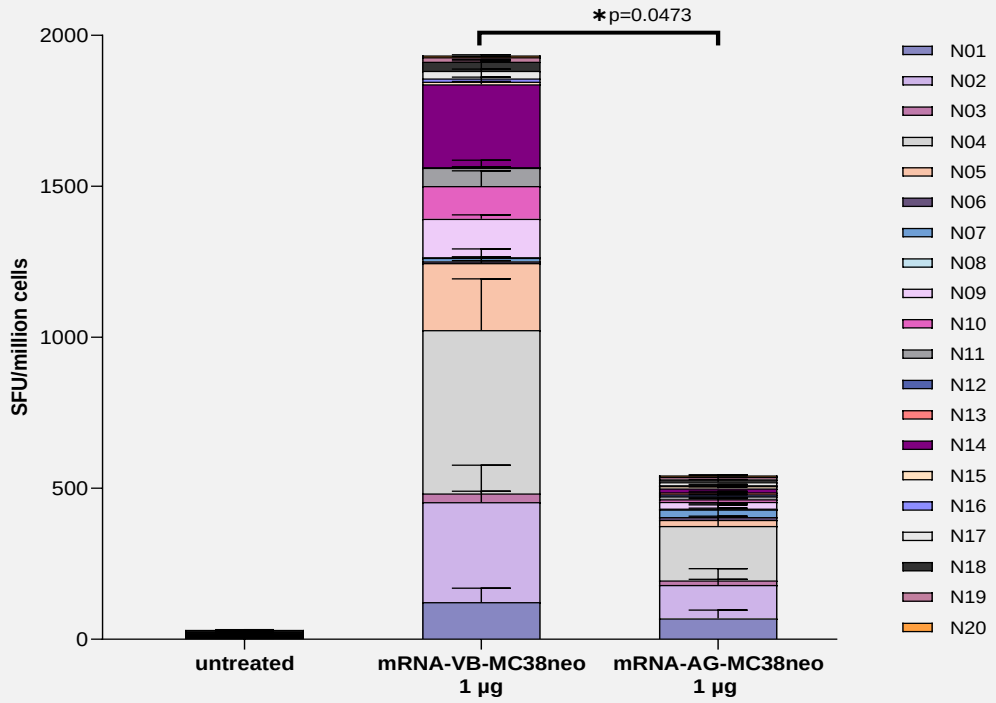
Groups:

1. mRNA-VB-MC38neo (1ug) in LNP intramuscular
2. mRNA-AG-MC38neo (1ug) in LNP intramuscular

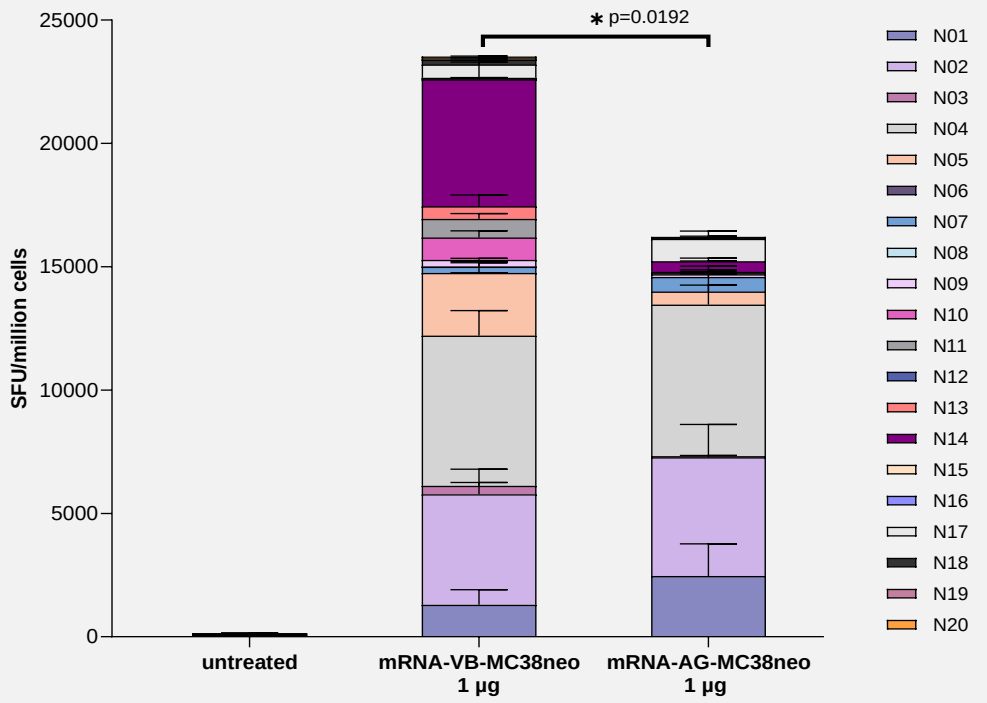
Vaccibody induces stronger immune responses than a neoantigen-only vaccine

IFN-γ+ fluorospot responses to MC38 neoantigens

Prime vaccination only (D14)

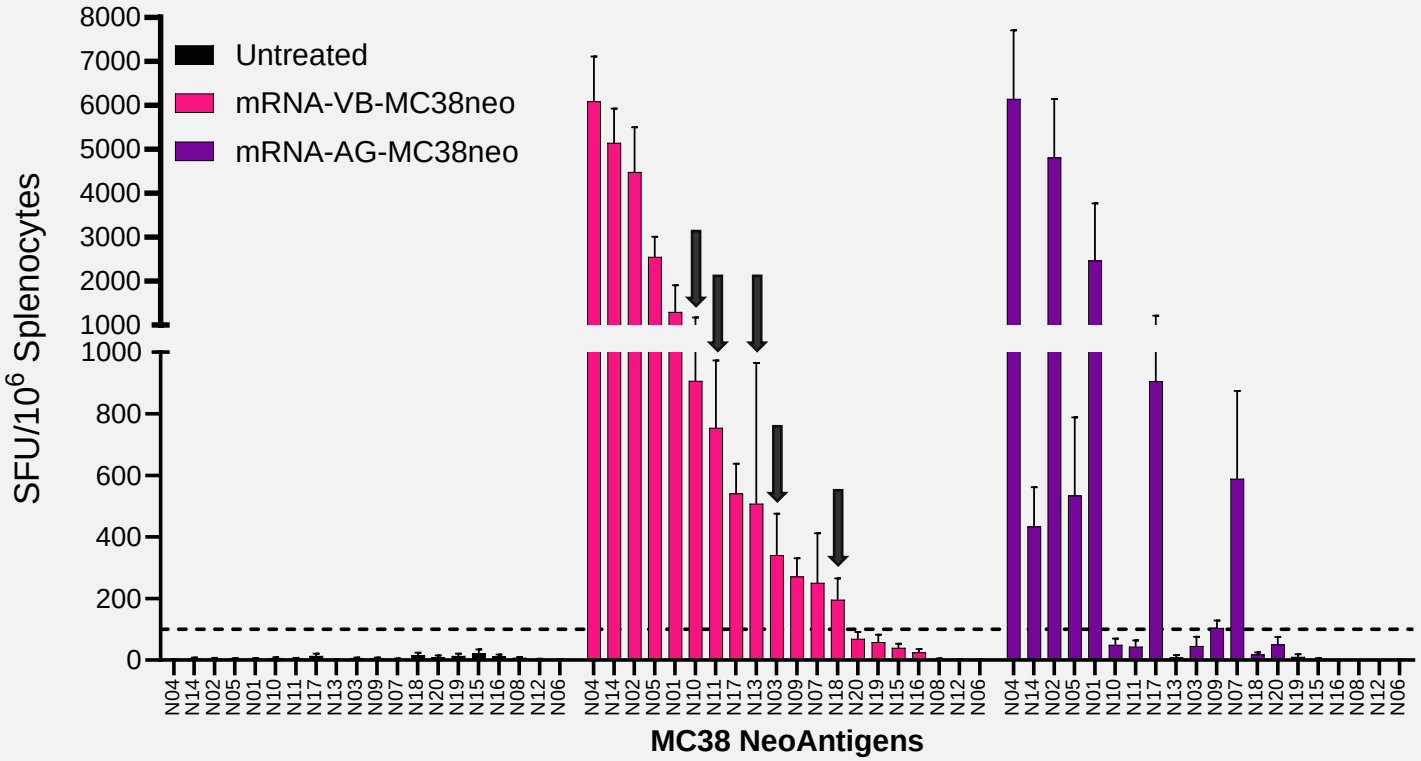


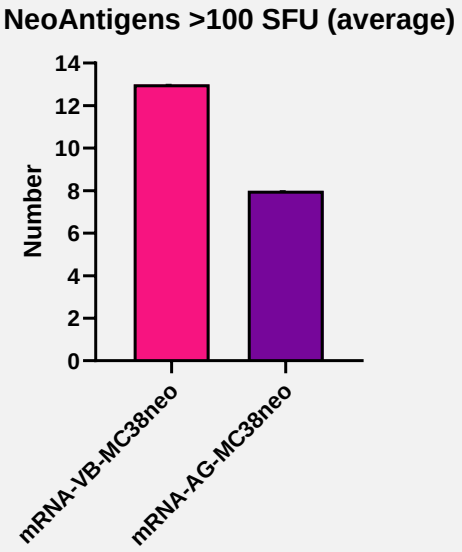
Prime + boost vaccination (D28)



Vaccibody generates a broader T cell response

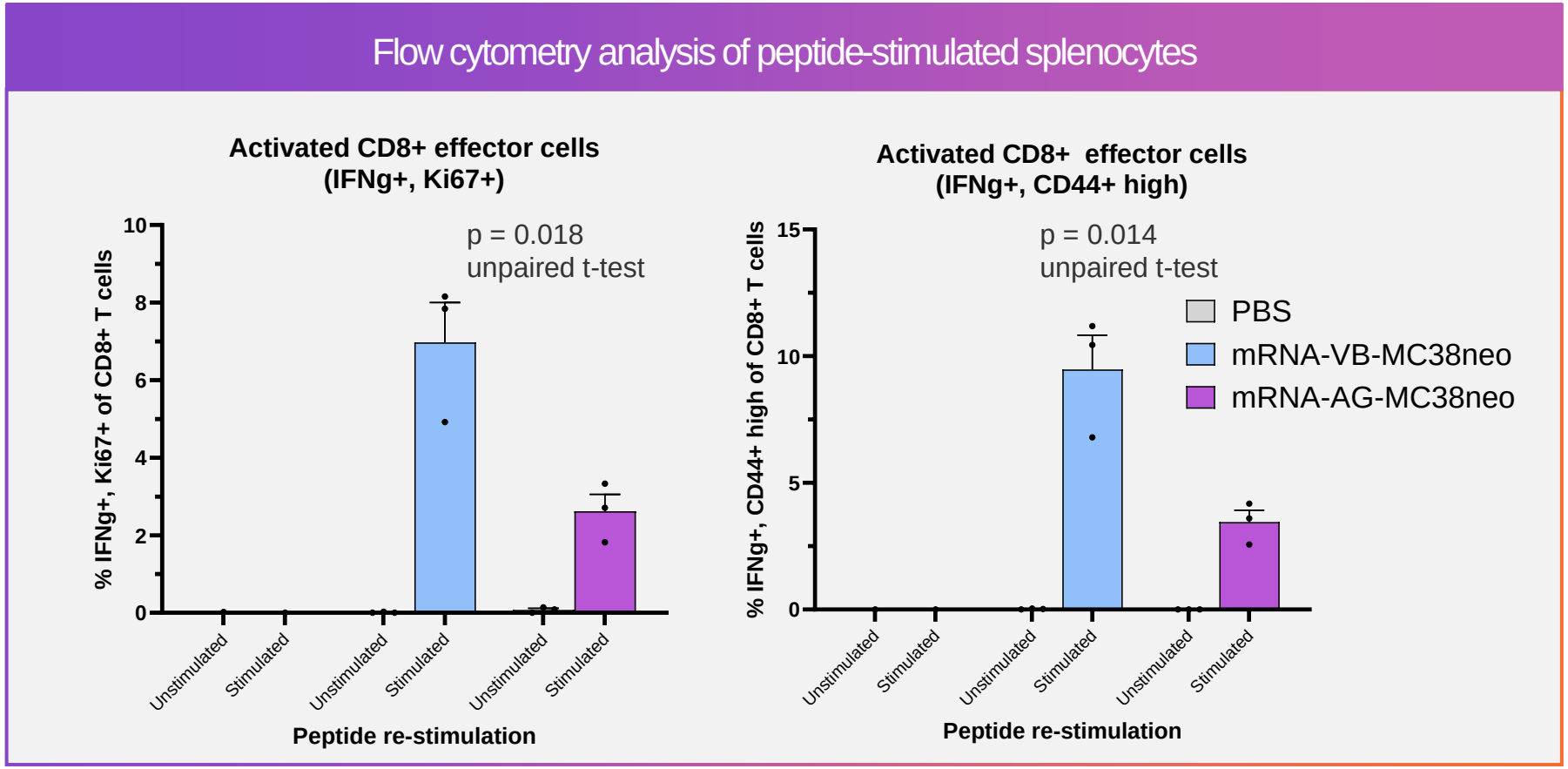
mRNA-encoded vaccibody induced responses to a greater number of neoantigens





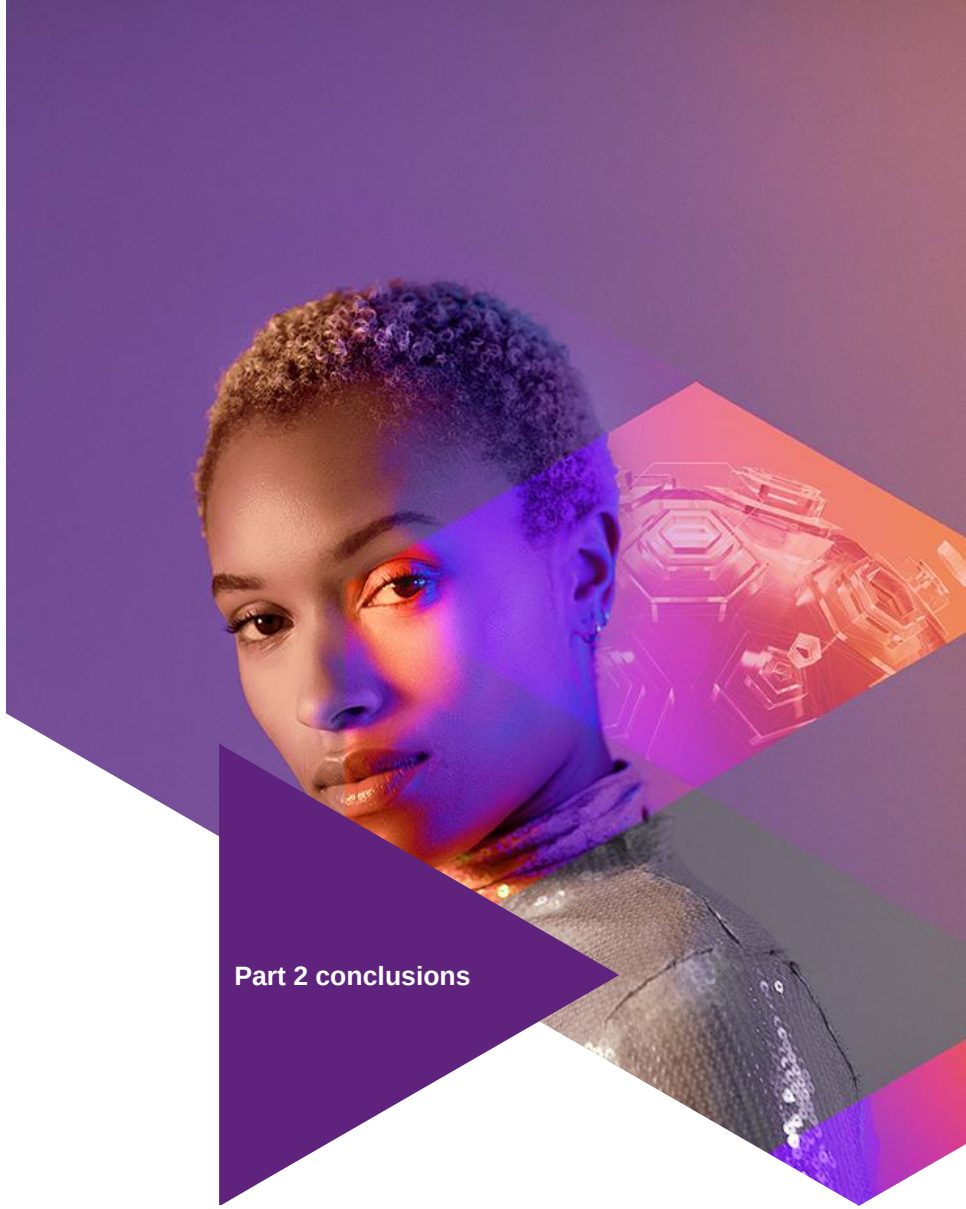
Flow cytometry analysis confirms a strong Vaccibody mRNA-LNP CD8 T cell response

mRNA-VB-MC38neo results in a higher percentage of activated CD8+ effector cells



Conclusions Part 2

- Vaccibodies encoding T cell epitopes or structured antigens can be delivered by mRNA and generate strong T cell and antibody responses in animals
- mRNA vaccination with Vaccibodies containing NeoAntigens results in broader and stronger T cell responses compared to mRNA delivery of the same epitopes
- mRNA vaccination with Vaccibodies is heavily CD8 focused and driven by the unique targeting to antigen presenting cells



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Synne Hougsnæs
Anna Lunde
Marit Renee Myhre

Contact
Mikkel Wandahl Pedersen
CSO
MWPedersen@nykode.com

THANK YOU