nykode therapeutics

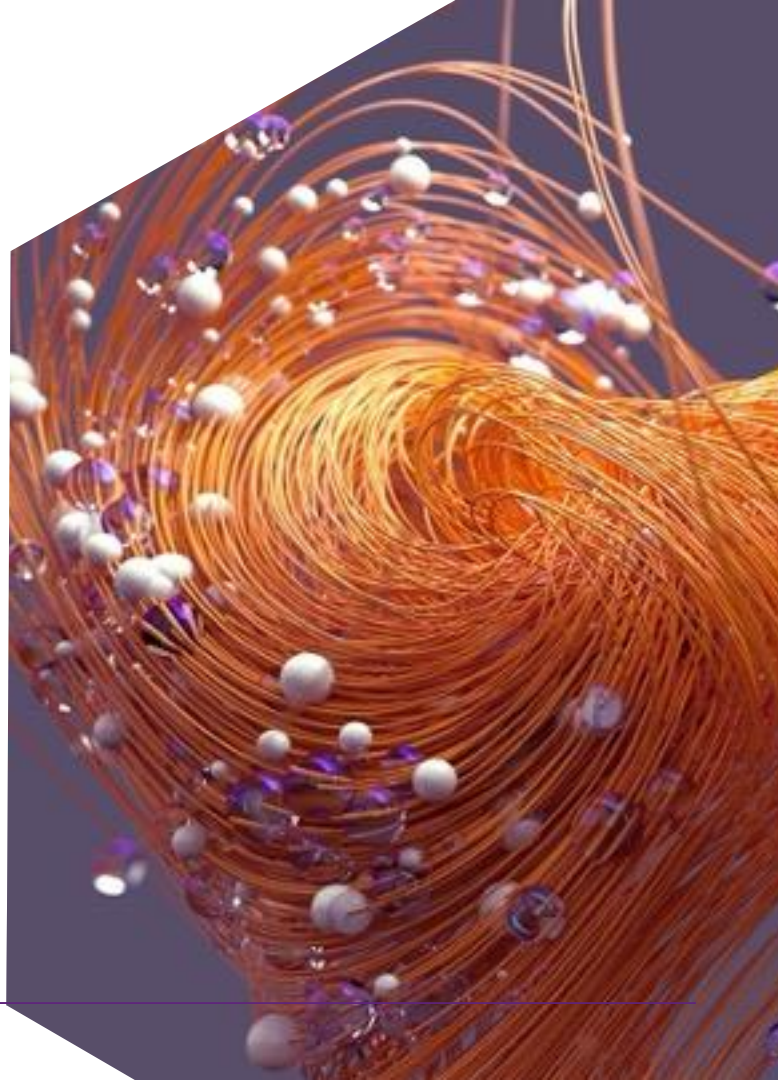
Targeting Cancer Antigens to Antigen Presenting Cells to Elicit Rapid, Broad and Dominant CD8 T Cell Responses

March 22, 2022

Keystone Symposium: Cancer Immunotherapy

Overview

- Clinical stage immunotherapy company with pipeline in oncology and infectious disease vaccines
- Vaccibody™ immunotherapy platform targets antigens to Antigen Presenting Cells (APCs) for a rapid, broad and controlled immune response
- Unique Vaccibody construct can deliver all major vaccine types: DNA, RNA, viral, fusion protein
- Recently changed name from Vaccibody to Nykode Therapeutics to capture preclinical activities within Ag-specific immune tolerance and further innovative drug design



Pipeline

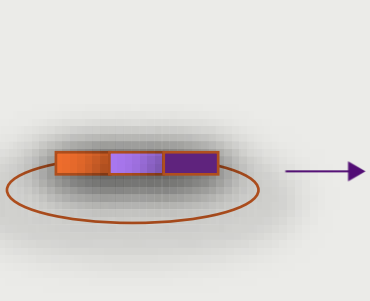
	Program	Indication	Discovery/ Preclinical	Phase 1	Phase 2	Phase 3	Partnerships
Nykode							
Oncology	**VB10.16 (off-the-shelf)**	**HPV16+ cervical cancer[3]**					
	Internal (off-the-shelf)	Undisclosed targets					
Infectious Disease	**VB10.COV2**	**SARS-CoV-2**					Adaptive[4]
	Internal	Undisclosed targets					
Partnered							
Oncology	VB10.NEO (individualized)	Melanoma, lung, bladder, renal, head and neck					Genentech[1] NEKTAR[2]
	VB10.NEO (individualized)	Locally advanced and metastatic tumors					Genentech[1]
	Regeneron (programs 1 – 3) (off-the-shelf)	Undisclosed					REGENERON[5]
Infectious Disease	Regeneron (programs 4 – 5)	Undisclosed					REGENERON[5]

1. Genentech has an exclusive license to VB10.NEO; 2. Collaboration with Nektar Therapeutics on combining NKTR-214 (bempegaldesleukin) with VB10.NEO in trial arm 5B (SCCHN); 3. Roche supplies atezolizumab; 4. Collaboration with Adaptive Biotechnologies on SARS-CoV-2 T cell vaccine; 5. Collaboration with Regeneron

Vaccibody APC-targeting platform is designed to induce a rapid, broad and lasting immune response

- Targets Antigen Presenting Cells (APCs) to induce T cells and B cells to combat cancer and infectious disease
- Ability to change the targeting unit enables different immune response profiles that can be tailored to specific diseases
- Delivery platform is agnostic to DNA, mRNA, viral vector vaccines
- Potential for combination therapies

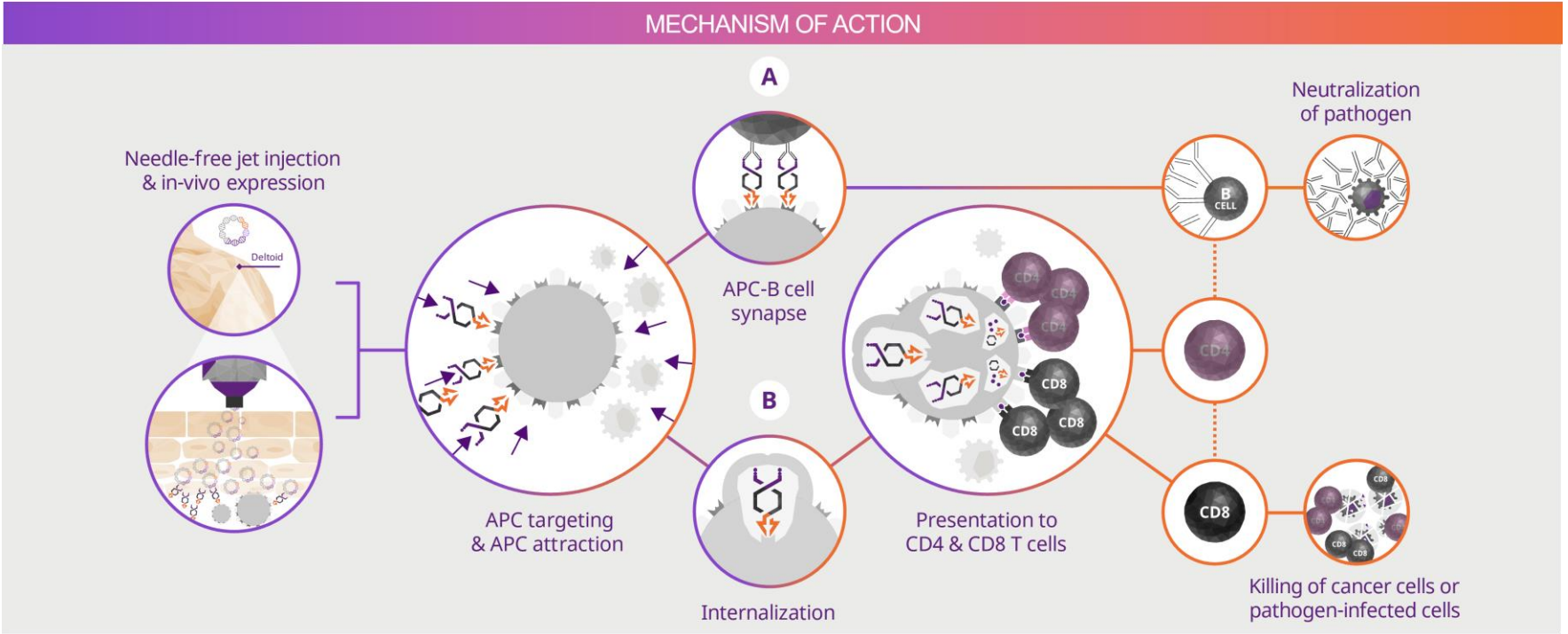
APC TARGETED VACCINE PLATFORM



- Targeting unit to attract and bind Antigen Presenting Cells (APC)
  - Molecules that bind surface receptors on APC, eg:
    - Natural ligands, including cytokines and chemokines
    - Bacterial proteins
    - scFv from mAb binding
- Dimerization unit for crosslinking targeted receptor on the surface of the APC
- Antigenic unit
  - Full-length antigens
    - Cancer, viral, bacterial, parasitic etc.
  - Multiple T cell epitopes
    - Individualized and shared cancer products
    - T cell products for infectious disease
    - T cell products for autoimmunity

We have achieved this by combining selected genes to encode novel vaccine molecules with desired properties

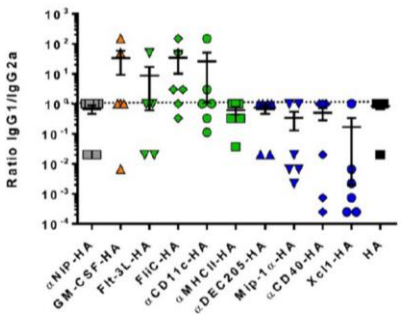
Unique MoA stimulates both killer T cells and neutralizing antibodies for a potent, disease-specific immune response



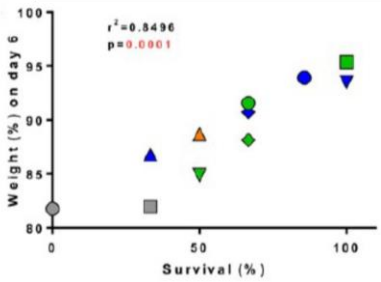
The targeting unit may be exchanged and thus Tailor the immune response profile to each disease's correlate of protection

INFLUENZA

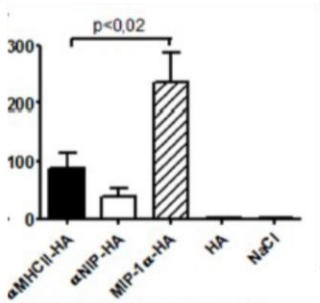
Targeting unit affects Th1/Th2 balance



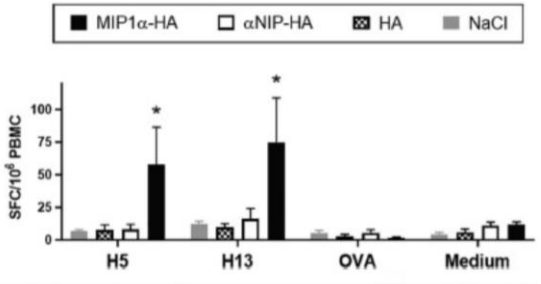
Targeting unit affects level of protection



Targeting unit affects level of CD8 T cell response



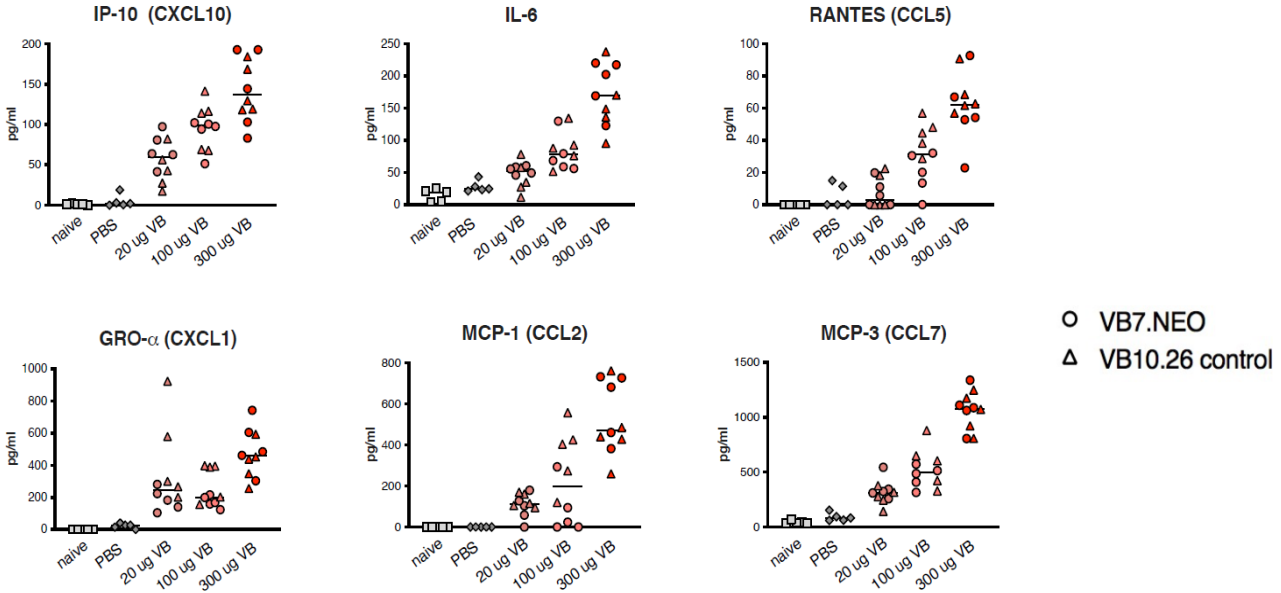
MIP-1α induces cross-reactive T cell responses



- Vaccibody's targeting unit binds surface receptors on APC
- Adapting the APC targeting unit affects the immune response profile
- Nykode can match targeting unit and antigen to the disease's correlate of protection

Systemic cytokine response detected early in response to i.m. plasmid DNA injection, in mice

- Low, dose dependent systemic cytokine response detected 6 hours post vaccination
- Independent on CCL3L1 targeting unit, hence driven by plasmid DNA

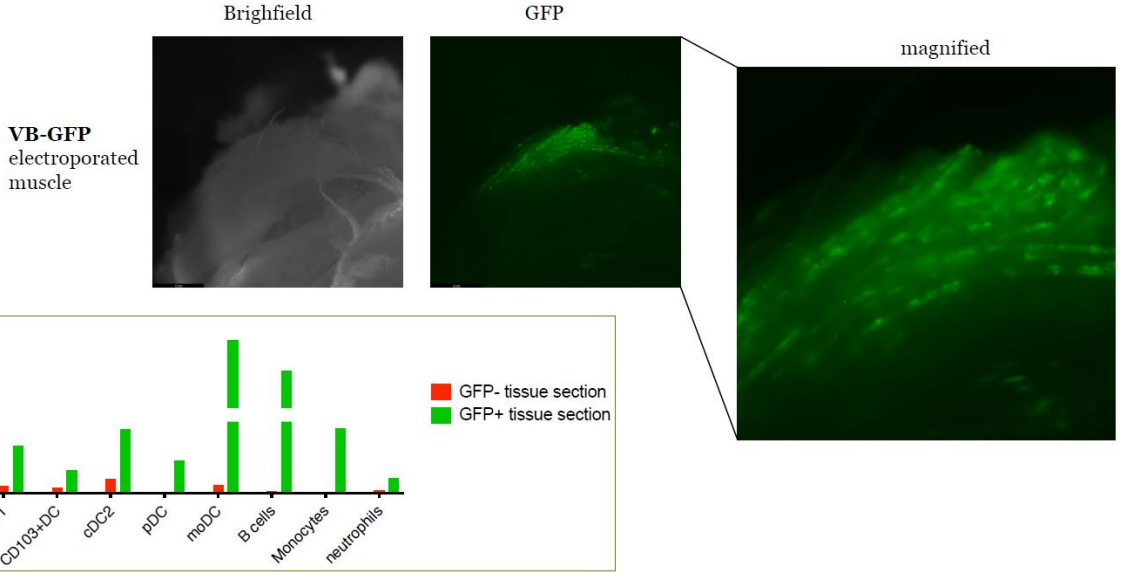


Genentech
A Member of the Roche Group

Siri Tahtinen S, Mark McCarron, et al (Genentech, Inc)

Immune cells infiltrate the muscle specifically in areas expressing the CCL3L1 Vaccibody protein, in mice

- Vaccibody protein expression can be detected directly in muscle cells by microscopy after i.m. DNA delivery.
- Dendritic cells, B cells and monocytes are attracted specifically to the CCL3L1 Vaccibody expressing muscle cells



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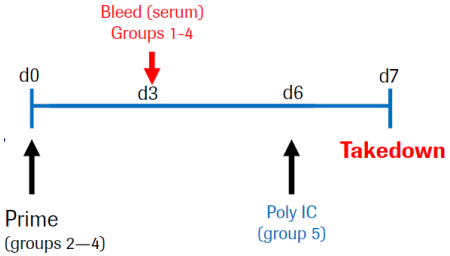
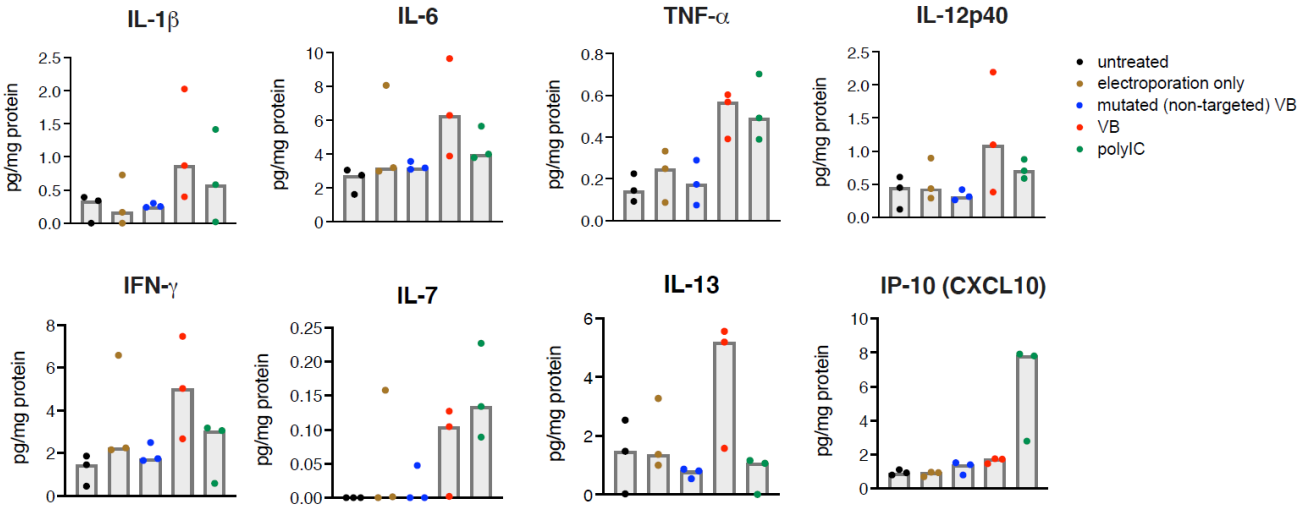
Vaccibody induced cytokine expression observed in the muscle at day 7 is dependent on functional CCL3L1 targeting unit, in mice



- Local intramuscular cytokine expression observed at day 7, dependent on functional CCL3L1 targeting unit



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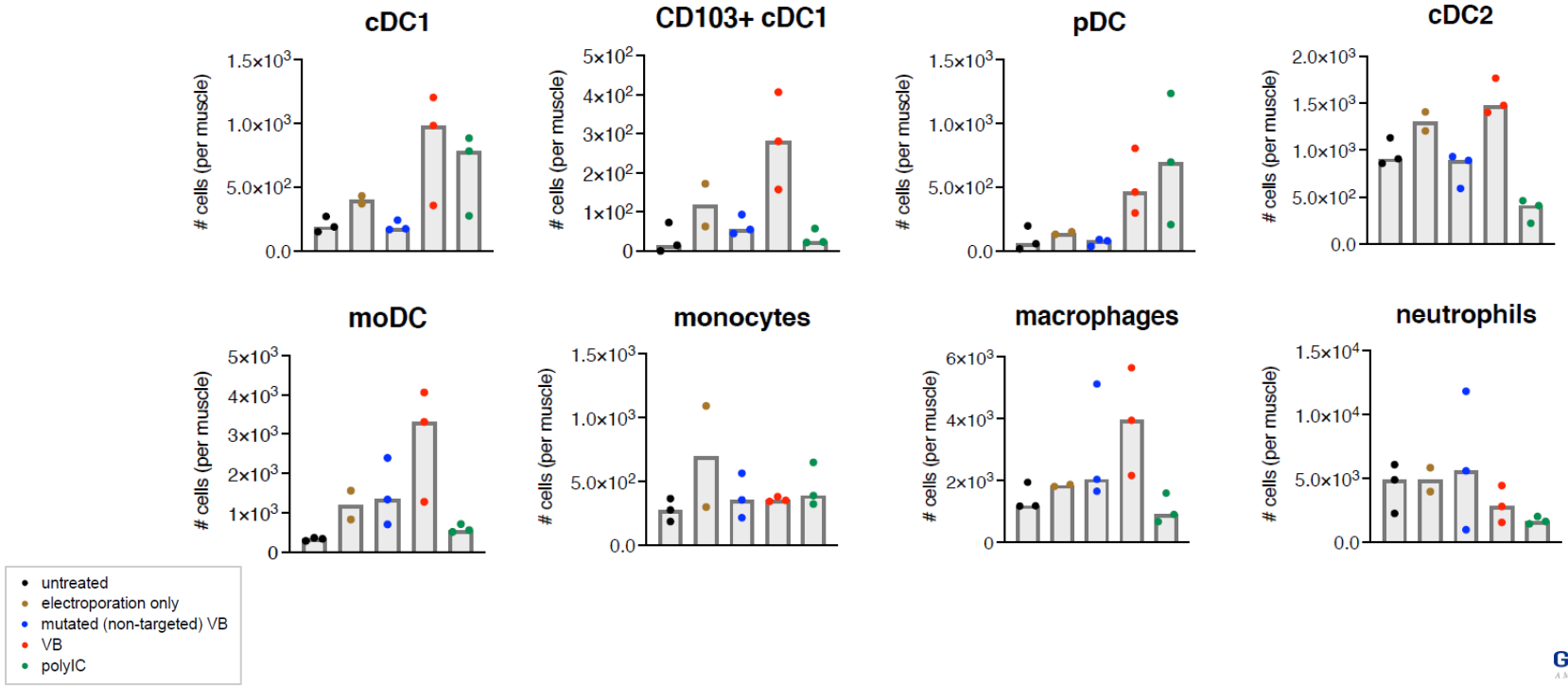
Note: poly IC is a positive control given at day 6

CCL3L1 Vaccibodies specifically induces infiltration of APC, primarily dendritic cells, in mice



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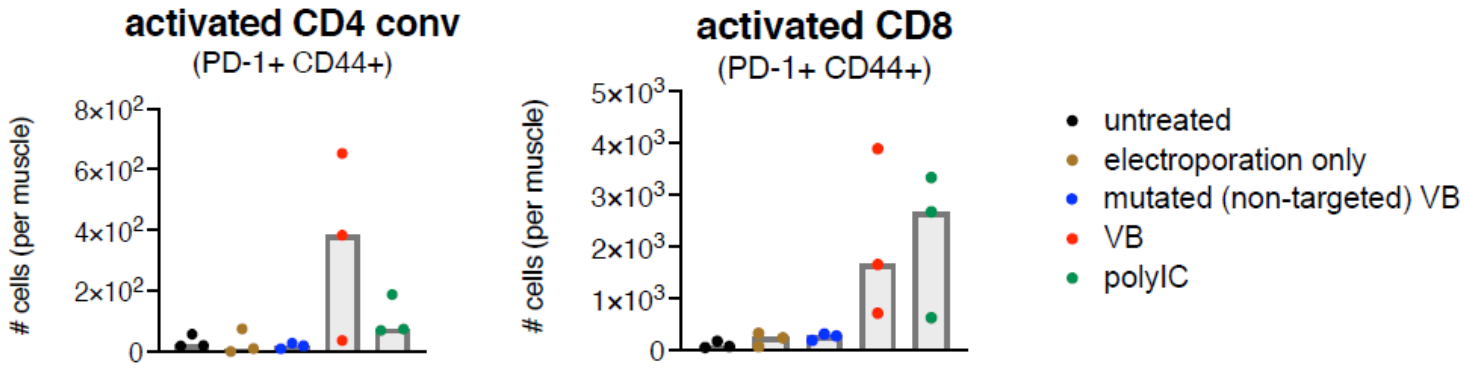
Note: poly IC is a positive control given at day 6

Activated CD4 and CD8 T cells in muscle is dependent on CCL3L1 targeting, in mice

Muscle



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Note: poly IC is a positive control given at day 6

VB10.NEO: Nykode's individualized cancer vaccine

Targeting antigen presenting cell

Proprietary neoantigen selection method

- Majority of selected neoepitopes are immunogenic
- Frequency of high-quality neoepitopes in vaccine and immune responses correlate with responses

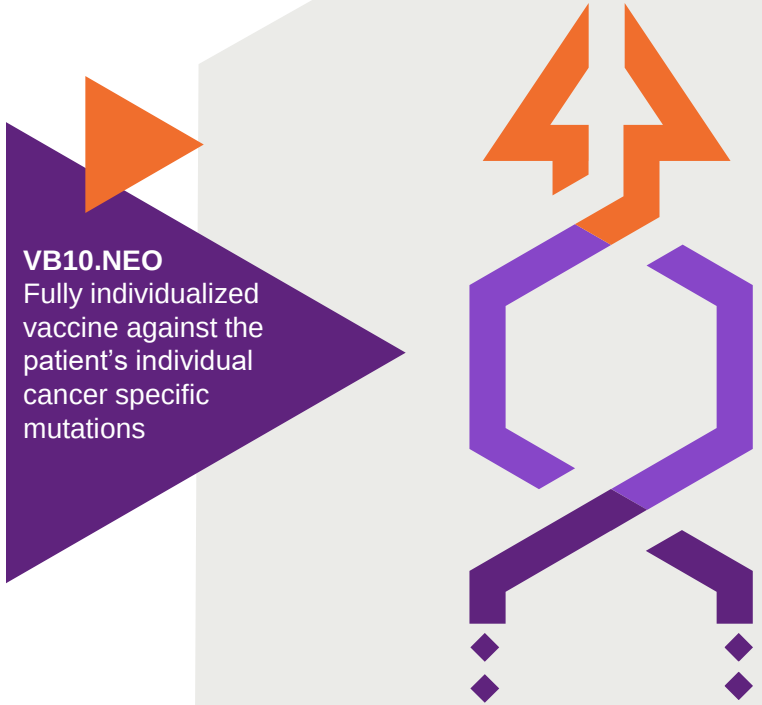
Promising immunogenicity and clinical data

- Phase I/IIa in >50 patients with melanoma, NSCLC, SCCHN, RCC and urothelial cancer

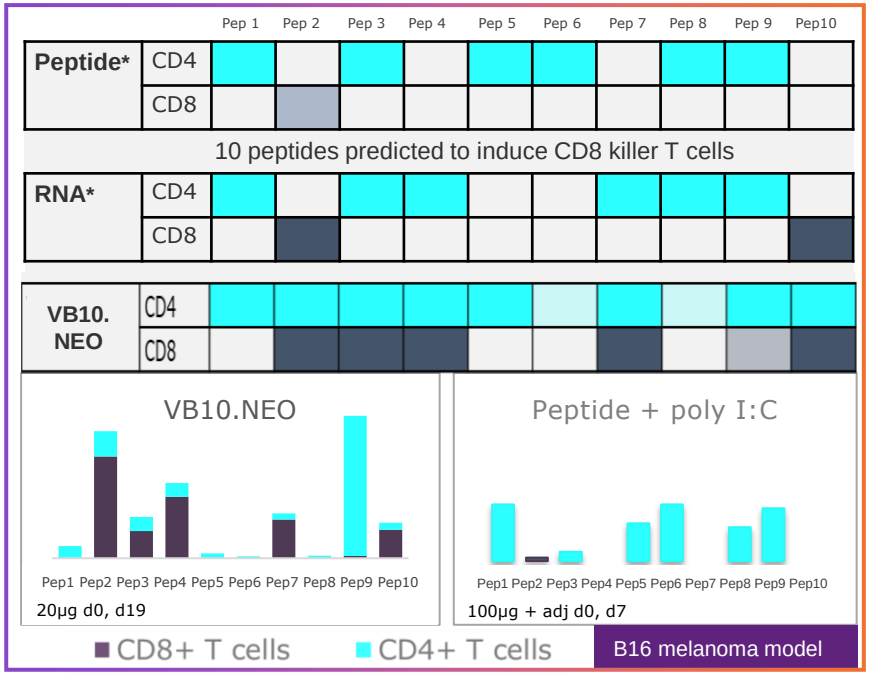
Delivered as DNA plasmid

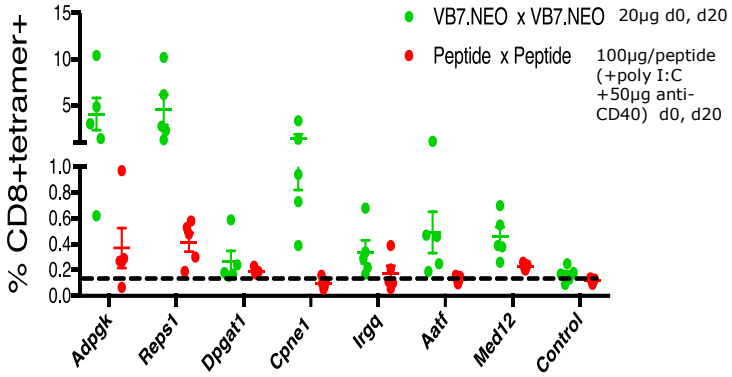
- Flexible, rapid and cost-effective manufacturing. 100% manufacturing success rate

Exclusively out-licensed to Roche and Genentech, 2020



CCL3L1 targeted Vaccibody induces effective cross-presentation resulting in broad, strong CD8 T cell responses





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MC38 colon carcinoma

Vaccibody's ability to achieve controlled cross-presentation by specific APC receptor targeting induces broader and stronger CD8 responses than non-targeted vaccine technologies

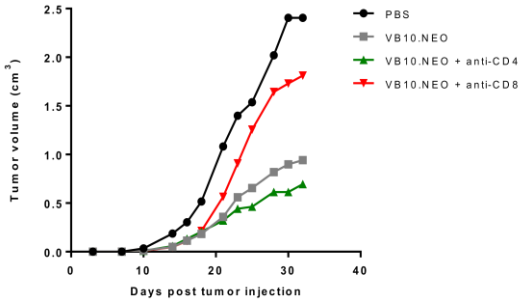
*Castle et al., 2012 and Kreiter et al., 2015

Siri Tahtinen S, Mark McCarron, et al (Genentech, Inc)

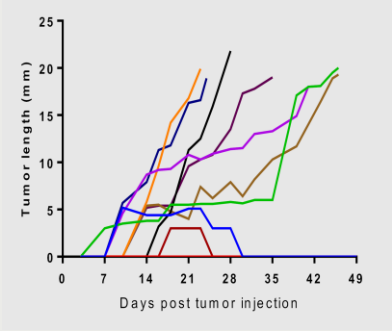
Neoepitope-specific CD8 T cells are essential for tumour protection

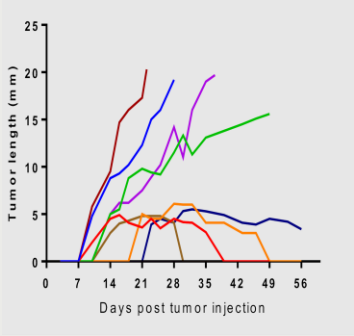
CT26 colon carcinoma model

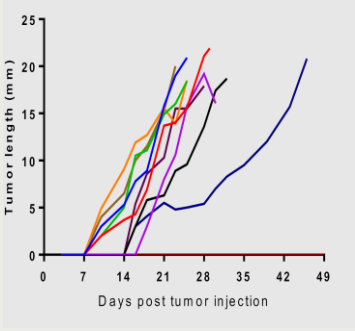
AVERAGE, ALL GROUPS



INDIVIDUAL GROWTH CURVES





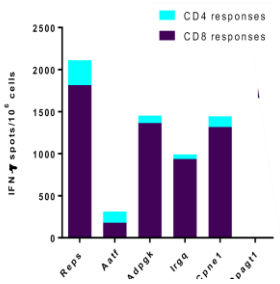


Depletion of CD8 T cells prohibit tumor protection in VB10.NEO vaccinated mice, indicating an essential role of neoepitope-specific CD8 T cells for anti-tumor efficacy

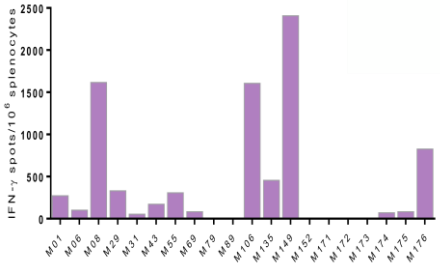
VB10.NEO: has proven to induce an effective local anti-tumor response

STRONG SCIENTIFIC RATIONALE AND PROVEN MECHANISM OF ACTION LEADING TO ANTI-TUMOR EFFICACY

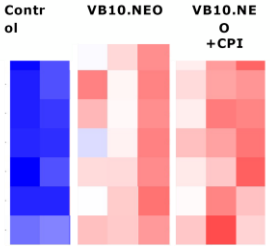
Neoepitope-specific CD8+ T cell response in spleen



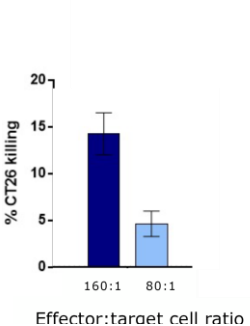
Neoepitope-specific T cell response in tumor



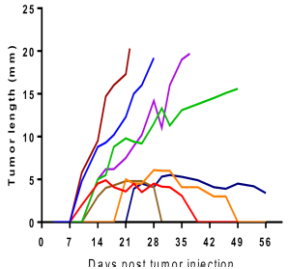
Influx of cytotoxic T cells in tumor (TILs)



TILs recognize and kill tumor cells

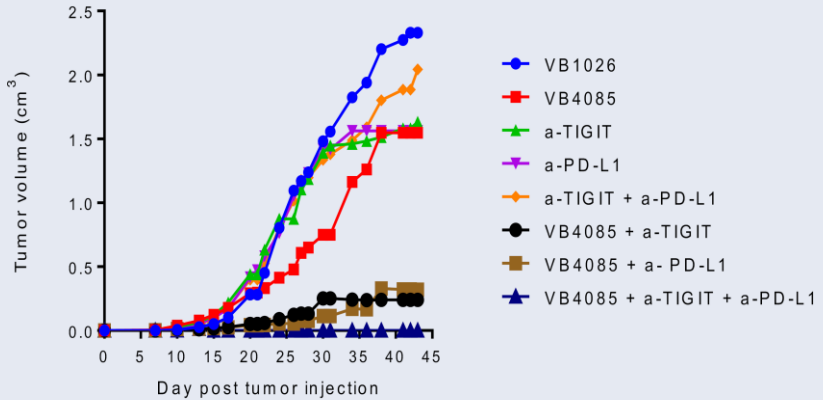


Tumor protective immune responses elicited in vaccinated mice (CD8 dependent)

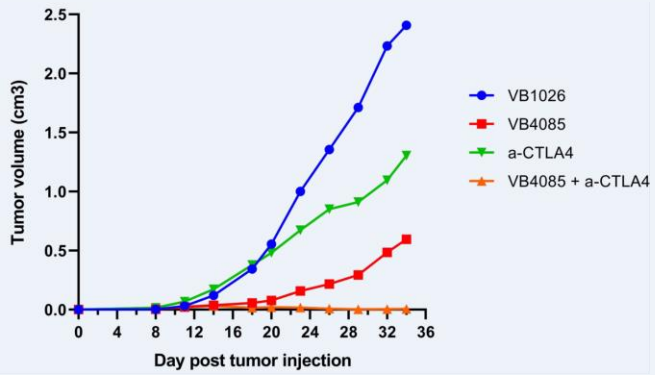


Synergistic effects combining Vaccibody and CPI regimen(s)

ANTI- PD-L1 AND ANTI-TIGIT



ANTI-CTLA-4



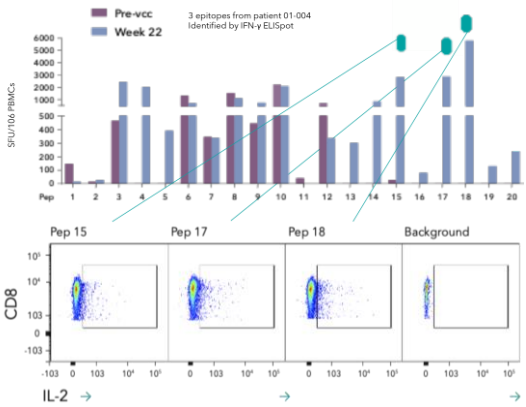
- VB plus anti-PD-L1, anti-TIGIT and anti-CTLA-4 mAbs all leads to synergistic anti-tumor efficacy
- Triple combination of VB plus anti-PD-L1 and anti-TIGIT leads to 100 % complete responses with significant contribution of VB

VB10.NEO: CD8 T cells and signs of clinical responses

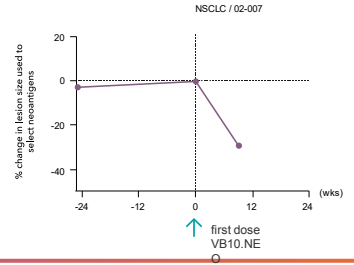
Neoepitope-specific CD8 dominating immune responses in SCCHN patients with clinical response

- Marked changes in lesion size development observed after initiating VB10.NEO
- Shrinkage of tumors and stabilization of progressing lesions
- Strong, dominant CD8 responses in patients with clinical responses

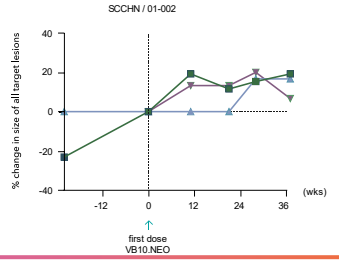
BROAD AND STRONG CD8 T CELL RESPONSES



STABLE DISEASE AT VACCINATION START



PROGRESSIVE DISEASE AT VACCINATION START



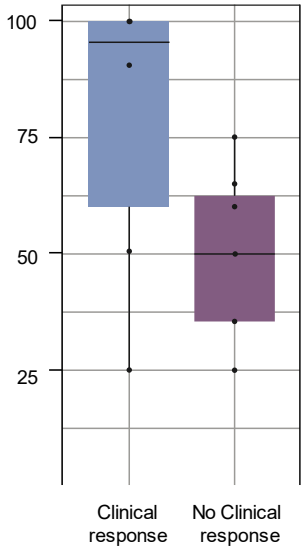
VB10.NEO: High quality neoepitopes and immune responses correlate with clinical responses

Patients with responses show highest frequency of high quality neoepitope and the strongest immune response profile

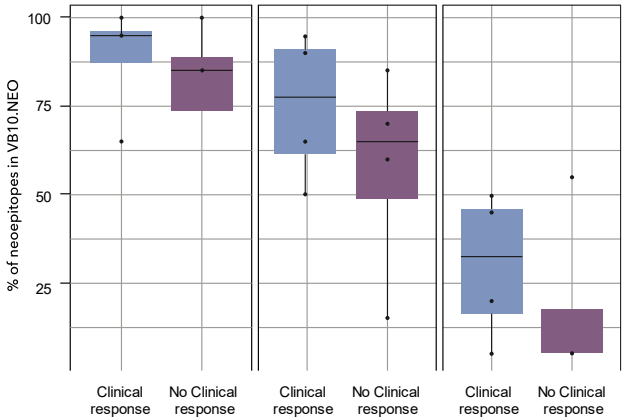
FREQUENCY OF HIGH QUALITY NEOEPITOPES VS CHANGE IN LESION SIZE

Patients with response after VB10.NEO vaccinations have:

- Highest frequency of high quality neoepitopes



FREQUENCY OF IMMUNOGENIC NEOEPITOPES VS CHANGE IN LESION SIZE

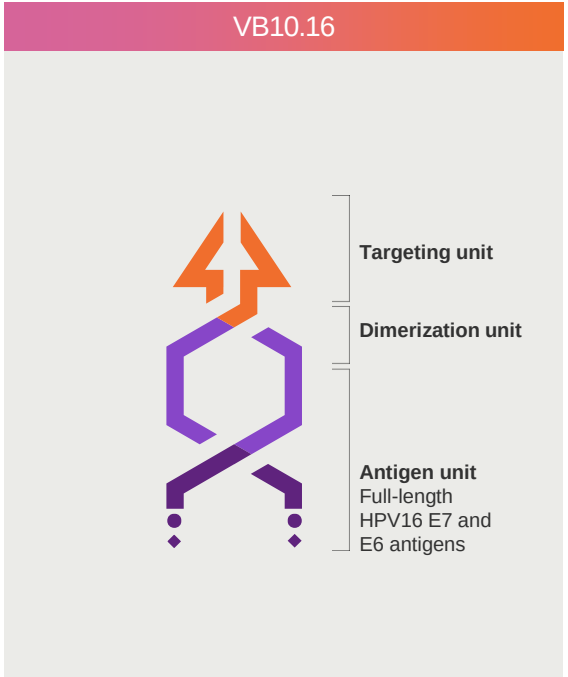


Patients with response after VB10.NEO vaccinations have:

- Highest frequency of immunogenic neoepitopes
- Highest frequency of increased response after vaccination
- Highest frequency of de novo immune responses

VB10.16: Therapeutic off-the-shelf HPV16 vaccine currently in Phase 2

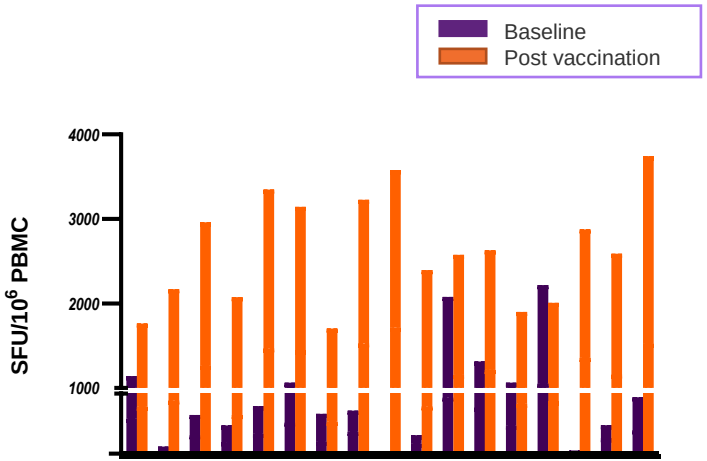
- Finalized Phase I/IIa study with VB10.16 monotherapy in HPV16+ precancerous cervical lesions, VB C-01
- Ongoing Phase II study of VB10.16 + atezolizumab in advanced cervical cancer, VB C-02
  - Interim clinical data to be presented 1H 2022
- Fully owned by Nykode



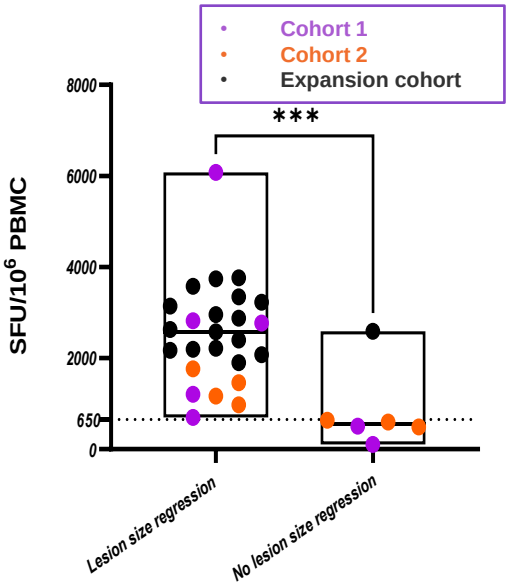
VB10.16: strong T cell responses with significant correlation to lesion size regression, VB C-01

- All patients in the expansion cohort elicited a strong HPV16-specific T cell response
- Highly significant correlation between vaccine-induced T cell responses and lesion size regression across all cohorts

STRONG HPV16-SPECIFIC T CELL REPSONSES IN ALL PATIENTS IN THE EXPANSION COHORT



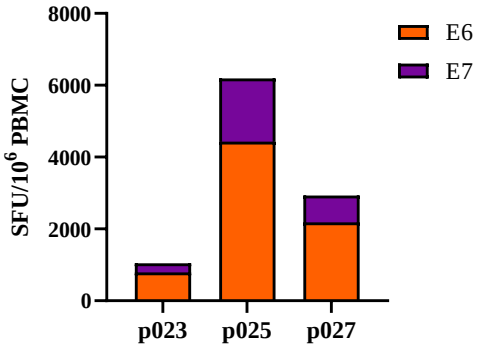
LESION SIZE REGRESSION CORRELATES WITH HPV-16 SPECIFIC RESPONSES



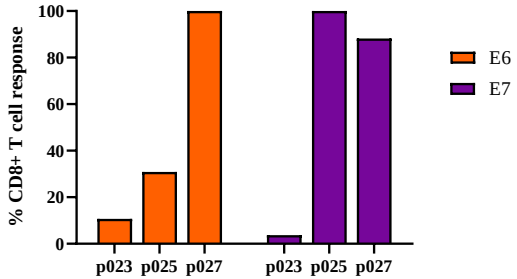
VB10.16: strong CD8 T cell responses in patients, VB C-01

- CD8 T cell response measured in 3 patients with CD4 depleted IFN-γ ELISpot
- Up to 100% of the HPV16 E7 and E6-specific IFN-γ response was contributed by CD8 T cells, confirming effective cross-presentation by chemokine-receptor targeting

3 patients with variable level of total T cell response was tested



The contribution of CD4 versus CD8 T cells were analyzed by a CD4 depleted ELIspot assay

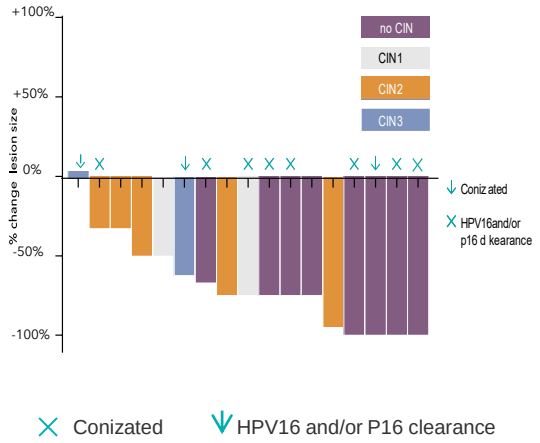


VB10.16: Strong additional clinical data as monotherapy in precancerous lesions, VB C-01

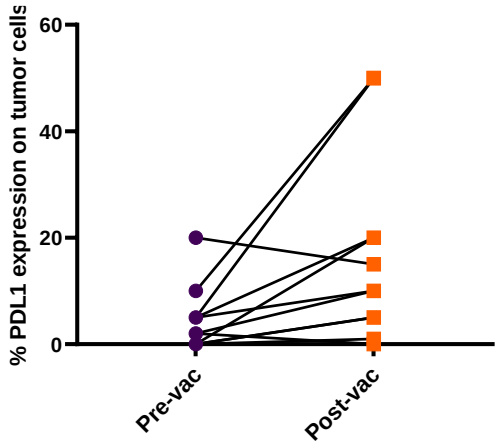
VB10.16 as a monotherapy in HPV16-positive, precancerous cervical lesions induces:

- Lesion size reduction in all patients in expansion cohort followed >4 months
- CIN regression to CIN1 or no CIN in 10 patients
- HPV16 and/or p16 clearance in 8 patients
- Well tolerated. No SAEs.
- Upregulation of PD-L1 in the lesions post vaccination, providing scientific rationale for combination with anti-PD-1/PD-L1 in cancer patients

LESION SIZE REDUCTION, CIN REGRESSION AND HPV16 AND/OR P16 CLEARANCE



UPREGULATION OF PD-L1 IN RESPONSE TO VACCINATION



Upregulation of PD-L1 expression in lesions after vaccination

Acknowledgement

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Ranveig Braathen
Bjarne Bogen

John Tregoning

Siri Tahtinen
Mark McCarron
Lelia Delamarre
Ira Mellman

UNLOCKING THE FUTURE OF MEDICINE

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