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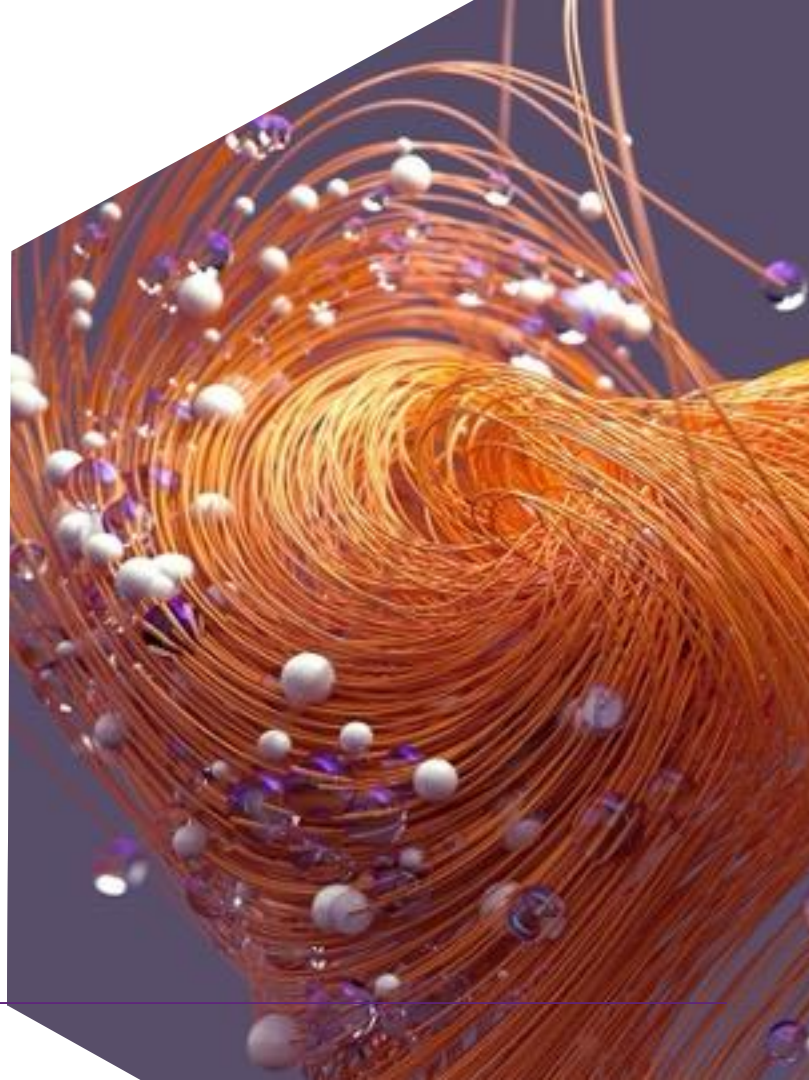
Using the Vaccibody™ platform to create new second and third generation vaccines against COVID

April 21st, 2022

World Vaccine Congress

Overview

- Clinical stage immunotherapy company with vaccine pipeline in oncology and infectious diseases
- Vaccibody™ immunotherapy platform targets antigens to Antigen Presenting Cells (APCs) for a rapid, broad and controlled immune response
- Unique Vaccibody construct can be delivered by 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

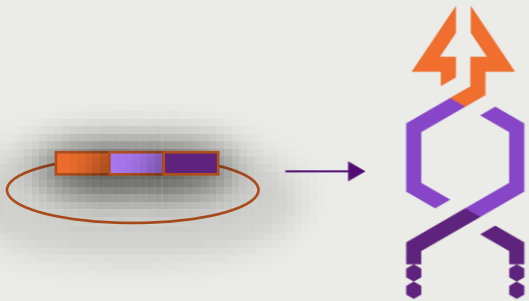
	Program	Indication	Discovery/ Preclinical	Phase 1	Phase 2	Phase 3	Partnerships
Nykode							
Oncology	VB10.16 (off-the-shelf)	HPV16+ cervical cancer[3]					Roche
	Internal (off-the-shelf)	Undisclosed targets					
Infectious Disease	**VB10.COV2**	**SARS-CoV-2**					Adaptive[4]
	Internal	Undisclosed targets					
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

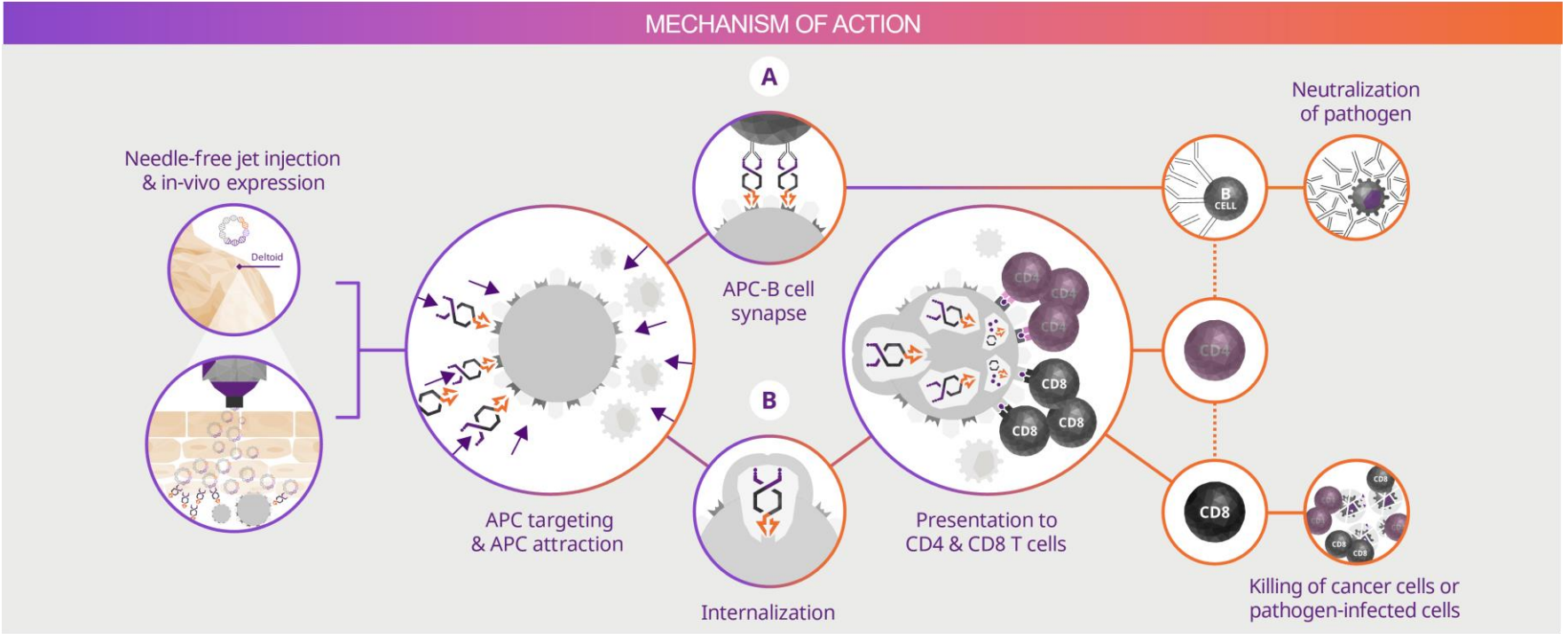
APC TARGETED VACCINE PLATFORM



- 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



With the Vaccibody™ platform Nykode has the potential to generate leading next generation COVID vaccine

Focus on Variants of Concern

- Neutralizing antibodies induced by the marketed Wuhan based vaccines wane over time
- Further reduced efficacy against Variants of Concern (VoC)
- **Both of Nykode's COVID candidates are engineered to provide broad and long-lasting protection against these emerging variants**
- **Nykode's VB10.2129 candidate includes two mutations of the Beta strain that are shared with Omicron**

Broad Based T-Cell Response

- Increasing evidence of the importance of broad T cell responses against COVID-19
- T cell response in vaccinated human subjects coincide with early protection and a higher proportion of CD8+ T cell responses is observed in mild disease
- Current vaccine approaches focus on Spike and do not generate broad based immune responses
- **Nykode's VB10.2210 candidate takes advantage of T cell epitopes identified by Adaptive Biotechnologies to generate rapid onset of broad T-cell immunity**

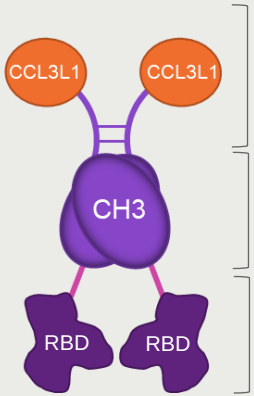
Nykode’s SARS-CoV-2 vaccine cadidates

Nykode currently advancing two COVID vaccine candidates with different approaches and potential to be used in combination approach

- both focused on addressing current and future variants of concern

VB10.2129 – RBD CANDIDATE

RBD vaccine tailored to the B1.351 (Beta) VoC to generate RBD-specific antibody and T cell immunity



Targeting unit

Dimerization unit

Antigen unit

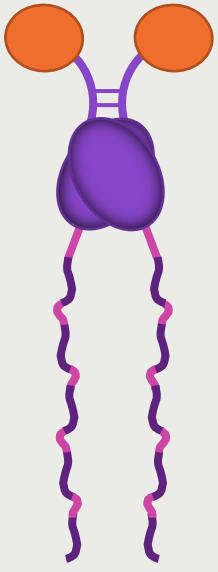
B1.351 VoC RBD

K417N, E484K and N501Y mutations*

*All 2 aa mutated also in Omicron VoC

VB10.2210 – T CELL CANDIDATE

T-cell epitope vaccine inducing broadly protective T cell responses



Targeting unit

Dimerization unit

Antigen unit
96+ Validated T cell epitopes from 8 antigens identified by Adaptive Biotechnologies

*includes conserved immunogenic T cell epitopes from 7 non-spike antigens which are not as affected by mutations in the current and future VoC, incl Omicron

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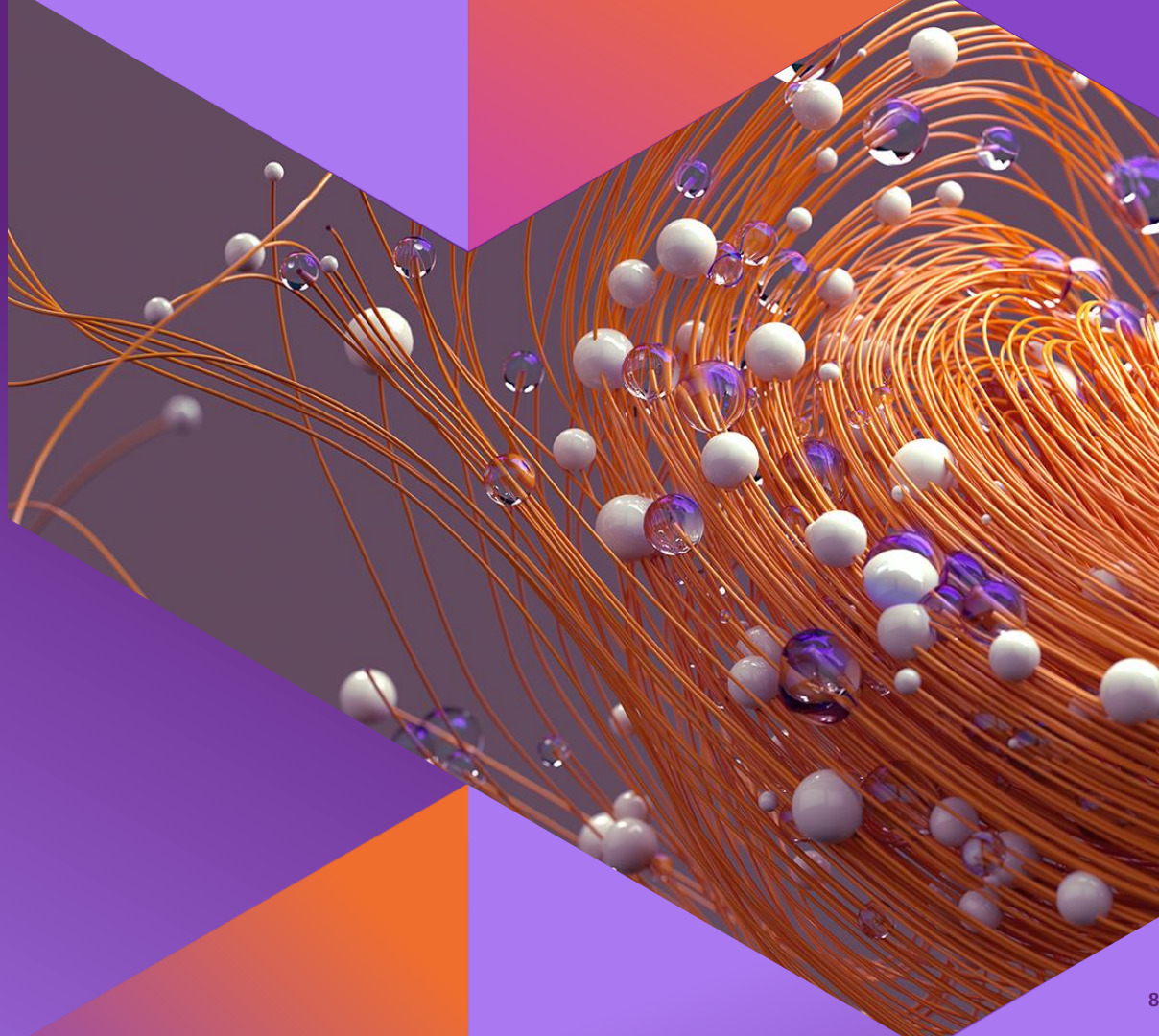
VB10.2129 – RBD CANDIDATE

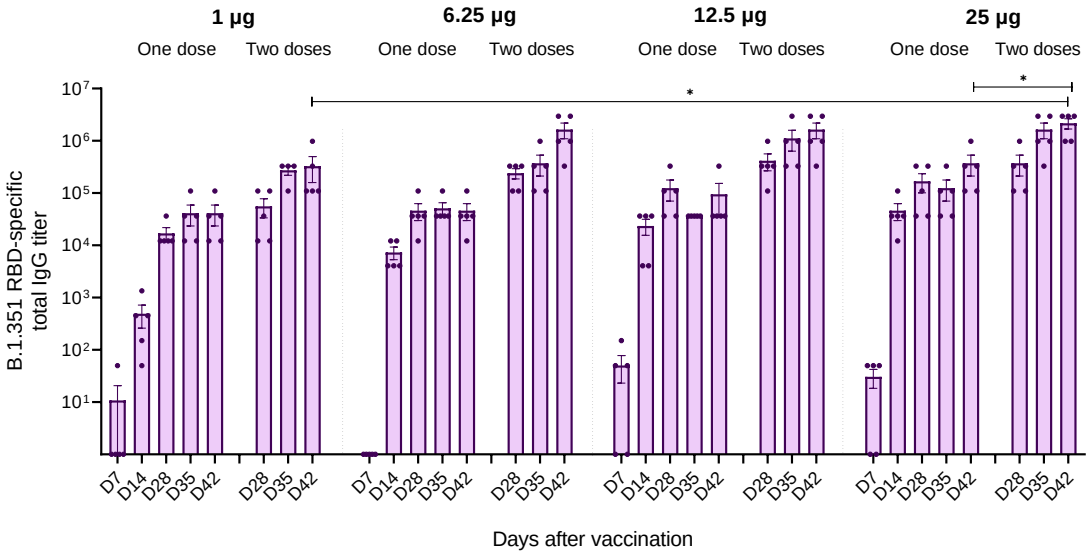


VB10.2129 induces rapid, strong and persistent antibody responses

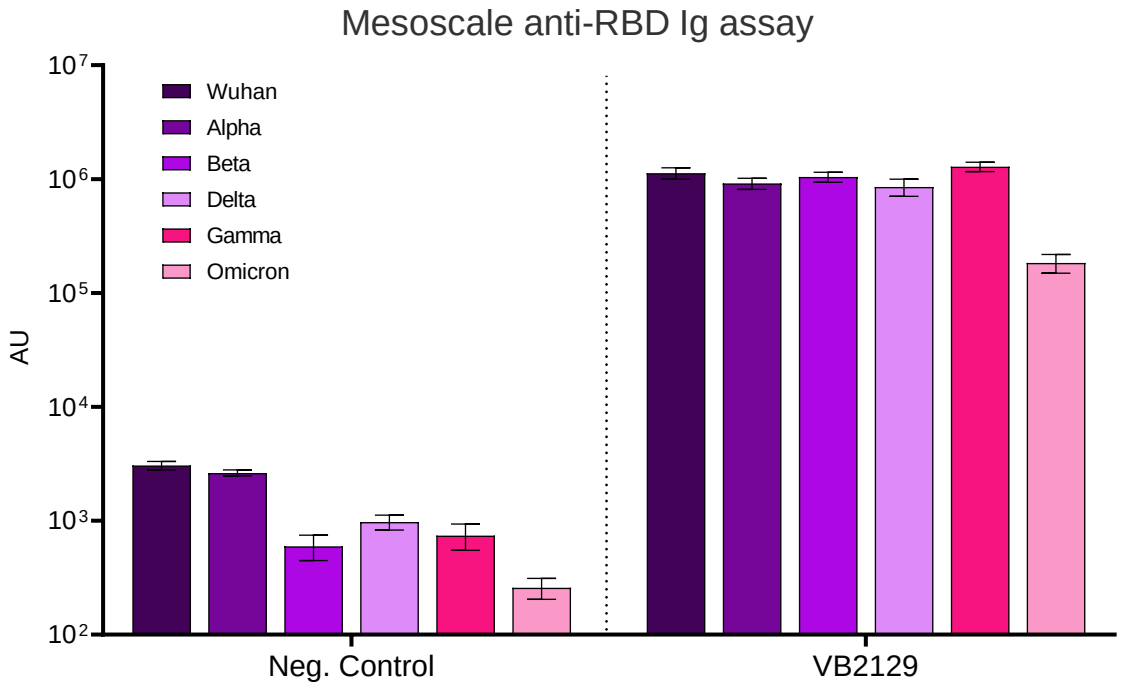
Rapid, strong and long-lasting antibody responses induced after vaccination with the B1.351 RBD specific vaccine

- Rapid: Ab detected already day 7 after one vaccination even with low dose (1µg)
- Strong responses: >10^6 endpoint titer
- Confirming the results achieved with the previously published Nykode RBD vaccine against Wuhan WA1/2020

RBD SPECIFIC ANTIBODY RESPONSES IN BALB/C MICE



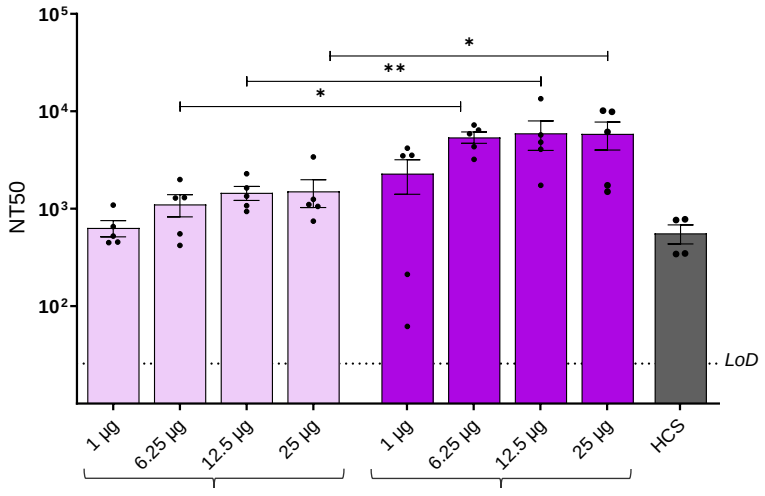
VB10.2129 induces high titers of cross-reactive antibodies



2x 25 µg
Day 42

RBD candidate VB10.2129 induces potent virus neutralization responses across VoC

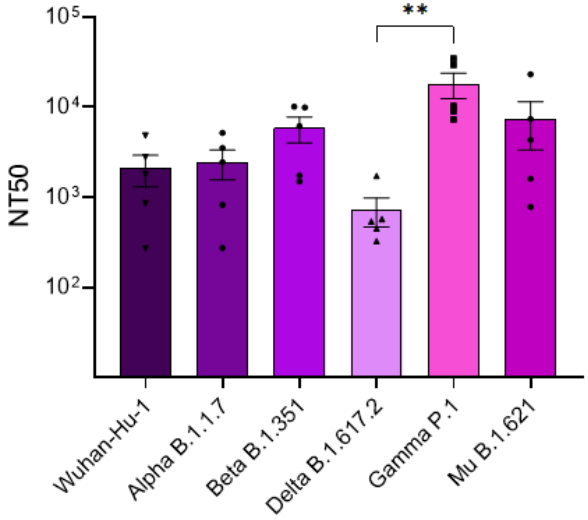
BETA – SOUTH AFRICAN VOC (PSEUDOVIRUS NEUTRALIZATION ASSAY)



Day 42

NT50: Neutralization titers that achieved 50% neutralization

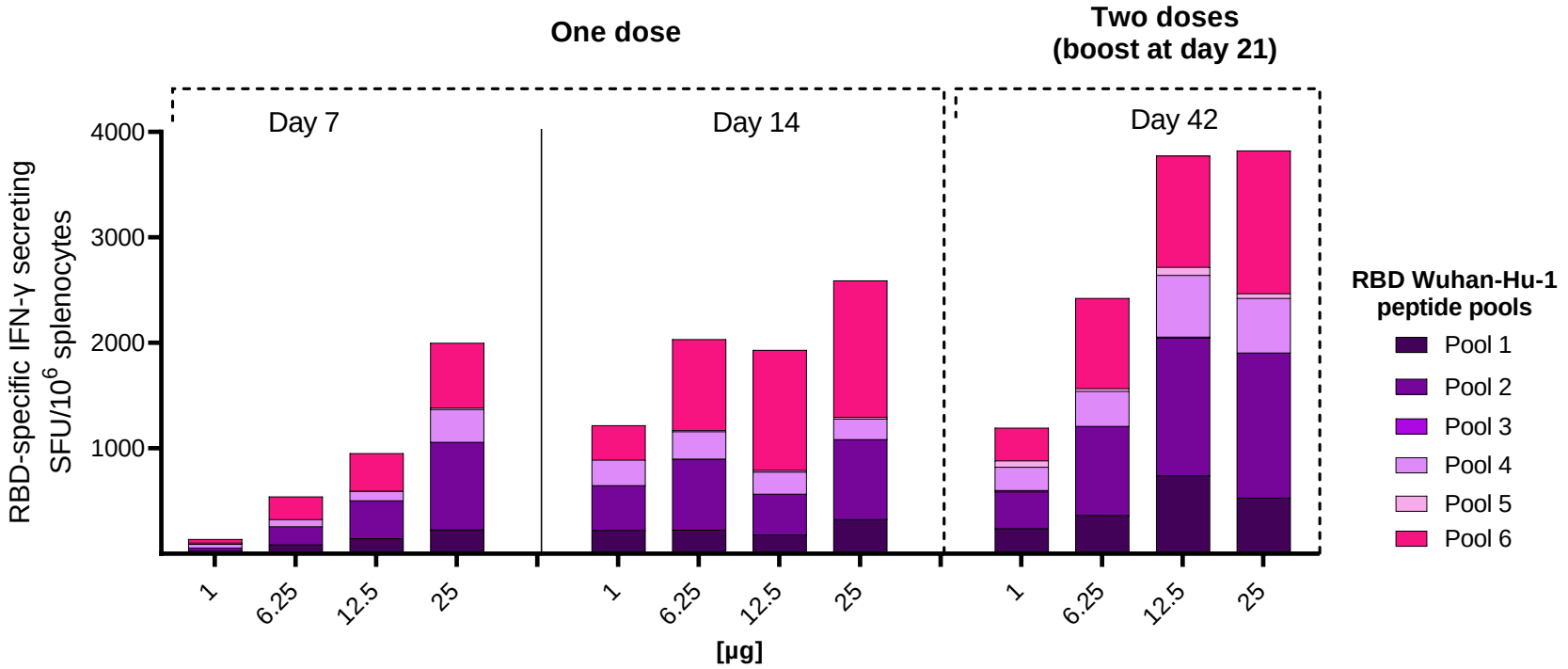
VARIANTS OF CONCERN (PSEUDOVIRUS NEUTRALIZATION ASSAY)



2x 25 µg
Day 42

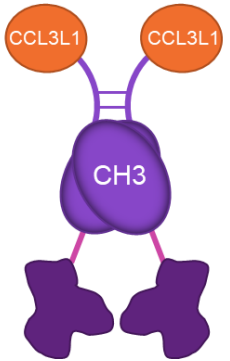
NT50: Neutralization titers that achieved 50% neutralization

RBD candidate VB2129 induces persistent T cell responses against RBD epitopes



Summary VB10.2129

- Include the RBD domain of B1.351 (Beta) variant of concern
- APC-targeted delivery encoded by DNA plasmid, formulated in PBS- with manufacturing, stability, distribution and safety advantages
- Consistently strong antibody responses induced in preclinical models
  - Validating the ability of the Vaccibody™ platform to induce antibody responses
  - Confirming ability to generate T cells to HLA-class I restricted epitopes
- Cross-neutralizing antibody responses to various VoC obtained
- Strong T cell responses across RBD epitopes
  - Verify ability to induce T cell responses on top of antibody responses



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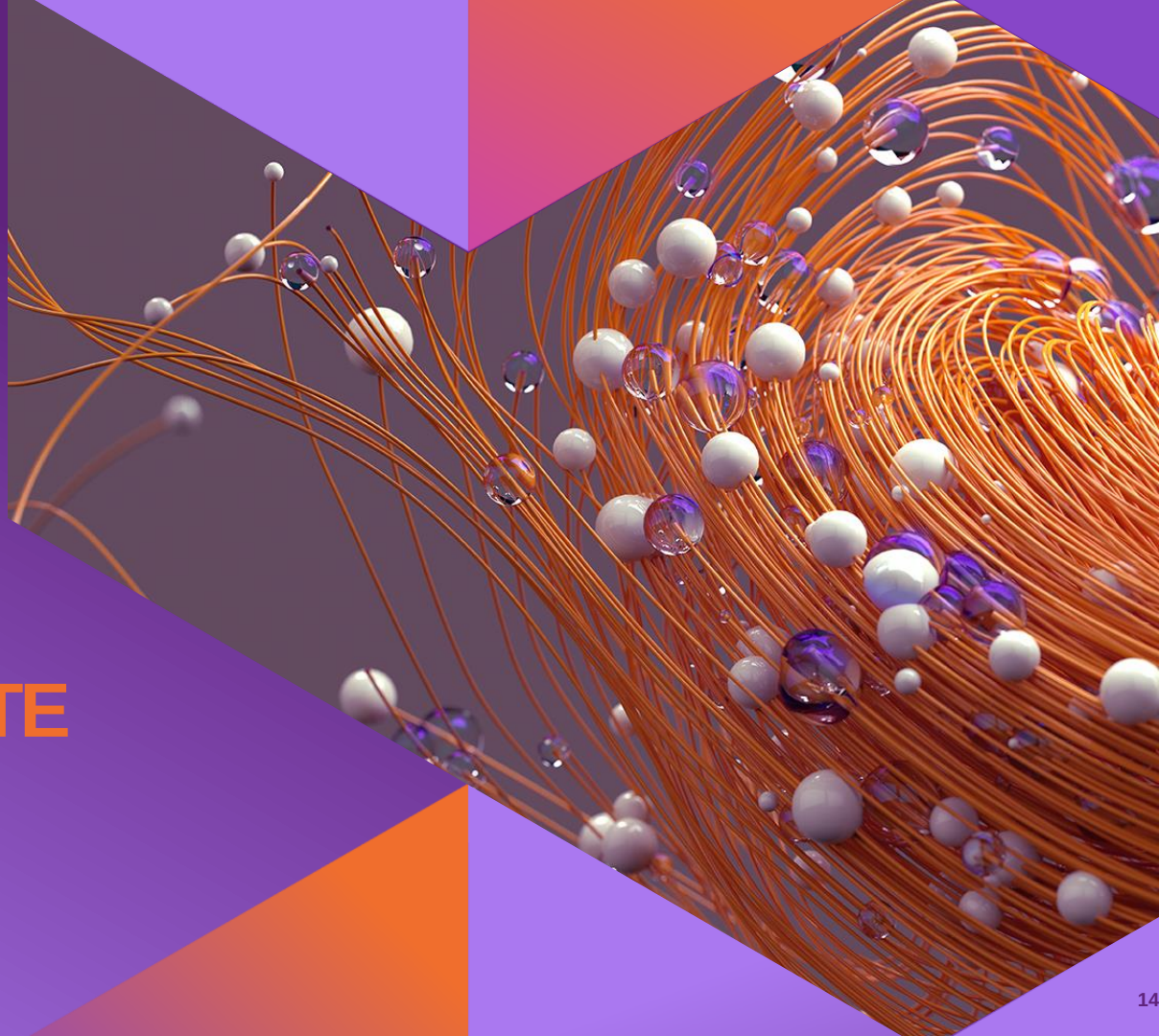
VB10.2210 – T CELL CANDIDATE



Rationale for T cell-based vaccines in more detail

Loss of neutralizing antibody capacity against recent VoCs has only minimally affected the ability of current vaccines to protect against severe disease, hospitalization and death

Durable cellular immune memory has been suggested to play a key role in this protection

In COVID-19 patients, T cell responses are observed across the viral proteome and not limited to surface proteins like Spike.

Mounting evidence for role of T cell immunity in protection against COVID-19

- SARS-CoV-2 specific memory T cells correlated with protection on secondary exposure
- T cell responses have been detected in individuals who failed to seroconvert following mild COVID-19
- Those who were infected with SARS-CoV-2 before getting vaccinated had a 65% to 82% lower rate of breakthrough infection compared with those who were vaccinated but never infected
- CD8 T cells play a key role in limiting SARS-CoV-2 disease severity, even in the absence of humoral immunity, e.g. in patients with B cell deficiency

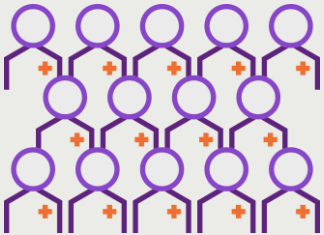
Efficacy across populations and future Variants of Concern (VoCs) would require a vaccine with a large set of validated T cell epitopes across multiple antigens with broad HLA coverage and a platform able to induce strong CD8 as well as CD4 T cell responses

Peng et al 2020 https://www.nature.com/articles/s41590-020-0782-6
Wyllie et al SIREN study UK https://www.medrxiv.org/content/10.1101/2020.11.02.20222778v1.full-text

https://jamanetwork.com/journals/jama/fullarticle/2785918

Adaptive Biotechnologies is the partner of choice for T cell based COVID-19 vaccines

Sequenced TCRs and identified expanded COVID-19 specific T cell clones in more than 6500 samples from COVID-19 patients.



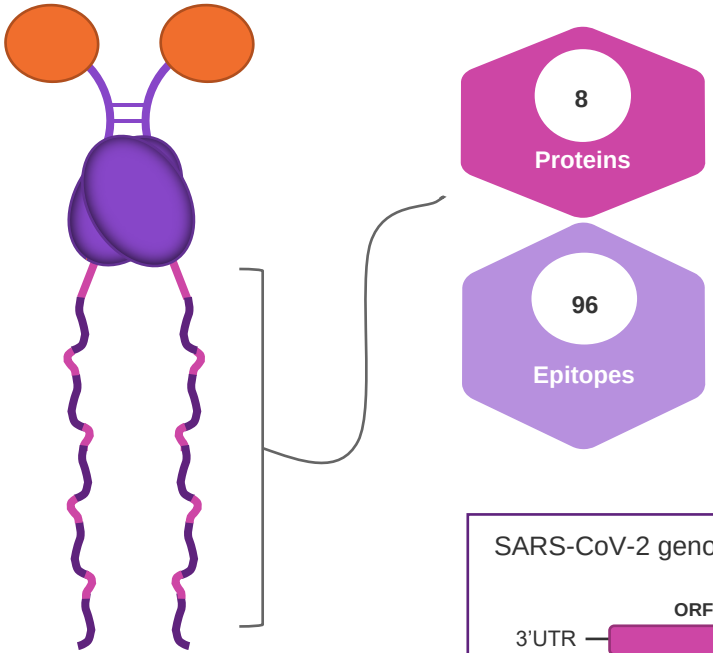
Mapped the TCRs to corresponding T cell epitopes, including functional cell-based assays.

Optimal combination of conserved and immuno-dominant T-cell epitope hotspots across 8 SARS-CoV-2 antigens were subsequently used for vaccine design.

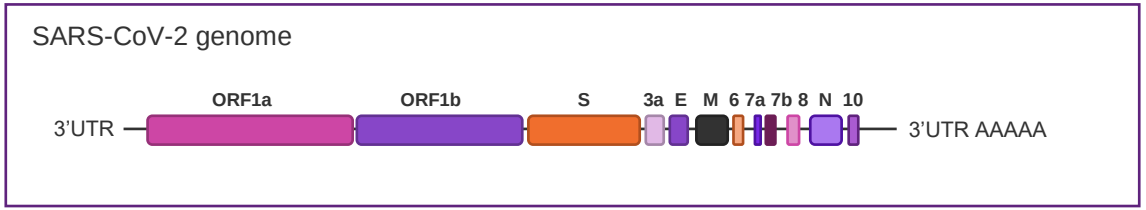
Adaptive launched T-Detect™ COVID, which is the first-in-class T-cell-based clinical test for Covid-19 with FDA Emergency Use Authorization.

To be implemented also for immuno-monitoring.

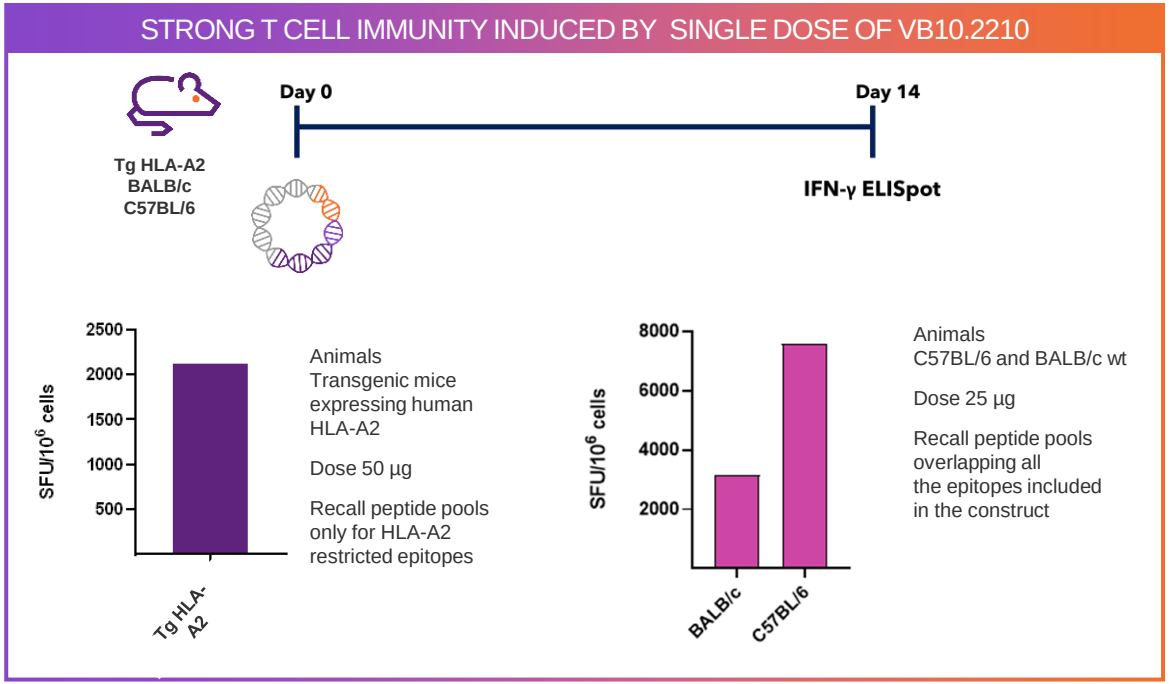
VB10.2210 includes a large set of conserved, validated T cell epitopes from 8 SARS CoV-2 genes



- High concentration of mutations in Spike are likely to affect both Spike-specific antibody and T cell responses
- VB10.2210 is designed to induce T cell responses against seven additional non-Spike antigens not affected by mutations in the VoC



Strong immunogenicity of VB10.2210 in 3 mouse models

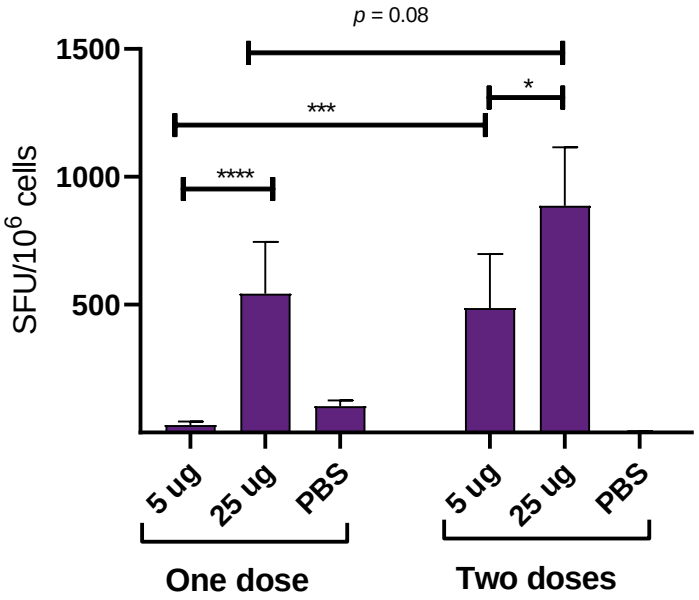


- VB10.2210 induces strong CD8 T cell responses post 1 vaccination against HLA-A2 specific epitopes in humanized HLA-A2 tg mice
- The strong T cell responses observed in two additional mice models show the breadth of the T cell response independent of HLA selection

HLA-A2 specific T cell responses induced in transgenic HLA-A2.1 mice upon vaccination with VB10.2210

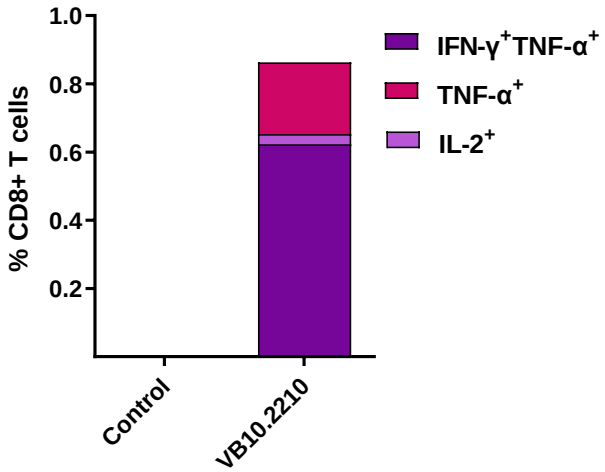
Recall peptide pools only for HLA-A2 restricted epitopes

DOSE RESPONSE AND SECOND DOSE EFFECT



Read-out at Day 14 (one dose), Day 35 (two doses)

PRO-INFLAMMATORY PROFILE

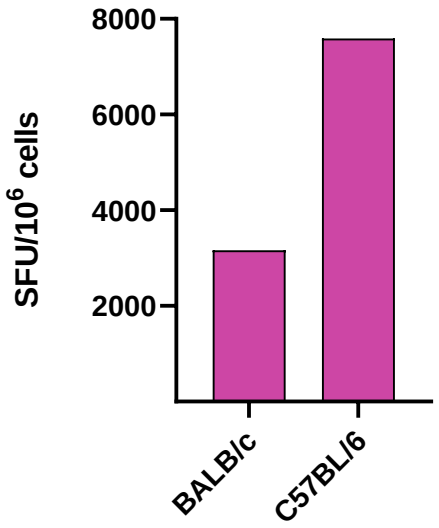


Read-out at Day 35 (two doses of 25µg)

VB10.2210 induces T cell responses across diverse MHC haplotypes in mouse models of different genetic backgrounds

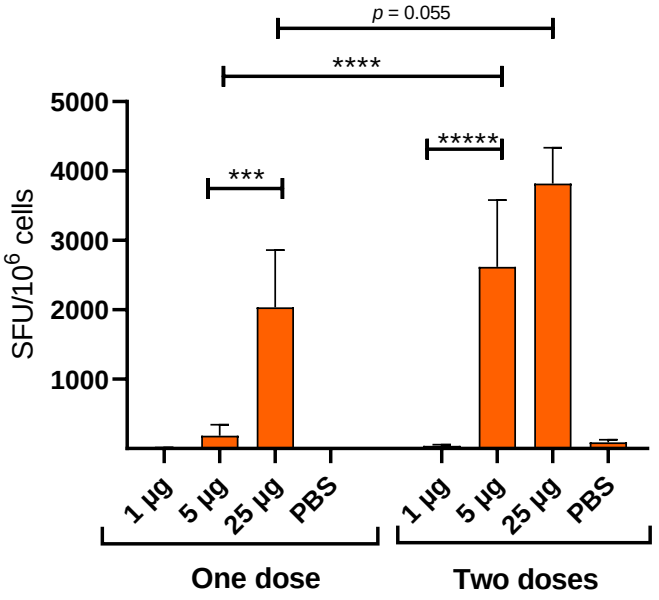
Recall overlapping peptides corresponding to T cell epitopes of broader restriction

SINGLE DOSE VACCINATION (25 µg)



Day 14

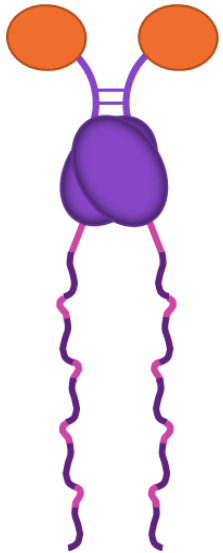
DOSE RESPONSE AND PERSISTENT T CELL IMMUNITY (C57BL/6)



Day 85

Summary VB10.2210

- Includes clinically validated T cell epitopes based on Adaptive's unique TCR and epitope matching technology from >6500 Covid-19 samples
- APC-targeted delivery encoded by DNA plasmid, formulated in PBS- with manufacturing, stability, distribution and safety advantages
- Consistently strong T cell immunity in transgenic HLA-A2.1 mice
  - Validating the T cell epitopes identified by Adaptive
  - Confirming ability to generate $CD8^+$ T cells to HLA-class I restricted epitopes
- Strong T cell responses in three different mouse models across multiple epitopes
  - Verify ability to induce T cell responses across diverse HLA haplotypes
- Persistent T cell immunity measured at day 85
  - Indicates established immunological memory



Phase 1/2 trial investigating the two candidates as diverse boosters in previously vaccinated subjects

A Phase 1/2, open label, dose escalation trial

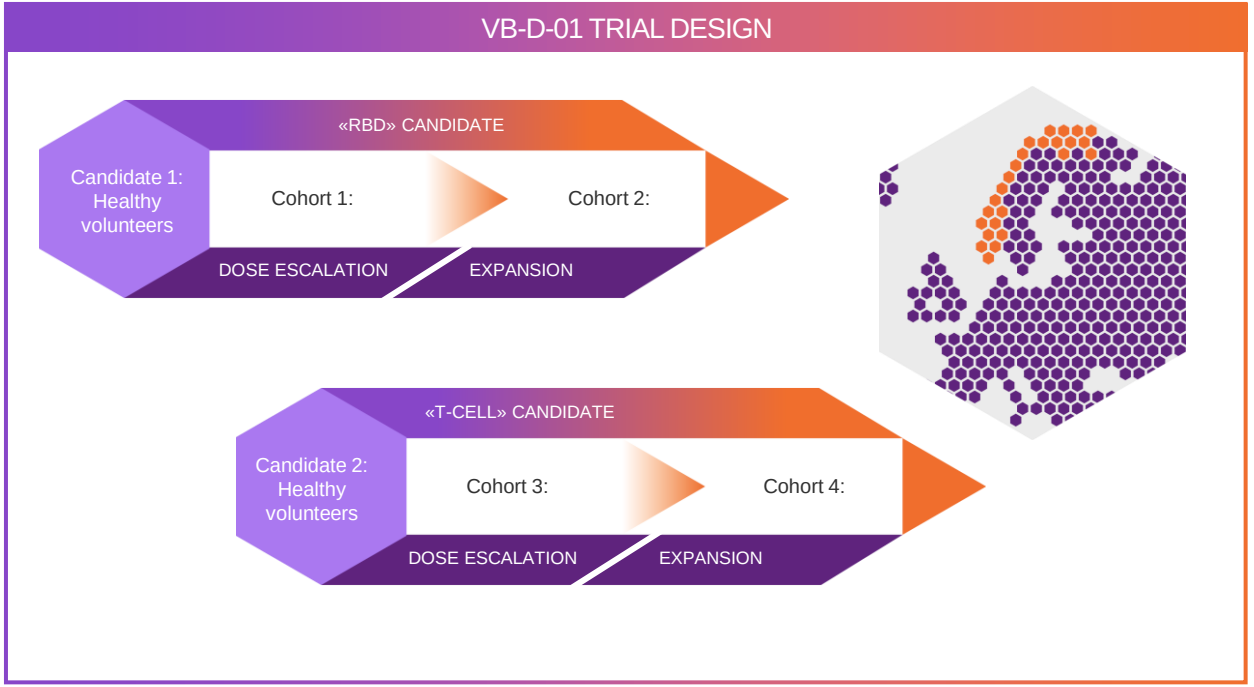
- First subject with RBD candidate dosed Nov. 3, 2021
- First patient with T cell candidate dosed Dec. 27, 2021

Cohort 3 fully enrolled for T cell candidate

Introduction of booster vaccination challenged the recruitment for the RBD candidate

- 2 dose levels fully enrolled in Cohort 1

Results expected in 3Q 2022



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Rikke Olesen
Mariane Høgsbjerg

Harlan Robins
Sharon Benzeno
Mark Klinger

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Contact:
Mikkel Wandahl Pedersen
Chief Scientific Officer
mwpedersen@nykode.com