nykode therapeutics

# Capital Markets Day

**May 12, 2022**

# 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.

# Today’s presenters from Nykode management; and Oslo University Hospital

## MICHAEL ENGSIG

**Chief Executive Officer**

Extensive experience from leading early-stage drug discovery through late-stage and commercial development

## AGNETE FREDRIKSEN

**Chief Innovation & Strategy Officer**

More than 20 years experience with APC-targeted vaccines from discovery to clinical development

- Co-founder Vaccibody/Nykode

## SIRI TORHAUG

**Chief Medical Officer**

More than 20 years experience within Clinical development and pharma scientific and medical affairs

## MIKKEL W. PEDERSEN

**Chief Scientific Officer**

More than 15 years experience with biologics drug discovery and development from both biotech and pharma

## HARALD GURVIN

**Chief Financial Officer**

Long career in the field of finance including:

- CFO at Flex LNG, listed on NYSE
- CFO at SFL Corporation, listed on NYSE

## KRISTINA LINDEMANN

**M.D., Ph.D.**

Associate professor and staff specialist at the Department of gynaecologic cancer and head of research group for gynecological oncology, Oslo University Hospital

- Leads the National advisory unit of gynaecologic cancer at Oslo University Hospital
- Received an ASCO merit award in 2018

# Agenda

01 **Business status and journey**

02 **Innovation strategy**

03 **Pipeline update**

04 **Research update**

05 **Business development and partnering strategy**

06 **Capital Markets Strategy, Financials and upcoming events**

07 **Q&A**

# 01 Business status and journey

## Another transformational year

# Pipeline

| | Program | Indication | Discovery/ Preclinical | Phase 1 | Phase 2 | Phase 3 | Partnerships | Upcoming Milestones |
|---|---|---|---|---|---|---|---|---|
| **Nykode** | | | | | | | | |
| **Oncology** | **VB10.16 (off-the-shelf)** | **HPV16+ cervical cancer[3]** | | | | | Roche [3] | 1H23: Updated data |
| | Internal (off-the-shelf) | Undisclosed targets | | | | | | |
| **Infectious Disease** | **VB10.COV2** | **SARS-CoV-2** | | | | | Adaptive [4] | 2H22: Interim data |
| | 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] | |

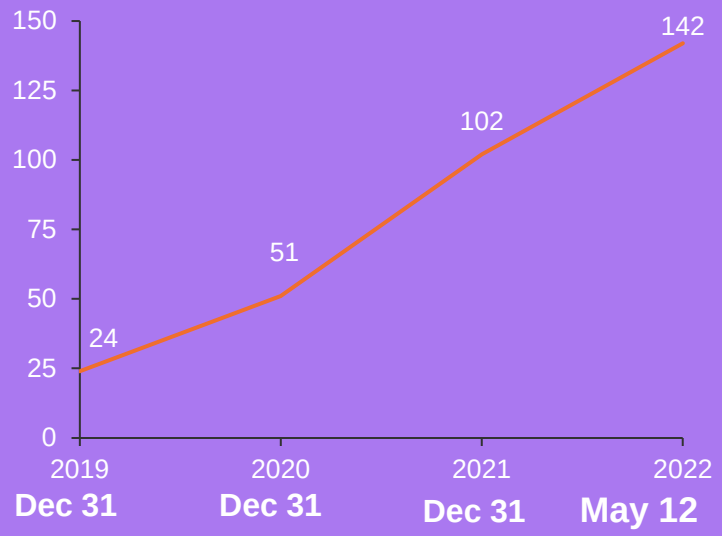
1. Genentech has an exclusive license to VB10.NEO; 2. Collaboration with Nektar Therapeutics on combining NKTR-214 (bempegaldesleukin) with VB10.NEO in trial arm 5B (SCCHN); 3. Roche supplies atezolizumab; 4. Collaboration with Adaptive Biotechnologies on SARS-CoV-2 T cell vaccine; 5. Collaboration with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

# Top-tier collaborations for cancer and infectious disease vaccines valued potentially more than $1.64 billion plus royalties

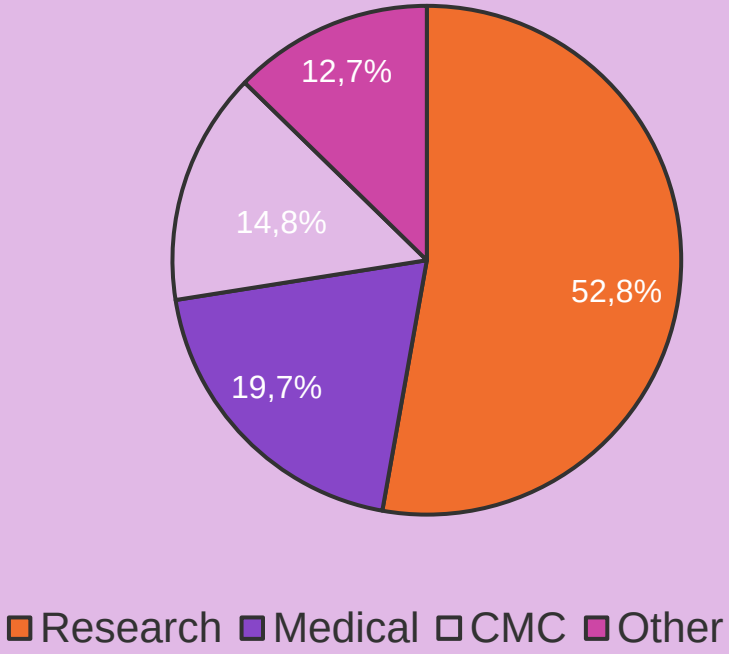
| Partner | Collaboration | Terms | Clinical Development |
|---|---|---|---|
| REGENERON | Multi-target license and collaboration agreement to develop 3 oncology and 2 novel infectious disease programs | $925M~<br>◆ $30M upfront<br>◆ $20M equity investment<br>◆ Potentially more than $875M in milestone payments<br>◆ Tiered high single-digit to low double-digit royalties | Regeneron to develop and potentially commercialize products<br><br>Nykode to supply technology and product supply through Phase 1 trials |
| Genentech A Member of the Roche Group | Worldwide, exclusive license and collaboration agreement to develop VB10.NEO, Nykode's individualized neoantigen cancer vaccine | $715M~<br>◆ $200M upfront/near term<br>◆ $515M in potential payments and milestones<br>◆ Tiered low double-digit royalties | Nykode to conduct clinical trials through Phase 1b study<br><br>Genentech to subsequently conduct clinical, regulatory, manufacturing and commercialization activities |
| Adaptive biotechnologies | Worldwide, exclusive rights to Adaptive's clinically validated SARS-CoV-2 T cell epitopes | ◆ Undisclosed | Nykode to design and develop T cell vaccines to specifically address SARS-CoV-2 variants of concern |

# Continued strong growth across the organization

## Number of employees




## Strong focus on R&D



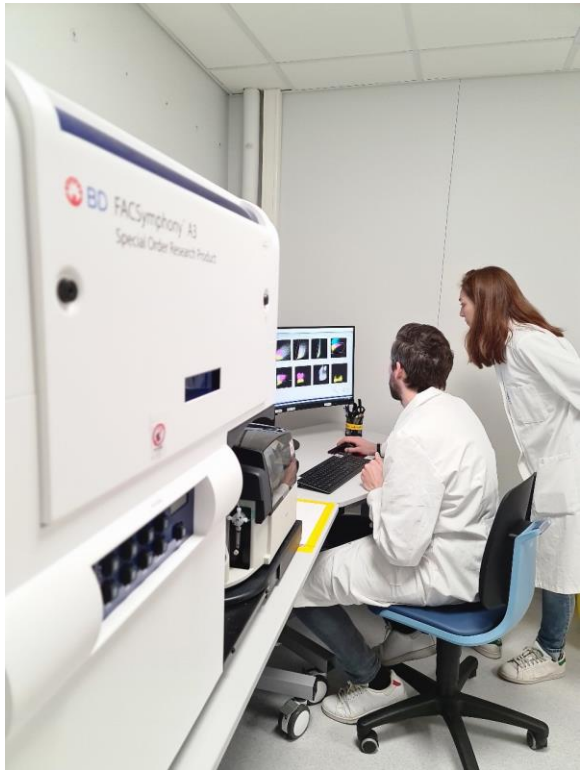

## Geographical footprint

| | |
|---|---|
| **Norway (HQ)** | 118 (83%) |
| **Denmark** | 24 (17%) |
| **Total** | **142** |

# New flagship lab opened in Oslo Science City

The heart of Nykode's innovation power-house

- Vaccine discovery
- Platform improvements and next generation products
- Process, analytical and formulation development
- Immune monitoring for clinical trials (GCLP)




# Strengthening the Nykode leadership team

## HARALD GURVIN, CFO

- Long career in the field of finance
- CFO at Flex LNG, listed on both the NYSE and Oslo Stock Exchange
- CFO at SFL Corporation, listed on the NYSE

## MIKKEL W. PEDERSEN, CSO

- More than 15 years experience with bio-logics drug discovery and development from Biotech and Pharma
- Head of Biologics Drug Design at Servier
- CSO of Symphogen a Danish biotech

## ELISE RAMSE, CHRO

- Extensive experience with HR and organizational development
- Head of People & Organization, Novartis Norway
- Leader of the Education Committee in The Life Science Cluster

## PETER FATUM, HEAD OF QA

- More than 25 years of experience from the pharma & medtech industry
- Head of Global GxP Compliance & Quality Systems in Sobi (Swedish Orphan Biovitrum AB
- Senior Global QA roles in ALK and Radiometer

# Added strong industry experience to the Board of Directors

- **Executive level, drug development experience**
- **Big Pharma**
- **US listed companies**

## MARTIN NICKLASSON, CHAIR OF THE BOARD AND CHAIR OF REMUNERATION COMMITTEE

Currently, serves as:

- Chair of Zealand Pharma A/S and on the board of Basilea Pharmaceutica Ltd.

Former positions includes:

- CEO Executive Officer of Biovitrum AB and Swedish Orphan Biovitrum AB (Sobi)
- Various Executive Vice President positions at AstraZeneca PLC

## BIRGITTE VOLCK, MEMBER OF THE BOARD AND CO-CHAIR OF R&D COMMITTEE

Currently serves as:

- Senior Vice President, Head of Clinical Development and Medical Affairs of Ascendis Pharma A/S (Nasdaq-listed) and on the board of Soleno Therapeutics Inc. (Nasdaq-listed)

Former positions includes:

- Head of R&D in Rare Diseases for GlaxoSmithKline; and CMO and SVP of Development at Swedish Orphan Biovitrum AB (Sobi)

# Continuing the internationalization with two new members

- **International executive level,**
- **Drug development and commercialization experience**
- **Extensive Biotech and Big Pharma experience**

## ELAINE SULLIVAN

Currently, serves as:
- CEO of Keltic Pharma Therapeutics Ltd
- Various Non-executive directorships including Active Biotech AB, Open Orphan PLC and IP Group plc amongst others

Former positions includes:
- CEO of Carrick Therapeutics, Ltd
- Eli Lilly and Company - VP, Global External Research and Development
- AstraZeneca Plc - VP and Head of New Opportunities Therapy Area; VP, Science and Technology

## ANNE WHITAKER

Currently serves as:
- Chairman of Aerami Therapeutics, Inc.
- Various other Non-executive directorships

Former positions includes:
- Various CEO and Chairman positions
- Senior Vice PresidentSanofi - President, Region Head for North America, Pharmaceuticals & Consumer Health
- GlaxoSmithKline –Senior Vice President and Business Unit Head, Cardiovascular, Metabolic and Urology; Senior Vice President, Global Leadership and Organization Development

# Proven Strategy to Generate First-in-Class Immunotherapies and Create Shareholder Value

## VISION

- To build the leading immunotherapy company developing game changing medicine across an expanding range of therapeutic areas

## UNIQUE THERAPEUTIC APPROACH

- Dual-focus on its differentiated platform and clinical projects
- Proprietary Vaccibody™ immunotherapy platform uniquely targets APCs to induce a strong CD8 killer T cell response
- Adaptable platform can quickly target emerging infectious diseases, including COVID-19

## NEXT GENERATION PLATFORM AND PIPELINE

- Pipeline of oncology and infectious disease vaccines includes partnered programs and wholly-owned clinical candidates

## STRONG VALIDATING PARTNERSHIPS

- Potentially > $1.64B in payments + royalties from top-tier partners Regeneron, Genentech and Adaptive

## CLINICALLY VALIDATED TECHNOLOGY

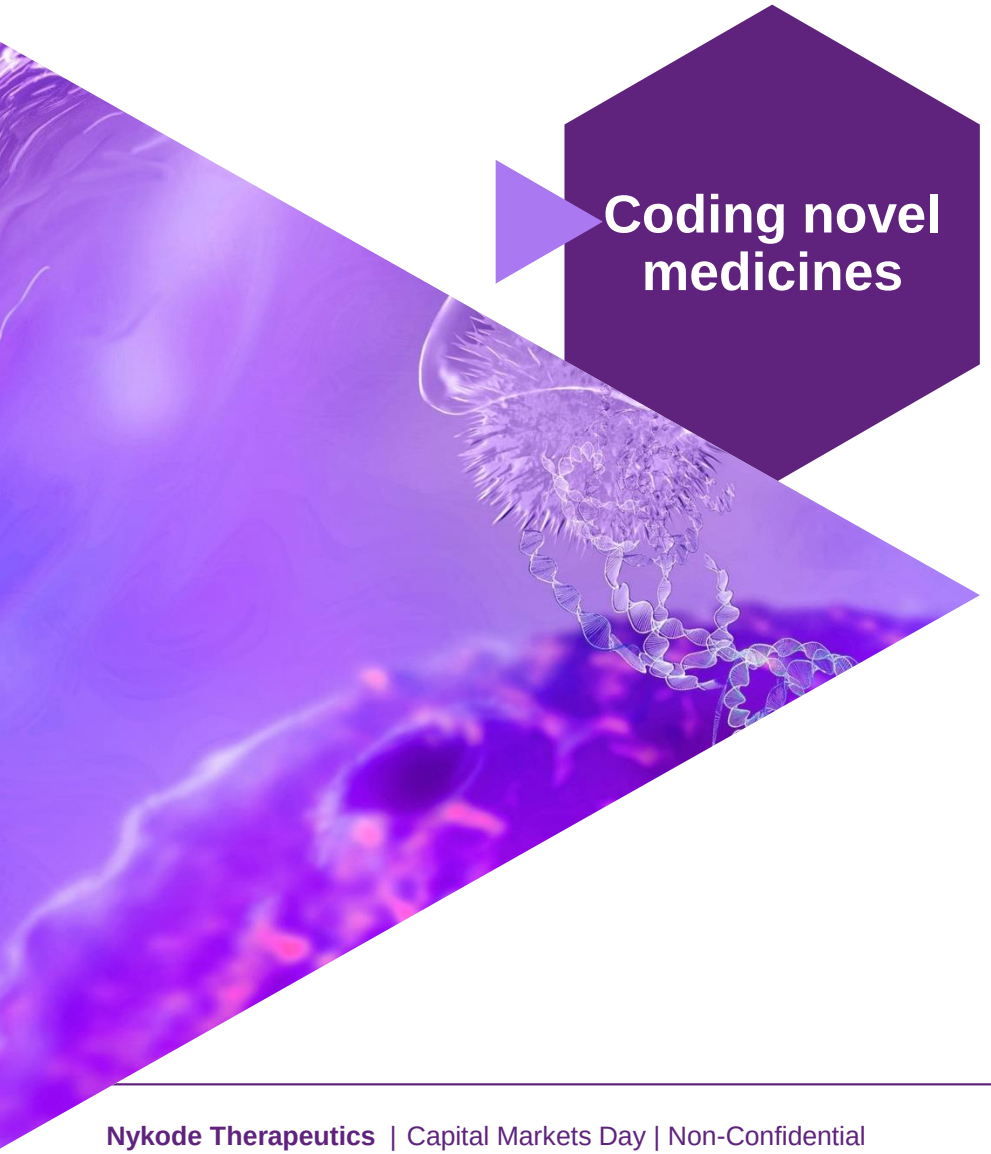
- Including positive interim results from Phase 2 HPV16+ cervical cancer program

## STRONG FINANCIAL POSITION

- Well capitalized with multiple significant catalysts in near-to-medium term

# 02 Innovation strategy

# Nykode’s innovation strategy




**The Innovation Strategy encapsulates our vision of finding new ways of coding medicine by breaking down conventional drug design**

Creating novel differentiated platform technologies applicable to fuel multiple products and optimize value-creation

**CONTINUE TO IMPROVE THE VACCINE PLATFORM**

**EXPANSION INTO NOVEL THERAPEUTIC AREAS AND NOVEL THERAPEUTIC MOLECULES**

**STIMULATE INNOVATIONS ACROSS THE ENTIRE ORGANIZATION**

# 03 Pipeline update

# Nykode development pipeline

*Clinical platform exposure*

EU & US exposure

5 clinical trials

8 countries

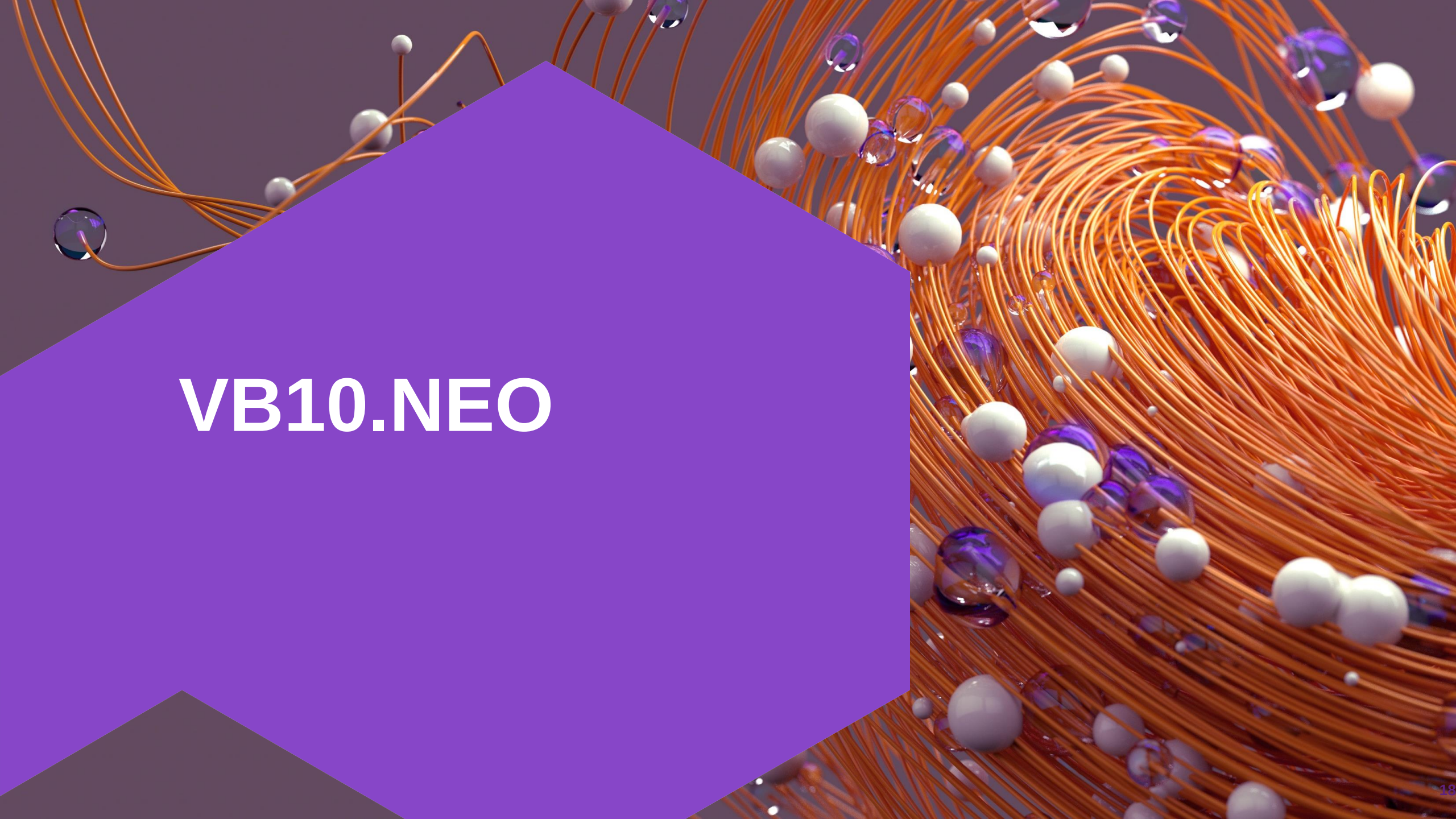
4 different compounds

12 different indications

>150 subjects exposed to our vaccines

>600 vaccines administered

- ❑ *Favorable safety profile – well tolerated as mono- and combination therapy*
- ❑ *Correlation of immune responses and clinical efficacy*
- ❑ *Clinically relevant and durable responses*


VB10.NEO

# **VB10.NEO:** Exclusively Licensed to Genentech

**Global, oncology collaboration between Nykode and Genentech to develop individualized neoantigen cancer vaccines across multiple tumor types**

nykode

Conduct clinical Phase1b trial testing 2 dose levels of VB10.NEO in combination with atezolizumab

Genentech
*A Member of the Roche Group*

Responsible, and bear all costs, for all further clinical, regulatory, manufacturing and commercialization activities for VB10.NEO

IN SUMMARY

- Research, bioinformatics and manufacturing collaboration
- Initial upfront and near-term payments of USD 200 million
- Potential milestone payments of up to USD 515 million
- Tiered low double-digit royalties on net sales

The Genentech collaboration was announced October 1st, 2020

# **VB10.NEO**: Individualized cancer DNA vaccine against various solid tumor types with locally advanced or metastatic disease

**Individualized treatment with broad potential across solid tumor indications**

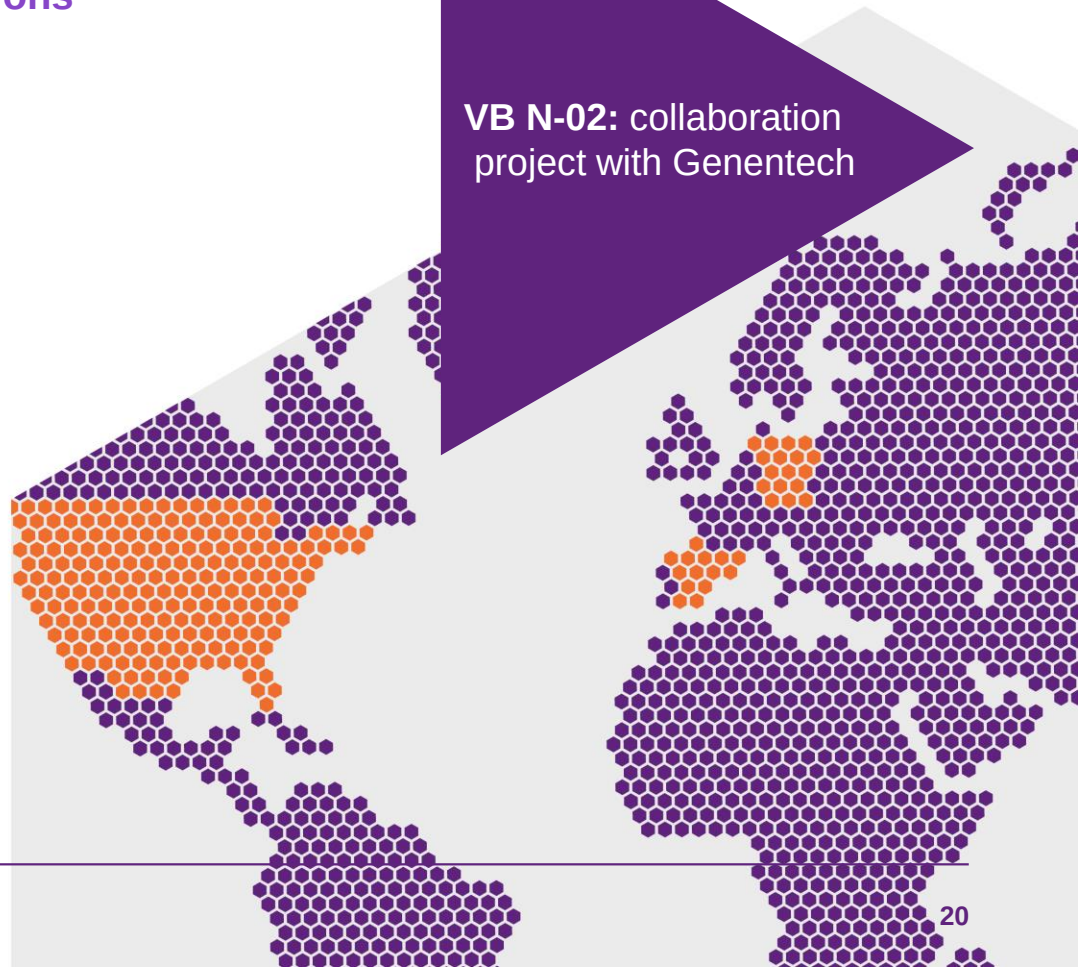
**N-01**

- Phase 1/2a trial with VB10.NEO in combination with CPI
- Recruitment finalized. Trial ongoing
- Conducted at 6 sites in Germany

**N-02**

- Dose escalation, phase 1b study of VB10.NEO in combination with atezolizumab (Tecentriq®)
- Planned enrollment up to 40 patients
- Recruiting sites open in US, Germany and Spain

**VB N-02:** collaboration project with Genentech



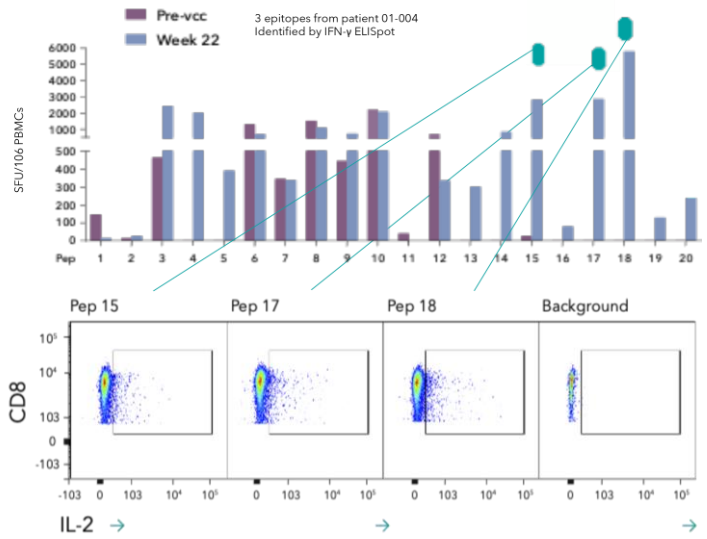
# **VB N-01:** Trial design facilitates efficacy readouts in each patient

*Signs of clinical efficacy correlated with strong dominant CD8 immune responses*

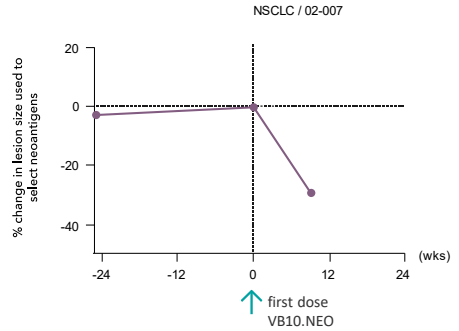
**Neoepitope-specific CD8 dominating immune responses in SCCHN patients with clinical response**

- Marked changes in lesion size development observed after initiating VB10.NEO
- Shrinkage of tumors and stabilization of progressing lesions

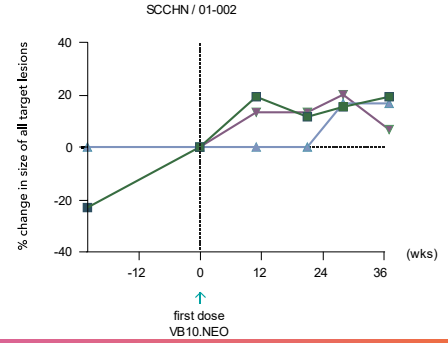
CHART 1

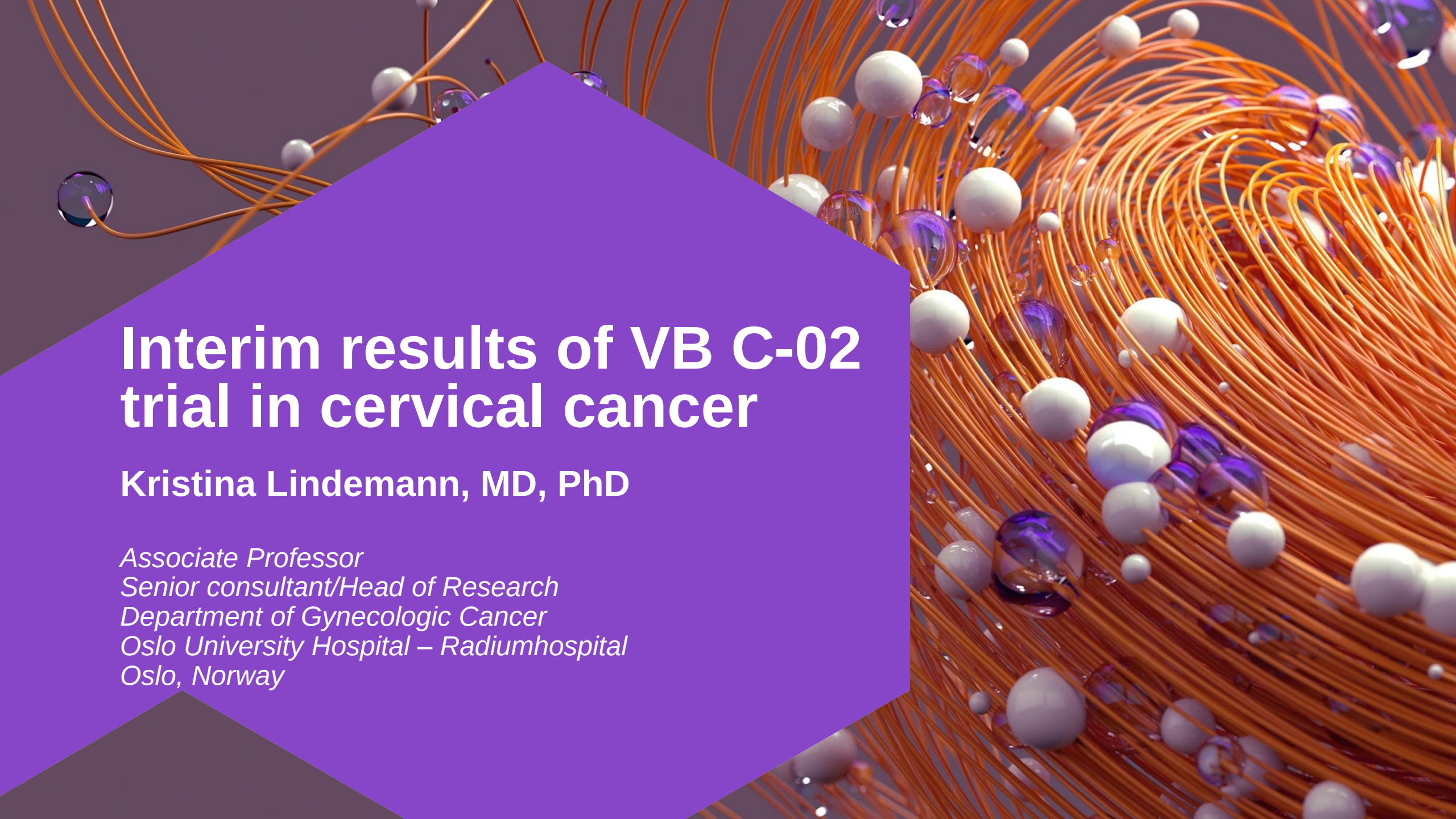



STABLE DISEASE AT VACCINATION START




PROGRESSIVE DISEASE AT VACCINATION START





# Interim results of VB C-02 trial in cervical cancer


**Kristina Lindemann, MD, PhD**

*Associate Professor*
*Senior consultant/Head of Research*
*Department of Gynecologic Cancer*
*Oslo University Hospital – Radiumhospital*
*Oslo, Norway*

# Kristina Lindemann – potential conflicts of interest

- **Personal financial interests**
- **GSK – Speaker**
- **MSD – Advisory board**
- **Eisai – Advisory board**

- **Institutional financial interests**
- **GSK – Study support**
- **AstraZeneca – Study support / Consultancy**
- **MSD – Study support / Advisory board**
- **Roche – Study support**
- **Nykode Therapeutics – Study support**

# Cervical cancer

*A leading cause of cancer death in women worldwide*

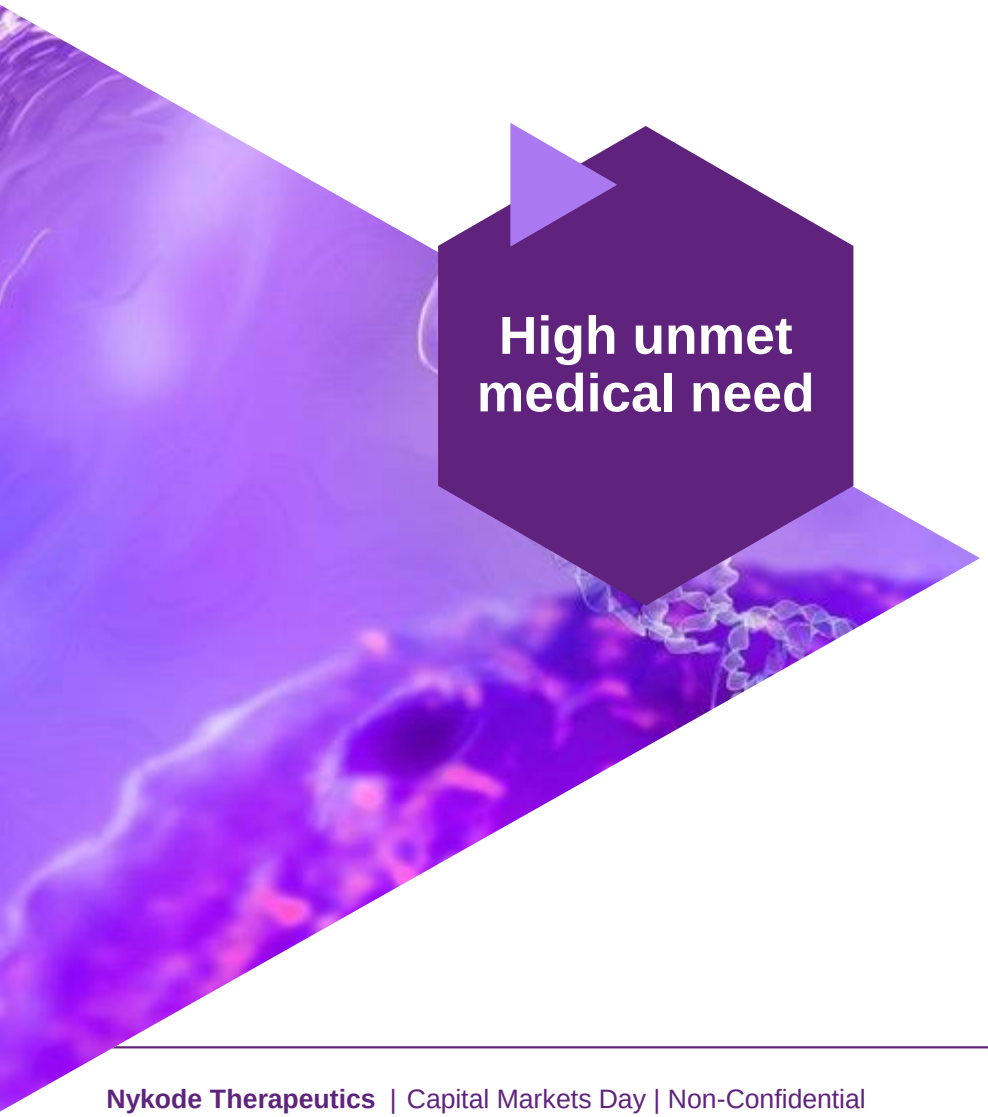
- Cervical cancer is the fourth leading cause of cancer death in women worldwide
- Each year nearly 600,000 women are diagnosed with cervical cancer worldwide
- Cervical cancer is often curable when detected early, but treatment options are more limited in advanced disease stages or when the cancer has spread




*EUCAN 2021; Bray et al.2018; Arbyn et al.2020; Crow 2012; Norwegian Cancer Registry 2020*

# Advanced cervical cancer

*Limited treatment options after progression on first-line treatment*




## Pembrolizumab is the only anti–PD-1 agent approved in the US as second-line therapy for patients with PD-L1 positive recurrent or metastatic cervical cancer

- US approval based on KEYNOTE-158 study that showed a modest response rate of 14% with all responses seen in PD-L1 positive patients

## Current ESMO guidelines do not recommend a specific treatment in patients with advanced/metastatic cervical cancer who progress on first-line treatment

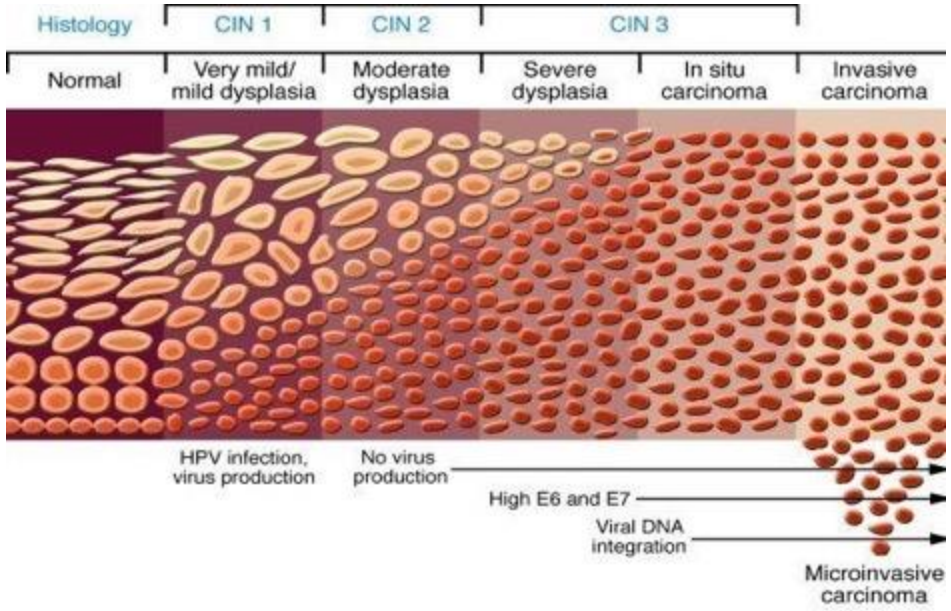
- Potential treatment options all have low response rates with short duration of response and poor survival



*Chung et al. 2019/2021; ESMO 2017.*

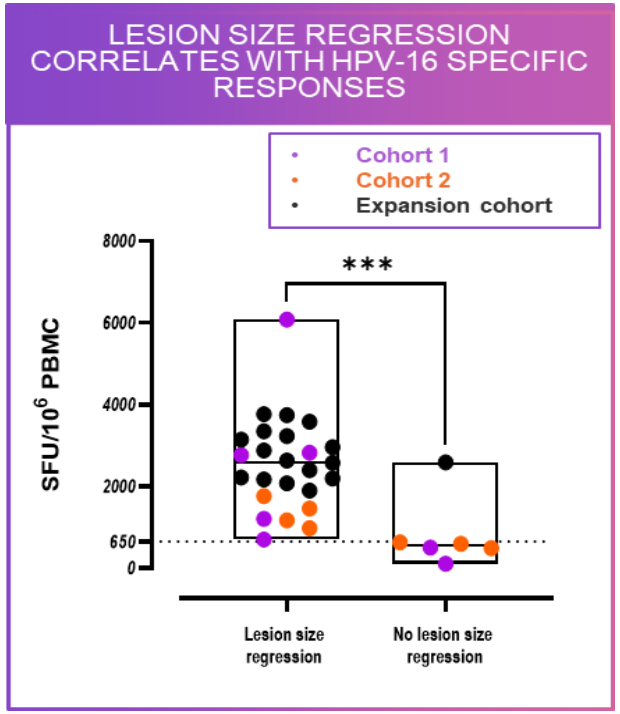
# HPV16 is an ideal target for off-the-shelf cancer vaccines

- High-grade cervical intraepithelial neoplasia (CIN) caused by infection with human papillomavirus (HPV) often precedes the development of cervical cancer
- Almost all cervical cancers are caused by HPV infection and HPV16 accounts for more than half of all cases
- HPV E6 and E7 viral antigens are only expressed by HPV-infected cells and thus act as tumor-specific antigens that are attractive targets for therapeutic cancer vaccines like VB10.16



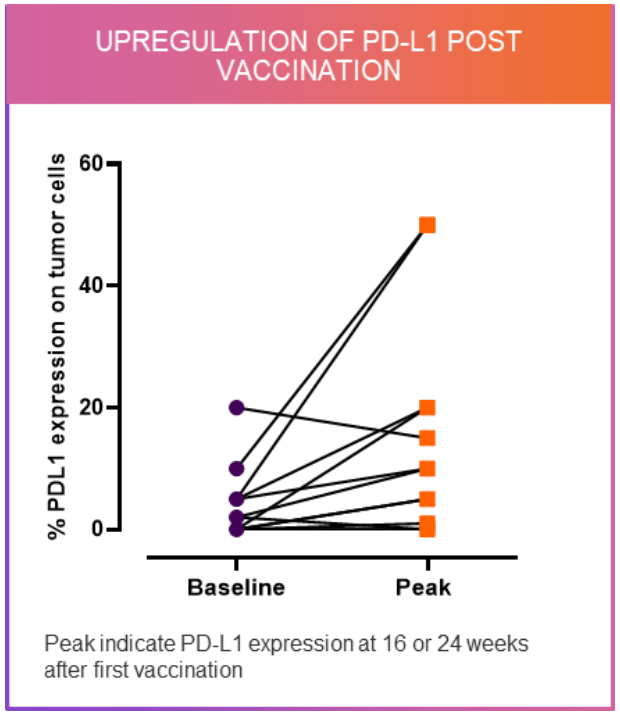

*Lowy et al. 2006*

# VB C-01: VB10.16 monotherapy in pre-cancerous cervical lesions: *strong signs of vaccine-induced clinical efficacy*




Highly significant correlation between vaccine-induced T cell responses and lesion size regression across all cohorts


Lesion size reduction in all patients in expansion cohort followed >4 months

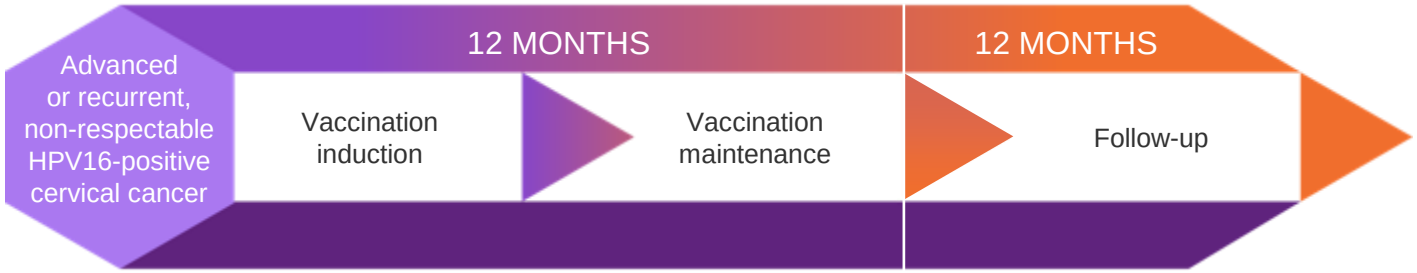



PD-L1 was upregulated in post-vaccination lesions suggesting that the vaccine may sensitize the lesion for CPI treatment

# **VB C-02:** VB10.16 in combination with atezolizumab 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, ORR (based on RECIST 1.1 by blinded independent central review)
- Fully enrolled with 52 patients
- Conducted in Europe in 6 countries (Germany, Belgium, Bulgaria, Czech Republic, Poland and Norway)
- Enrolled patients received treatment with 3 mg VB10.16 in combination with 1200 mg atezolizumab for up to 48 weeks.



# Interim analysis

*Number of patients included in the pre-planned interim analysis*

| Population | N |
|---|---|
| **Enrolled patients** | 50 |
| **Efficacy Analysis Set (EAS)**<br>At least one available post-baseline scan at cut off date* | 39 |
| *Completed Treatment* | *6* |
| *Discontinued* | *21* |
| *Ongoing* | *12* |
| **Safety Analysis Set (SAS)**<br>At least one dose of VB10.16 + atezolizumab at cut off date* | 50 |

- *Cut off date is 14 February 2022; first post-baseline scan was taken at week 9*
- *7 patients on treatment had not yet reached week 9 at cut off date*

# Baseline characteristics of EAS population

*C-02 included a heavily pre-treated population with advanced cervical cancer*

| Characteristic | | N (%) |
|---|---|---|
| **Age (mean)** | | 48.9 yrs |
| **Age (median)** | | 47.0 yrs |
| **Ethnicity (White)** | | 39 (100%) |
| **Prior systemic treatment lines** | | |
| | **1** | 12 (31%) |
| | **2** | 15 (39%) |
| | **3** | 9 (23%) |
| | **4** | 1 (2%) |
| | **5** | 2 (5%) |
| **Prior surgery** | | |
| | **Y** | 19 (49%) |
| | **N** | 20 (51%) |
| **Prior radiotherapy** | | |
| | **Y** | 31 (80%) |
| | **N** | 8 (20%) |
| **Prior chemotherapy** | | |
| | **Y** | 39 (100%) |
| | **N** | 0 (0%) |

| Characteristic | | N (%) |
|---|---|---|
| **ECOG** | | |
| | **0** | 22 (56%) |
| | **1** | 17 (44%) |
| **PD-L1 status at baseline** | | |
| | **TIC 0 (<5%)** | 12 (31%) |
| | **TIC 1 (5-10%)** | 3 (8%) |
| | **TIC 2 (>10%)** | 19 (49%) |
| | **Missing** | 5 (13%) |
| **Histology** | | |
| | **Squamous cell** | 28 (72%) |
| | **Adenocarcinoma** | 8 (21%) |
| | **Missing/unknown** | 3 (7%) |
| **Metastases*** | | |
| | **Liver** | 7 (18%) |
| | **Lung** | 17 (44%) |
| | **Other** | 19 (49%) |
| **Extra-pelvic metastases present** | | |
| | **Yes** | 35 (90%) |
| | **No** | 4 (10%) |

*Sum >100% as 4 patients had both liver and lung metastases

# Best overall response by blinded independent central review

*Promising clinical activity in majority of patients with advanced cervical cancer including PD-L1 negative patients*

| BOR rate | N (%) |
|---|---|
| **Complete Response** | 2 (5%) |
| **Partial Response** | 6 (15%) |
| **Stable Disease**<br>*SD+* | 17 (44%)<br>*9* |
| **Progressive Disease** | 13 (33%) |
| **NE** | 1 (3%) |

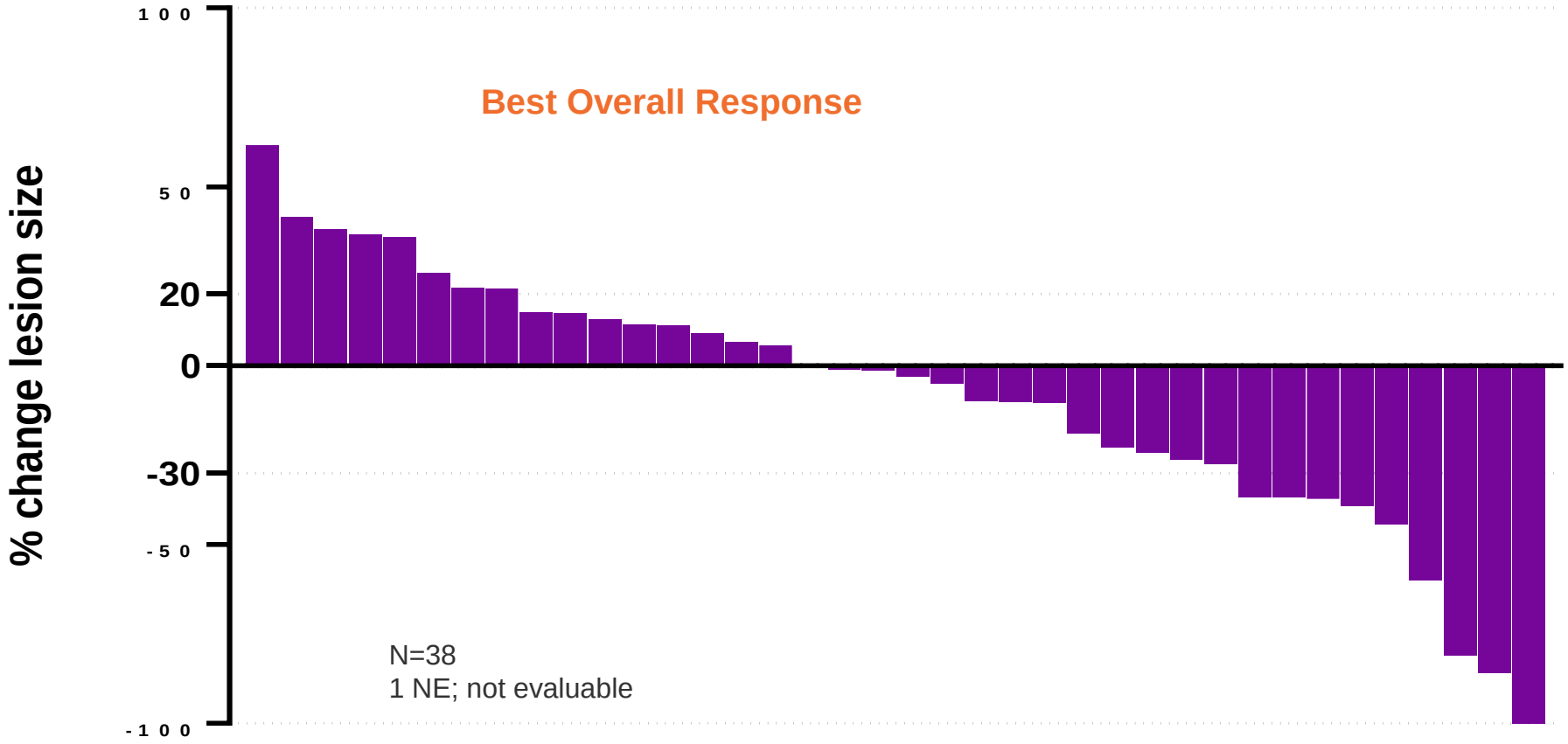
- *Assessment using RECIST v1.1 criteria*
- *SD+ = Stable Disease with shrinkage in target lesion(s)*
- *NE = non-evaluable*

**ORR = 21%** (8/39 patients)

**DCR = 64%** (25/39 patients)

**Median follow up time (range) = 6 months**
**(3-20 months)**

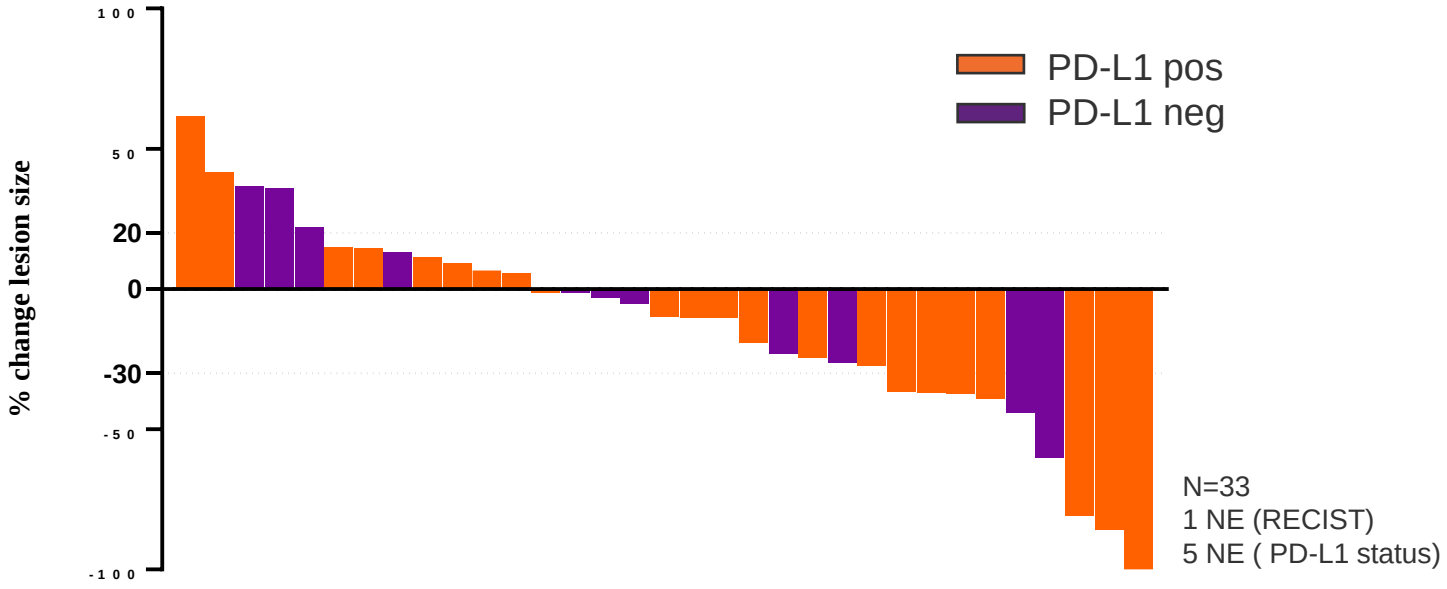
# Anti-tumor activity was observed in majority of patients including 9 patients with SD+




*SD+ = SD with shrinkage in target lesion(s)*

# Anti-tumor activity was observed both in patients with positive and negative baseline PD-L1 status

## Tumor regression in PD-L1 +/-



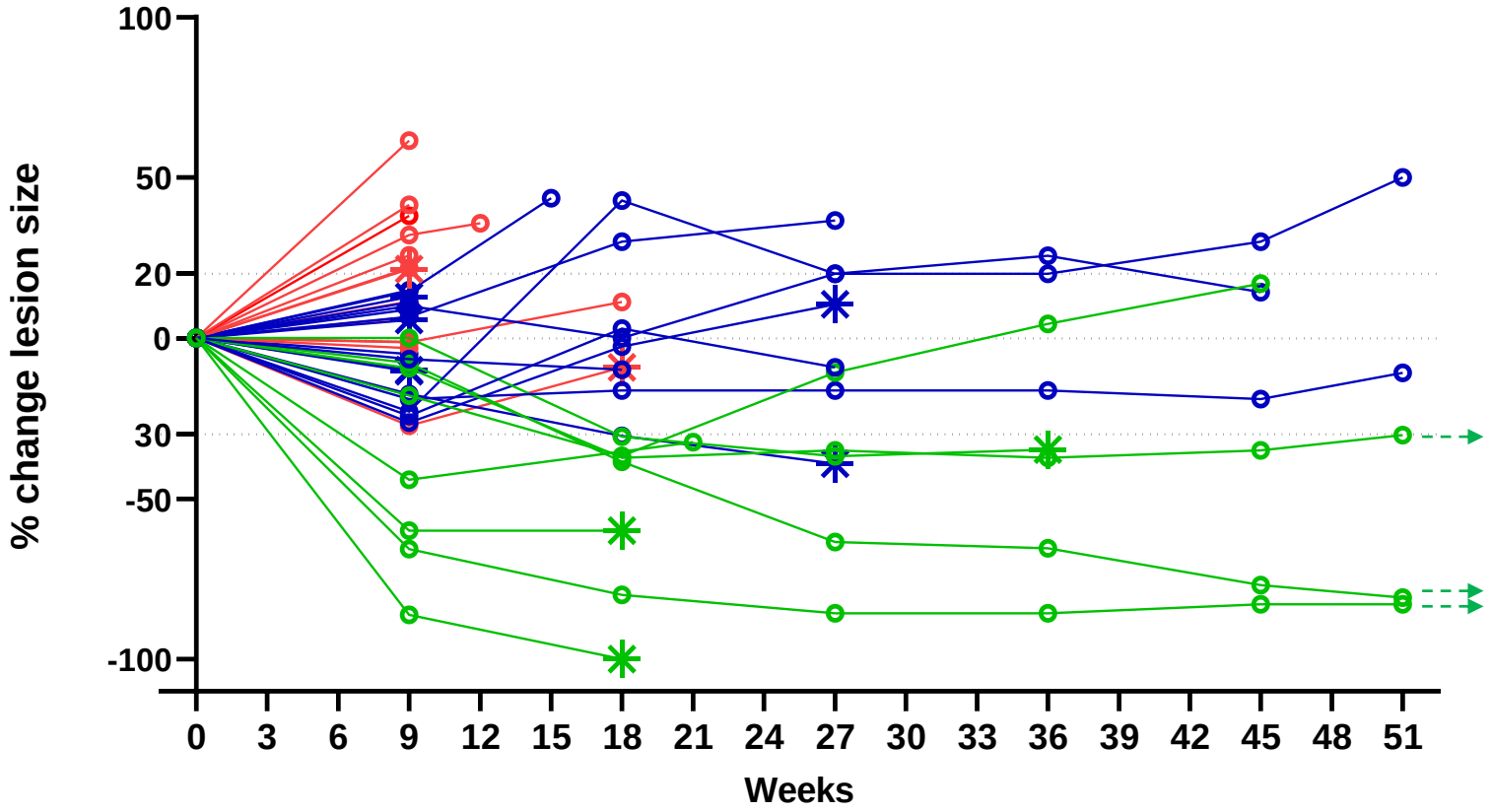

| PD-L1 status | ORR (n/N) | DCR (n/N) |
|---|---|---|
| **Positive** (TIC 1-2) | **27%** (6/22) | **77%** (17/22) |
| **Negative** (TIC 0) | **17%** (2/12) | **58%** (7/12) |

**These findings support that VB10.16 in combination with atezolizumab may enhance clinical responses also in PD-L1 negative patients where CPI monotherapy is not approved**



- PD-L1 was scored by TIC (Tumor and immune cell) scoring using Ventana SP263 platform (Roche Diagnostics)
- PD-L1 status at baseline was available in 34 patients, 1 PD-L1 negative patient was NE according to RECIST

# VB10.16 in combination with atezolizumab showed promising efficacy with durable responses




Complete/Partial Response
Stable Disease
Progressive Disease

- Durable responses in the DCR population
- 6 out of 8 ORR patients have an ongoing response

* Subjects with ongoing study treatment at cut off date (n=12)
3 responders who completed study treatment showed ongoing response on last available scan (Week 51)

N=38
1=NE; not evaluable
Treatment period week 0-48

# Safety and tolerability

*VB10.16 was generally well-tolerated and has a favorable safety profile*

## TRAEs considered related to VB10.16

| System Organ Class<br>Preferred Term | Any Grade N=50 (%) | Grade 3 N=50 (%) | Grade 4-5 N=50 (%) |
|---|---|---|---|
| **All TRAEs related to VB10.16** | 15 (30) | 1 (2) | - |
| **General disorders and adm. site conditions.** | 8 (16) | - | - |
| Administration site pain | 2 (4) | - | - |
| Fatigue | 1 (2) | - | - |
| Injection site bruising | 2 (4) | - | - |
| Injection site discomfort | 2 (4) | - | - |
| Injection site haematoma | 1 (2) | - | - |
| Injection site pain | 1 (2) | - | - |
| **Injury, poisoning and procedural complications** | 1 (2) | - | - |
| Infusion related reaction | 1 (2) | - | - |
| **Metabolism and nutrition disorders** | 1 (2) | - | - |
| Decreased appetite | 1 (2) | - | - |
| **Musculoskeletal and connective tissue disorders** | 3 (6) | 1 (2) | - |
| Arthralgia | 1 (2) | 1 (2) | - |
| Myalgia | 1 (2) | - | - |
| Pain in extremity | 1 (2) | - | - |
| **Skin and subcutaneous tissue disorders** | 4 (8) | - | - |
| Erythema | 1 (2) | - | - |
| Pruritus | 2 (4) | - | - |
| Rash | 2 (4) | - | - |

AE=adverse event; TRAE=treatment-related adverse event

VB10.16 in combination with atezolizumab was generally well-tolerated

- TRAEs of any grade related to either VB10.16 or atezolizumab was seen in 64% of patients.
- 5 patients (10%) experienced TRAEs of grade 3.
  - 1 patient (2%) experienced a TRAE of grade 3 related to VB10.16.
- No TRAEs of grade 4-5 were reported
- No deaths related to either VB10.16 or atezolizumab.

50 patients were included in the safety population for the interim analysis. Median number of VB10.16 doses given was 5 (range 1-11).

# Patient case 1

*T cell excluded and PD-L1 negative tumor with clinical response*

**Patient**
66 years old female with squamous cell cervical carcinoma – diagnosed in November 2019 and enrolled in February 2021 with progression following radiotherapy and one line of chemotherapy

**Clinical status**
Completed 24 weeks of study treatment with no signs of progression

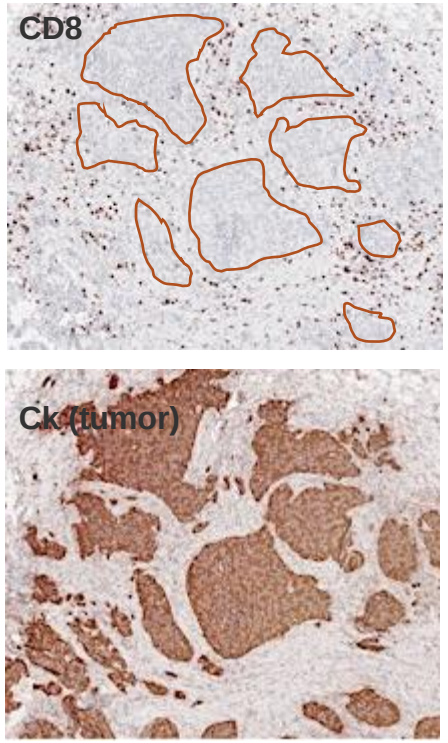
**Tumor response status**
Partial Response at Week 9 and ongoing response

**HPV16 specific T cell response**
Increased post vaccination

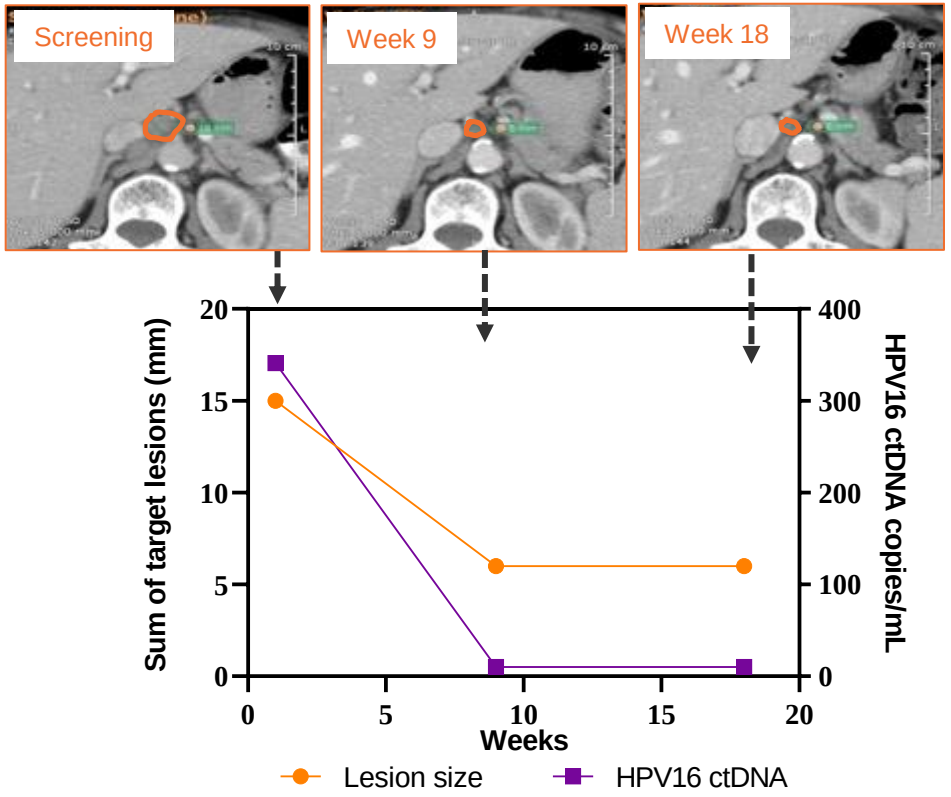
**Tumor microenvironment at baseline**
T cell excluded and PD-L1 negative

**HPV16 circulating tumor DNA kinetics**
Clearance observed from week 9

**T cells present in stroma, but excluded from the tumor area**




**Shrinkage of target lesion (retrocaval lymph node)**




HPV16 ctDNA analysed by ddPCR.
PD-L1 scored by SP263 Ventana using vCPS/TIC

# Patient case 2

*Deepening and durable clinical response*

**Patient**
55 years old female with squamous cell cervical carcinoma – diagnosed in November 2019 and enrolled in August 2021 with progression after radiotherapy and two previous systemic treatments

**Clinical status**
Completed study treatment (48 weeks) with no signs of progression at last follow-up scan

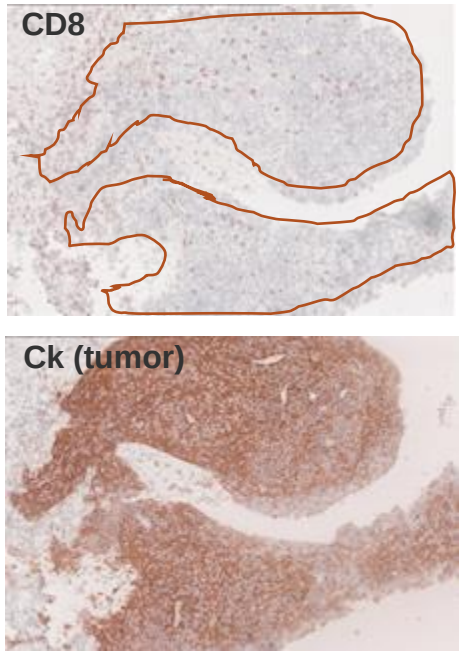
**Tumor response status**
Partial Response at Week 18 and signs of deepening anti-tumor response

**HPV16 specific T cell response**
Increased post vaccination

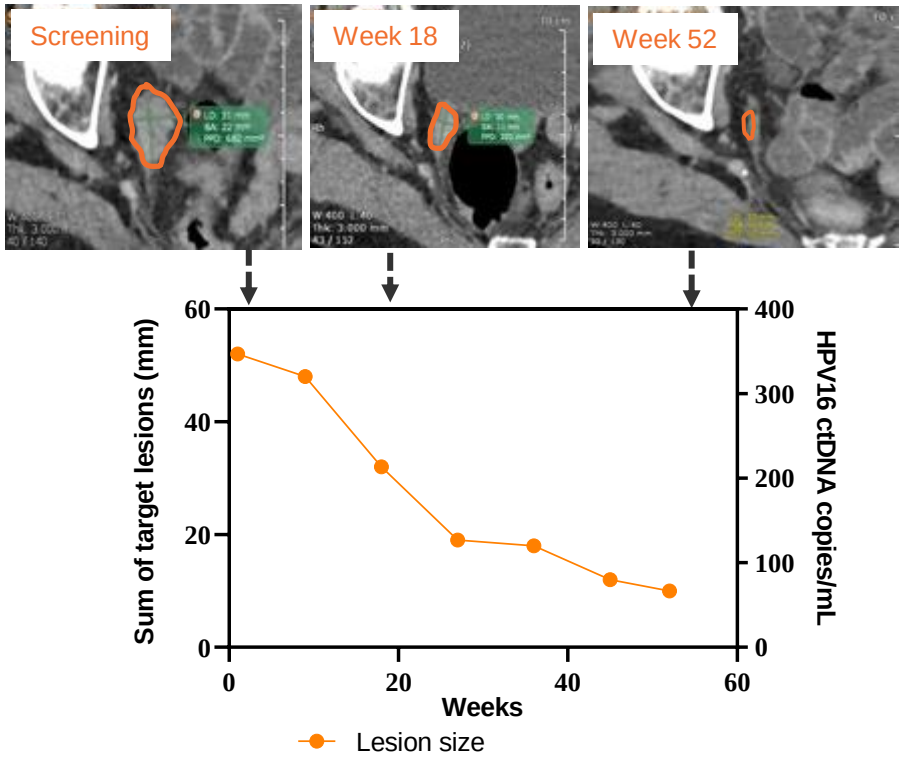
**Tumor microenvironment at baseline**
T cell infiltrated and PD-L1 positive

## T cells present in tumor tissue

CD3+CD8+Ki67+




## Shrinkage of target lesions (pelvic lymph node)




HPV16 ctDNA < LOD (not detected)
HPV16 ctDNA analysed by ddPCR.
PD-L1 scored by SP263 Ventana using vCPS/TIC

# VB C-02 Interim Analysis – Conclusion

- VB10.16 in combination with atezolizumab showed promising efficacy in heavily pre-treated patients with advanced HPV16+ cervical cancer who have a high unmet medical need
- VB10.16 in combination with atezolizumab showed durable responses with a very high DCR in advanced cervical cancer patients
- Efficacy was observed in patients with both PD-L1 positive and PD-L1 negative tumors, as well as non-inflamed tumors
- HPV16-specific IFN-γ T cell responses increased post vaccination in the majority of subjects and were associated with clinical efficacy indicating induction of clinically relevant T cell responses
- Complete clearance of HPV16 ctDNA was significantly correlated with clinical outcomes indicating that HPV16 ctDNA may be an early marker of response to treatment
- VB10.16 in combination with atezolizumab has a favorable safety profile

**The anti-tumor activity seen in the PD-L1 negative population may potentially open up for treatment of a new subset of patients**

# **VB10.16:** Therapeutic cancer DNA vaccine against HPV16 induced pre-malignancies and malignancies

**Expanding the clinical development into multiple indications**

**C-01**

HPV16+ Pre-cancerous cervical lesions

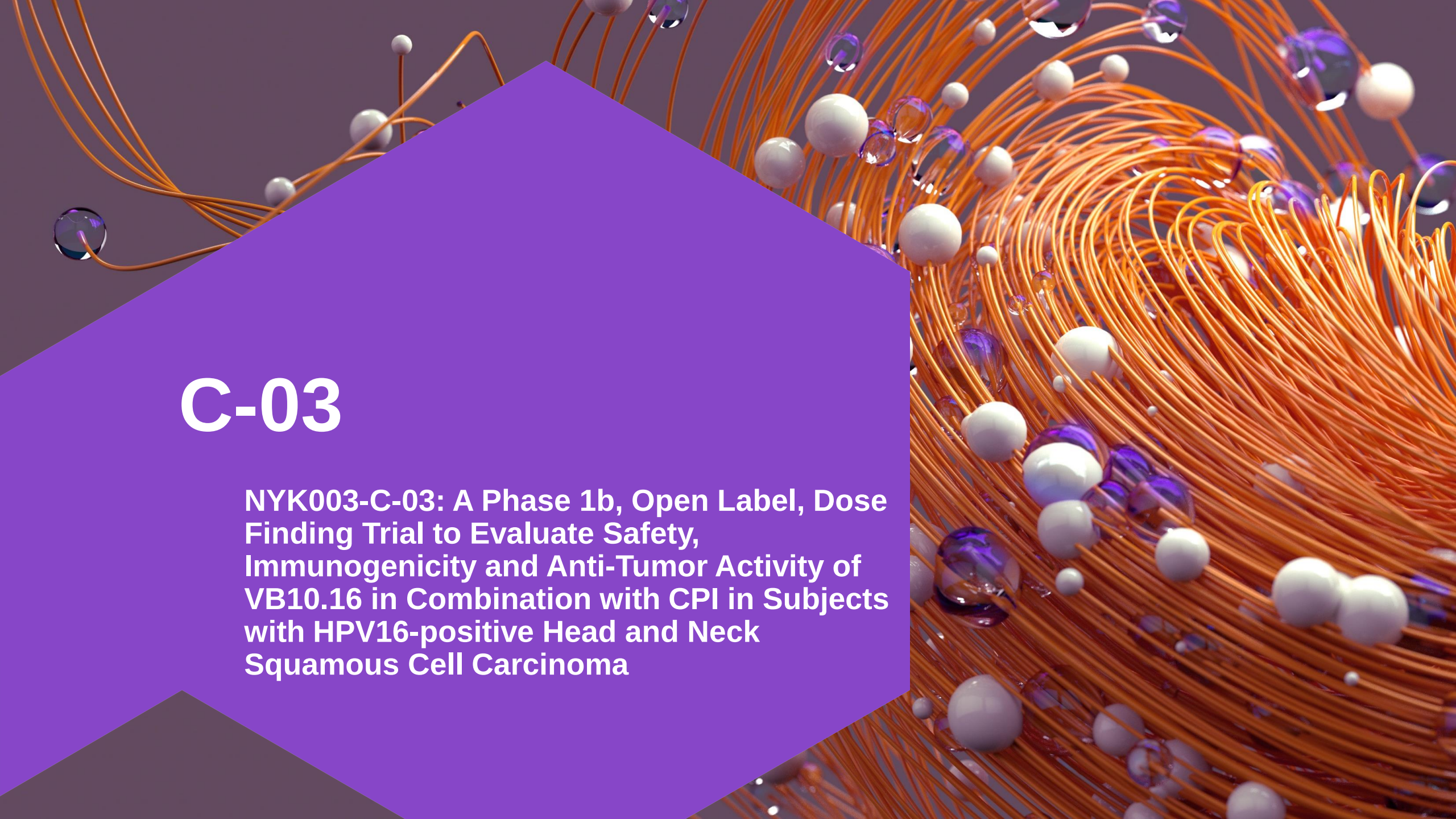
**C-02**

Advanced HPV16+ cervical cancer

**C-03**

HPV16+ Head & Neck squamous cell carcinoma

**VB10.16**
Off the shelf vaccine targeting foreign viral antigens



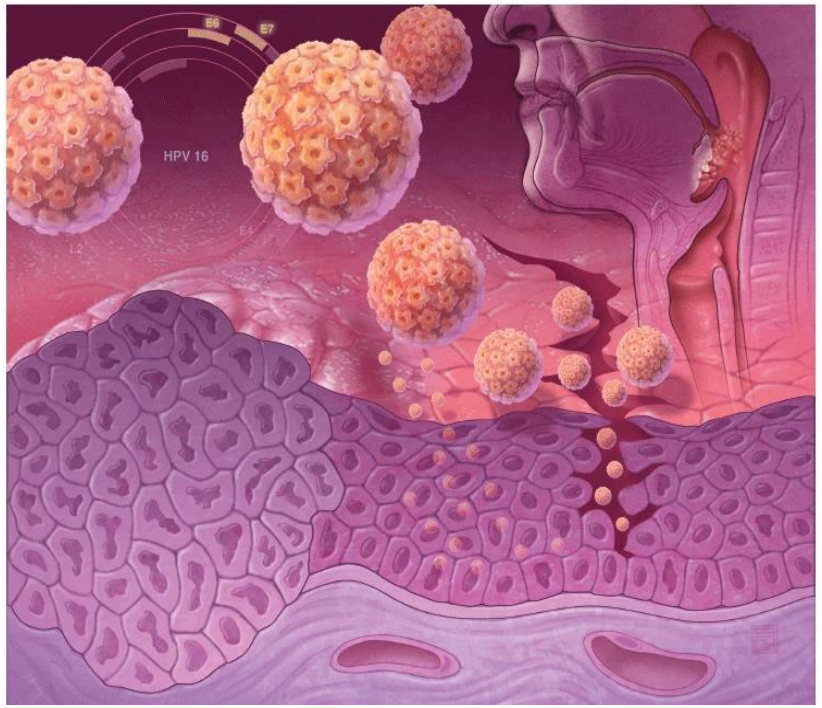
# C-03

**NYK003-C-03: A Phase 1b, Open Label, Dose Finding Trial to Evaluate Safety, Immunogenicity and Anti-Tumor Activity of VB10.16 in Combination with CPI in Subjects with HPV16-positive Head and Neck Squamous Cell Carcinoma**

# HPV16-positive squamous cell head and neck cancer

*Continued increase in cases worldwide*

- **The number of patients with squamous cell head and neck cancer (HNSCC) has risen substantially during the last decades and around 560,000 patients are now diagnosed yearly**
- **This rising incidence in HNSCC is mainly attributed to Human Papilloma Virus (HPV) infections - HPV16 accounts for nearly 90% of such cases**
- **HNSCC can be managed effectively in early stages, but most patients are diagnosed at advanced stages where treatment outcomes are less favorable**




*Johnson et al. 2020; Cancer Network 2015*

# NYK003-C-03 Phase 1b trial

*Combining VB10.16 with a checkpoint inhibitor (CPI)*

- **The use of immunotherapy is currently limited to PD-L1+ recurrent or metastatic advanced HNSCC**
- **Responses to immunotherapy in this advanced setting are limited with modest response rates (ORR ranging from 13-17%)**

- **Nykode is currently planning a dose escalation trial of VB10.16 in combination with CPI in patients with HPV16-positive HNSCC**
- **Safety, efficacy and immunogenicity of multiple VB10.16 dose levels will be assessed**

- **Trial builds on the encouraging clinical efficacy and favorable safety profile that was observed with VB10.16 in combination with CPI in patients with HPV16-positive cervical cancer (C-02 trial)**

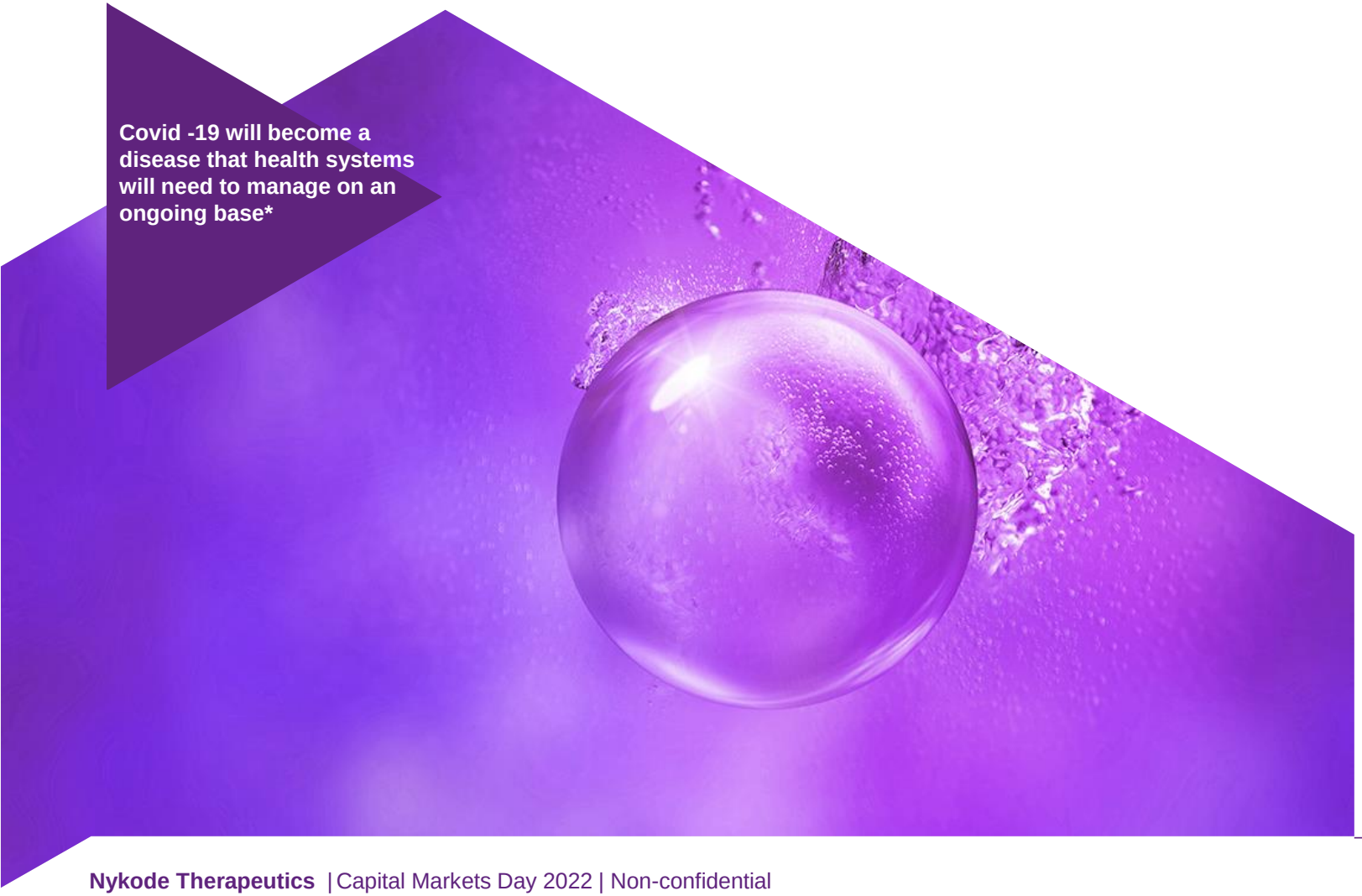
- **Planned trial initiation H2 2022**

*Ferris et al. 2016; Burtness et al. 2019*

# VB10.COV2

# SARS COV2: A continuous global health threat

*Need for new vaccine approaches*




With SARS CoV2 a new global human pathogen has emerged. It will stay with us and has to be addressed by health systems globally

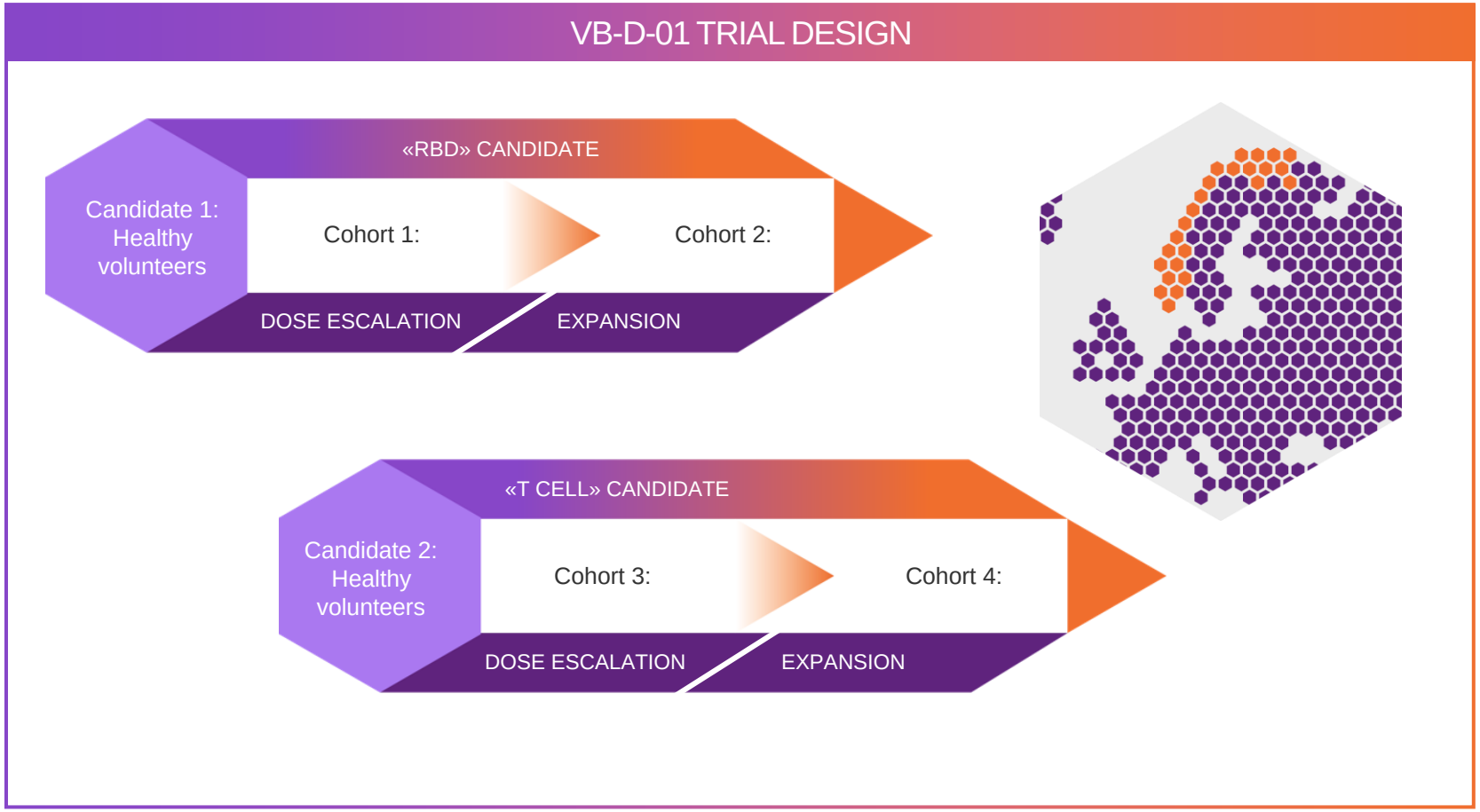
SARS CoV2 new Variants of concern (VoC) are still emerging

Approved vaccine immunity seems to be short lived, especially in vulnerable target populations like elderly and immune compromised

* (FDA advisory committee, 4.Apr.2022)

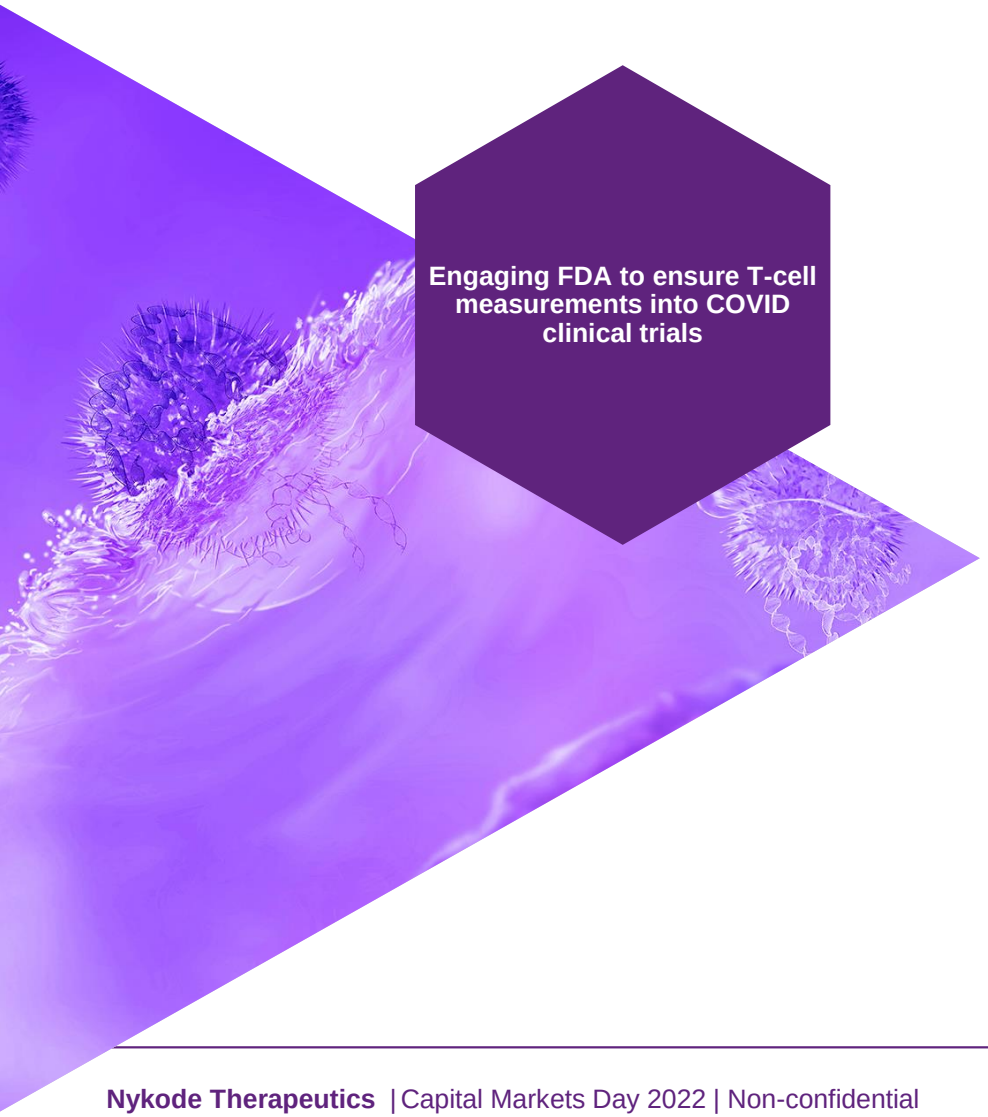
# Phase 1/2 trial investigating two candidates as a diverse booster in previously vaccinated subjects

- A Phase 1/2, open label, dose escalation trial with two SARS-CoV-2 virus vaccine candidates (C1) and (C2)
- C1: First subject dosed 03 Nov 2021
  - Ongoing enrollment in the 3 dose level in Cohort 1
- C2: First subject dosed 27 Dec 2021
  - Fully enrolled all 3 dose levels in Cohort 3
- Expected results in 2H 2022




 ClinicalTrials.gov Identifier: NCT05069623

# T-cell vaccine rationale




Future VOCs are not unilaterally likely to be milder or cause a lower disease burden

Based on efficacy studies with approved Spike based vaccines, T-cells appear central in maintaining the protection against severe disease and death across current VoCs.

COVID-19 vaccines inducing a broader T cell immunity across populations may therefore be a good way to prevent severe disease across future VOCs

***Nykode focuses on our T-cell candidate***
***Awaiting data from the ongoing phase 1 trial VB D-01***

# 04 Research update

# Agenda

- Discovery pipeline update
- Platform improvement strategy
- Tolerizing vaccines

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# Discovery pipeline update

# Discovery pipeline

| Program | Indication | Early Discovery | Late discovery | Pre-clinical | Phase 1 | Partnerships | Upcoming Milestones |
|---|---|---|---|---|---|---|---|
| **Oncology** | | | | | | | |
| **Off the shelf** | | | | | | | |
| Regeneron program 1 | – | ● | ○ | ○ | ○ | Regeneron[6] | |
| Regeneron program 2 | – | ● | ○ | ○ | ○ | Regeneron[6] | |
| Regeneron program 3 | – | ● | ○ | ○ | ○ | Regeneron[6] | |
| NYK011 | Undisclosed target | ● | ○ | ○ | ○ | | Selection of lead |
| **Infectious disease** | | | | | | | |
| Regeneron program 4 | - | ● | ○ | ○ | ○ | Regeneron[6] | |
| Regeneron program 5 | - | ● | ○ | ○ | ○ | Regeneron[6] | |
| NYK004 | Undisclosed pathogen | ● | ● | ○ | ○ | | Selection of lead |
| NYK005 | Undisclosed pathogen | ● | ● | ○ | ○ | | Selection of lead |

6. Developed under license to Regeneron

# Regeneron collaboration

Multitarget collaboration with the aim of using Nykode's modular vaccine platform combined with Regeneron's unique antigen selection expertise to discover and develop

- Two vaccine programs within infectious diseases
- Three vaccine programs within oncology

The collaboration off to a good start

- Progressing according to plans
- Lots of energy, good discussions and knowledge sharing

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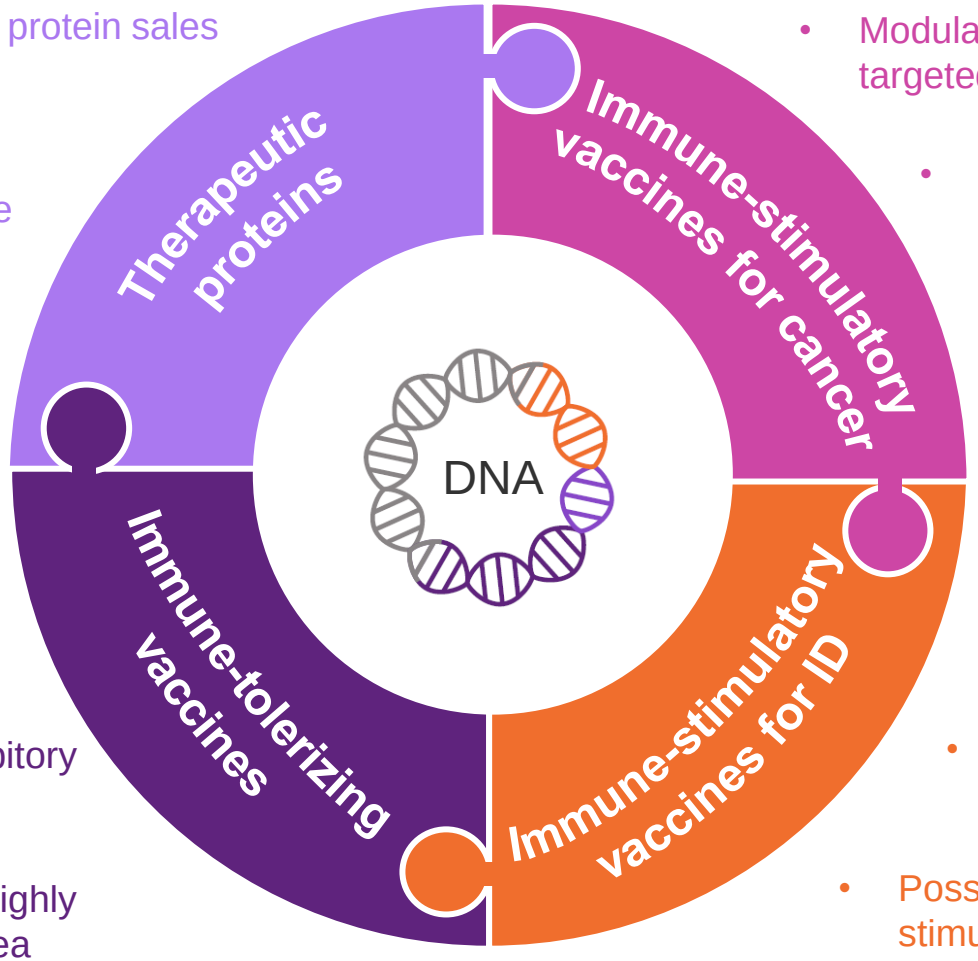
# Platform improvement strategy

# Preambles to technology platform improvement

- Nykode's pipeline as of today consists of infectious disease and cancer vaccines, which are based on the Vaccibody™ platform
- The ability of the Vaccibody platform to induce T cell responses is well proven in preclinical as well as clinical studies
- The ability to induce strong antibody responses demonstrated in pre-clinical studies
- To keep ahead of competition Nykode invests significant time and resources in improving the technology platform
- Although Vaccibody vaccines are platform agnostic, DNA is our preferred delivery platform
- The potential of DNA as a vehicle for proteins and polypeptides of all sorts is enormous and something Nykode will explore and exploit to make groundbreaking new medicines

# DNA platform provides near endless opportunities

- 2022 (F) Global therapeutic protein sales ~USD 300 Billion[1]
- In situ production of recombinant therapeutic proteins highly attractive
- DNA mediated delivery offers advantages over RNA



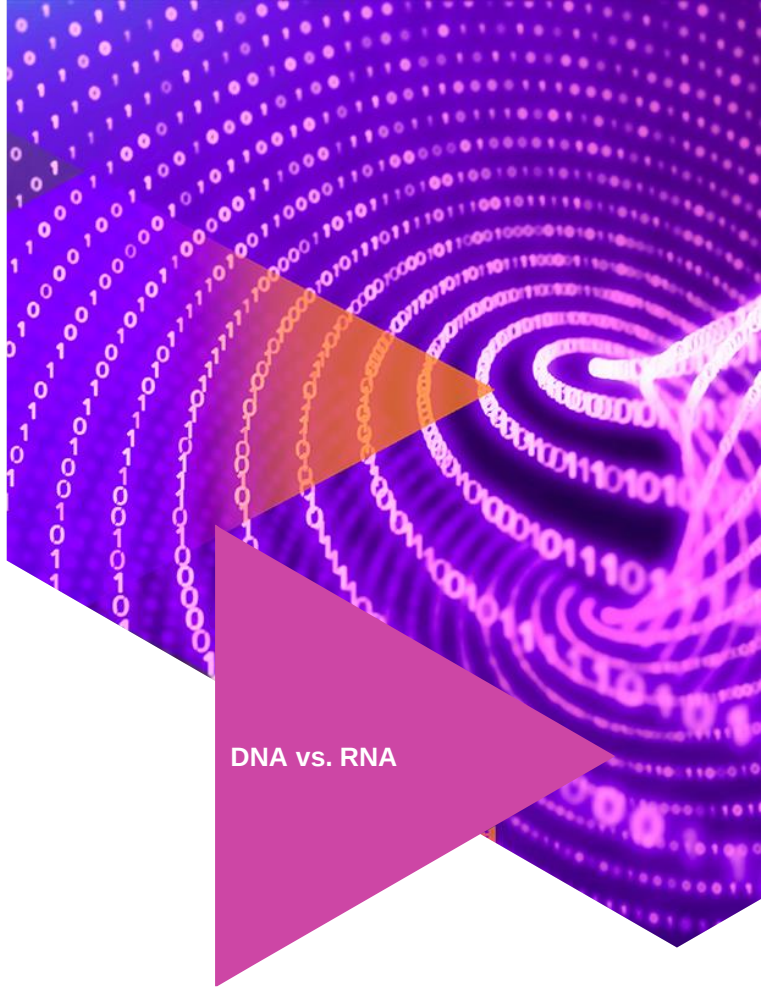

- Modular and flexible antigen presenting cell targeted vaccines
- Clinically proven technology for inducing T cell responses
- Possibility to include immune stimulatory polypeptide code

- Changing the code of the targeting unit makes specific delivery of antigens to tolerizing DCs achievable
- Possibility to include immune inhibitory polypeptide code
- Opens a commercially highly attractive therapeutic area

- Modular and flexible vaccines targeted to APCs and B cells
- Preclinically validated to induce potent antibody and T cell responses
- Possibility to include immune stimulatory polypeptide code

1. GlobalData, Drugs database

# Why DNA and not RNA?

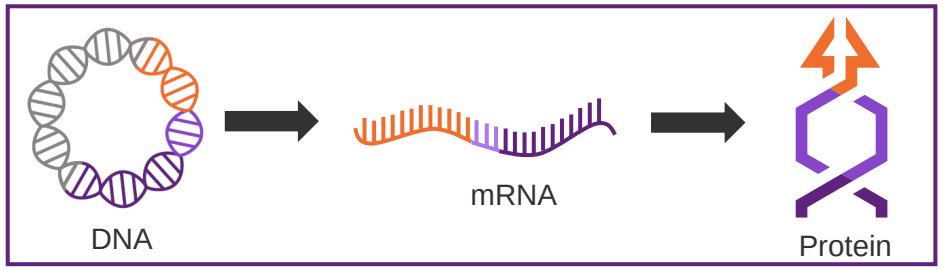



## The “success” of the COVID19 vaccines have glorified mRNA technologies but significant challenges remain

- Unspecific delivery of the mRNA may cause unwanted inflammation as seen in e.g., heart muscle in younger males[1]
- mRNA together with key LPN constituents stimulates IL1-beta production resulting in systemic reactions such as fever and chills[2]
- Together these issues limits the tolerable dose of mRNA delivery
- Short lived mRNA leads to rapid peak protein levels, which impacts the quality of the therapeutic response
- Require freezing in storage and transport

## DNA provides an attractive alternative

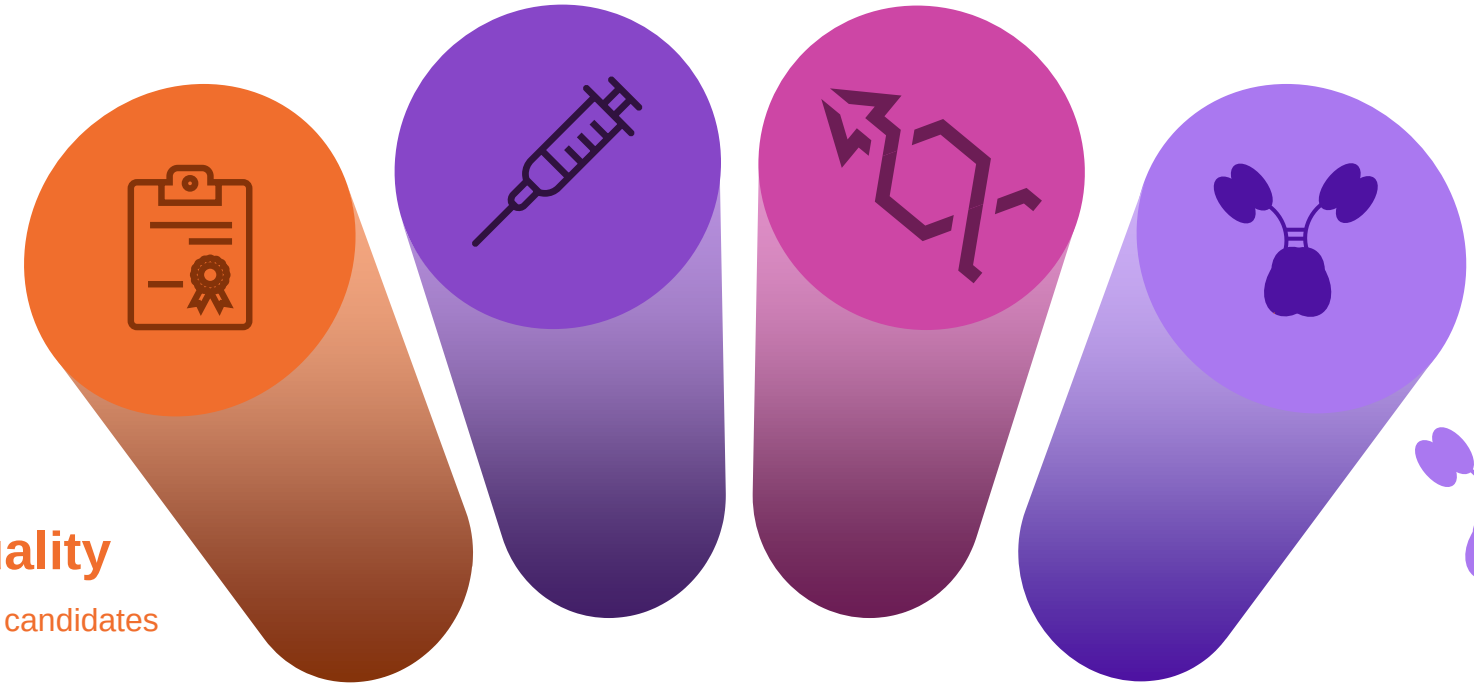
- Favorable toxicity
- Slower and longer protein production
- Favorable manufacturing and storage - no frozen storage issues
- Possible to code larger and more complex protein constructs






1. Ling RR et al. 2022, Lancet Respir Med, doi: 10.1016/S2213-2600(22)00059-5
2. Tahinen et al. 2022, Nature immunology 23, 532-542

# Four-pillar platform improvement strategy



## Construct quality

Focusing on the quality of vaccine candidates

## Dose and delivery*

Explore and optimize dose, plasmid size and delivery methods

## Novel vaccine formats

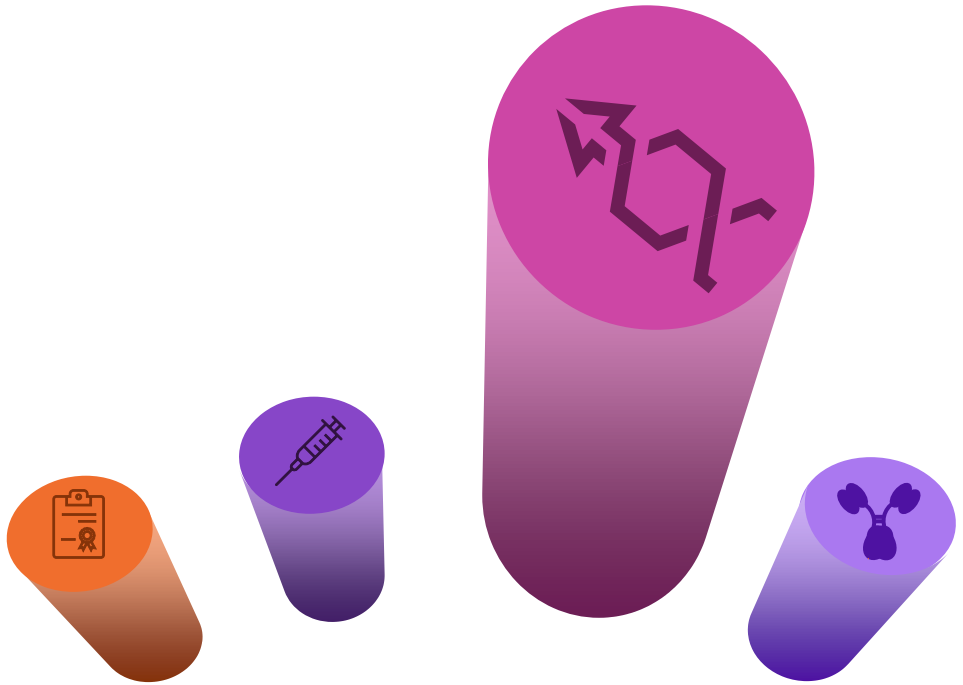
Develop novel formats with optimized and directed immune responses

## Non-vaccines

Explore opportunities for delivering non-vaccine proteins using the DNA platform

* Close collaboration with CMC

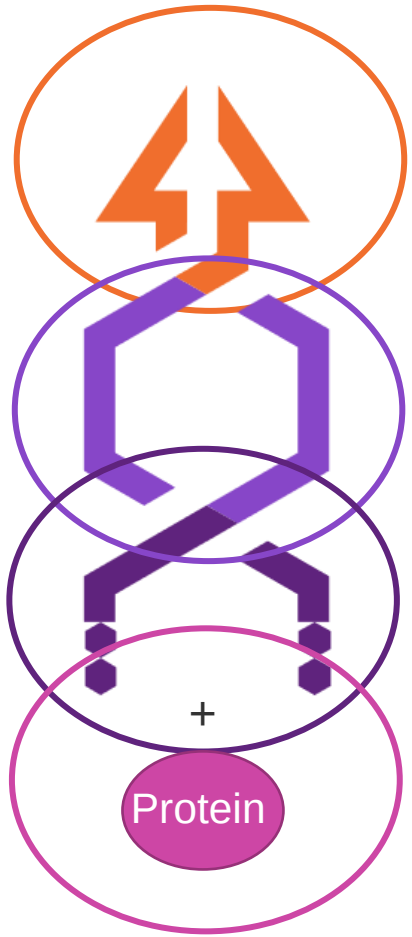
# Focus of today will be novel vaccine formats



## Novel vaccine formats

Develop novel formats with optimized and directed immune responses

# Numerous new codes designed and evaluated experimentally




## Targeting unit

- Targeting of multiple different receptors on different APCs
- Multiple natural ligands and antibody like molecules

## Dimerization unit

- Several new designs
- Smaller units, more units

## Antigenic unit

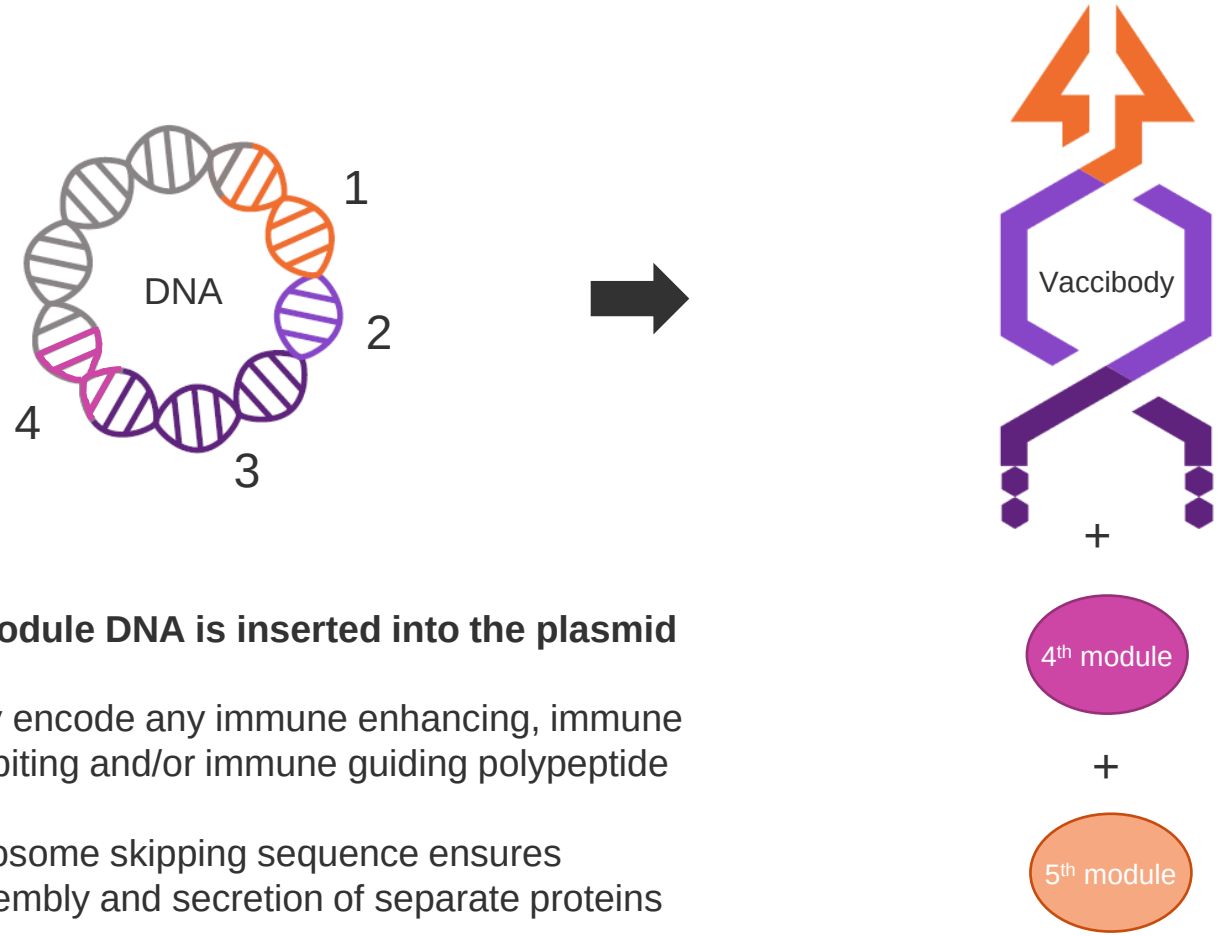
- Combinations of structured antigens and T cell epitopes into one vaccine construct

## New codes

- Addition of new codes encoding natural peptide ligands and receptor extracellular domains

- These efforts have resulted in a significant broadening of our patent portfolio
- Providing additional layers of protection to Nykode's technology platform

# 4th Module
## Adding gas pedal, brake and/or steering wheel

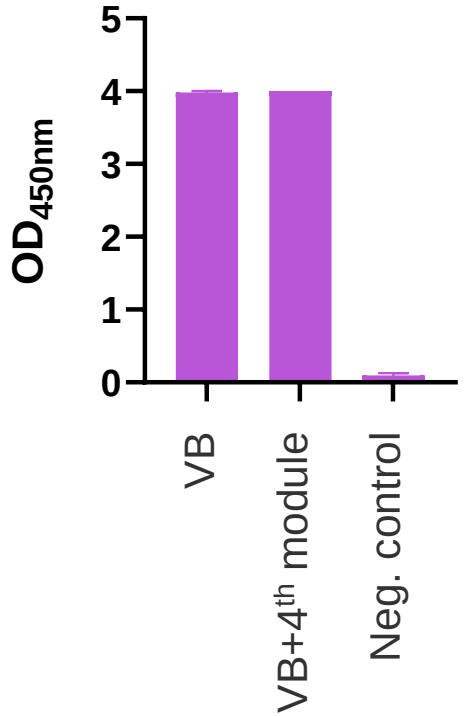



**A 4th module DNA is inserted into the plasmid**

- May encode any immune enhancing, immune inhibiting and/or immune guiding polypeptide
- Ribosome skipping sequence ensures assembly and secretion of separate proteins

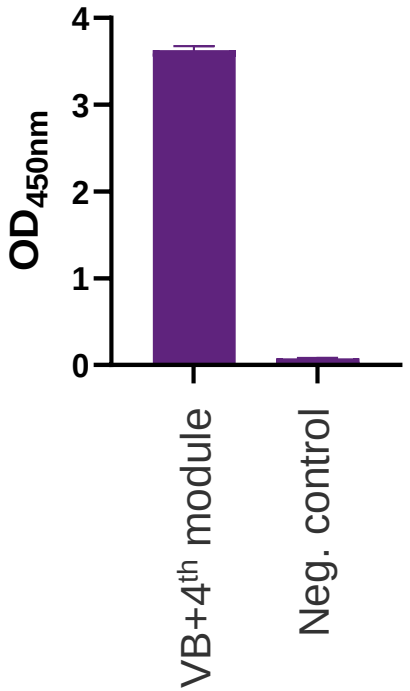
# 4th module has no impact on secretion of the Vaccibody

### 4TH MODULE HAS NO IMPACT ON VACCIBODY SECRETION



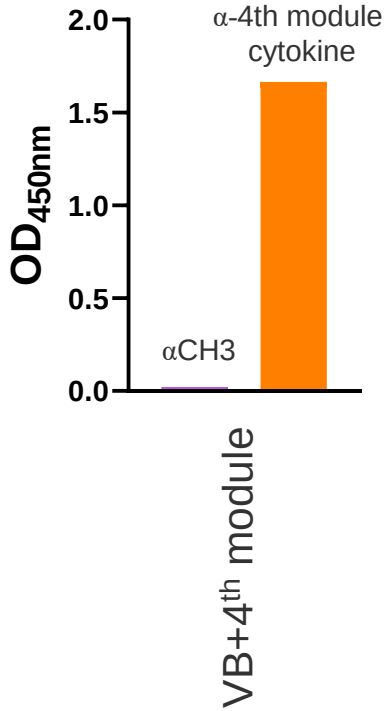

Coat: α-antigen
Detection: α-CH3

### 4TH MODULE CYTOKINE HIGHLY SECRETED



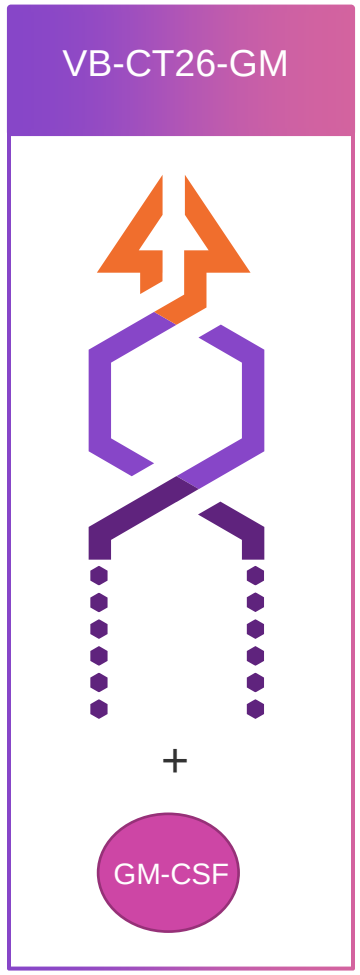

Coat: α-4th module cytokine
Detection: α-4th module cytokine

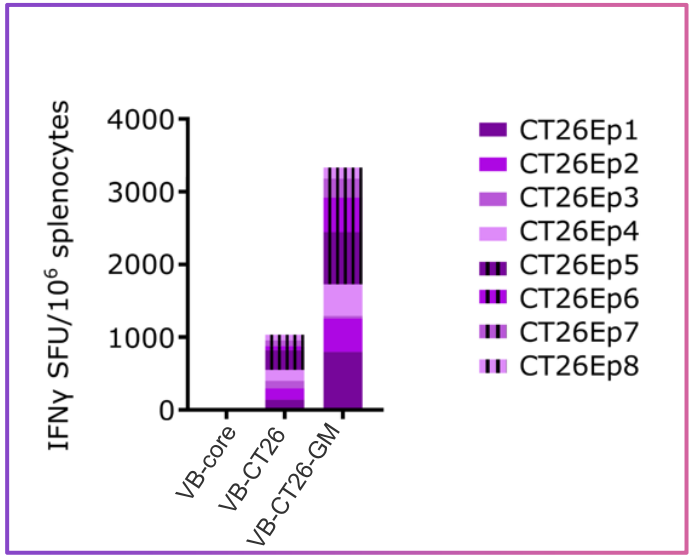
### SECRETED 4TH MODULE CYTOKINE BINDS TO TARGET RECEPTOR

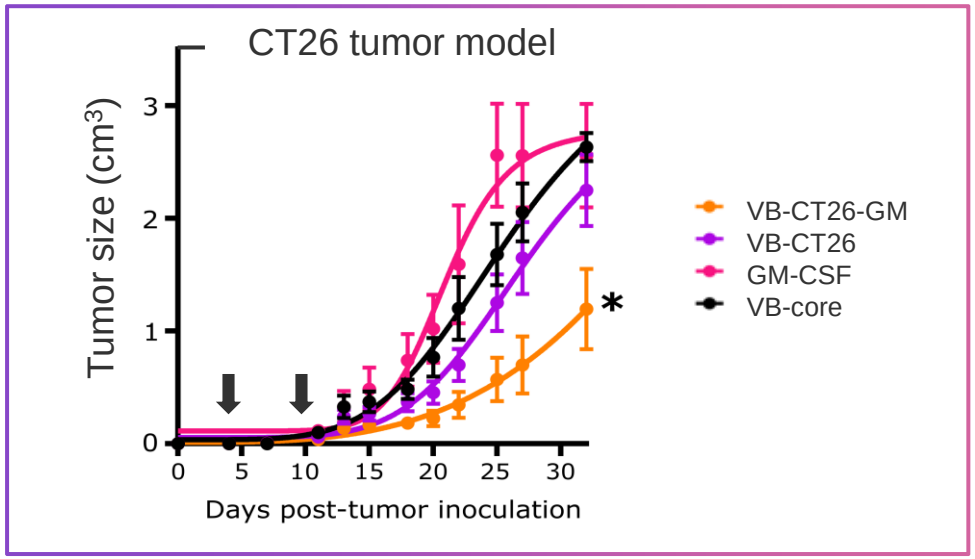


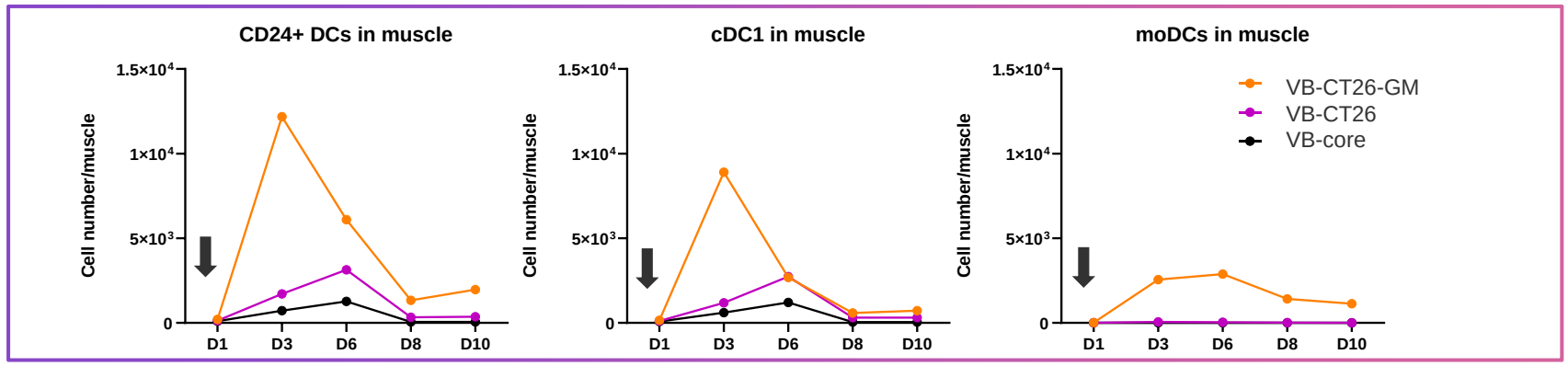

Coat: 4th module cytokine receptor
Detection: α-CH3 or α-4th module cytokine

# 4th module cytokine boosts T cell and anti-tumor responses driven by a tumor specific antigen vaccine



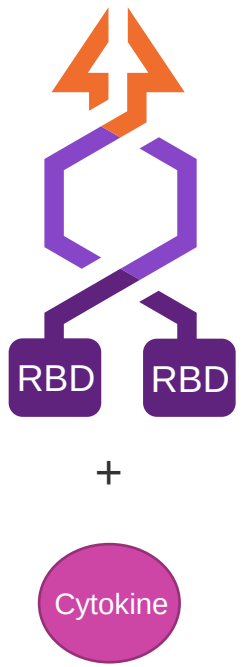

DC: Dendritic cell, VB-core: Vaccibody without antigenic unit, GM: GM-CSF



Data presented at AACR Annual meeting 2022

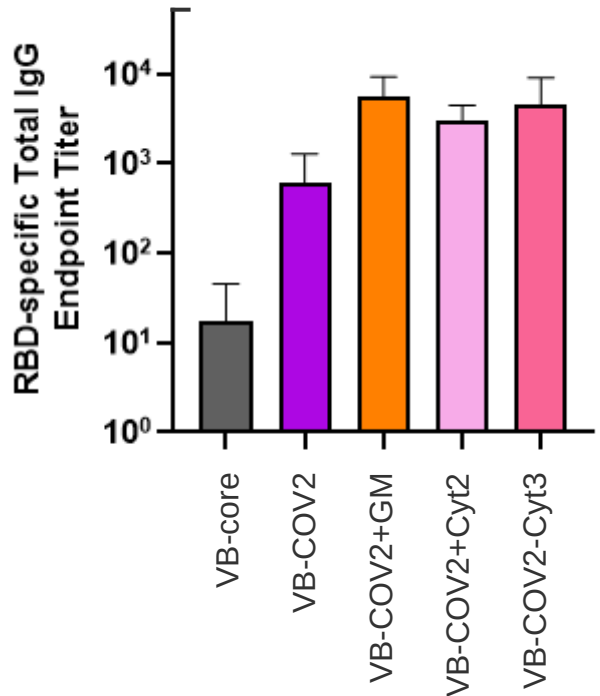
# 4th module cytokines boost T cell and antibodies responses induced by a SARS-COV-2 subunit vaccine

## VB-COV2



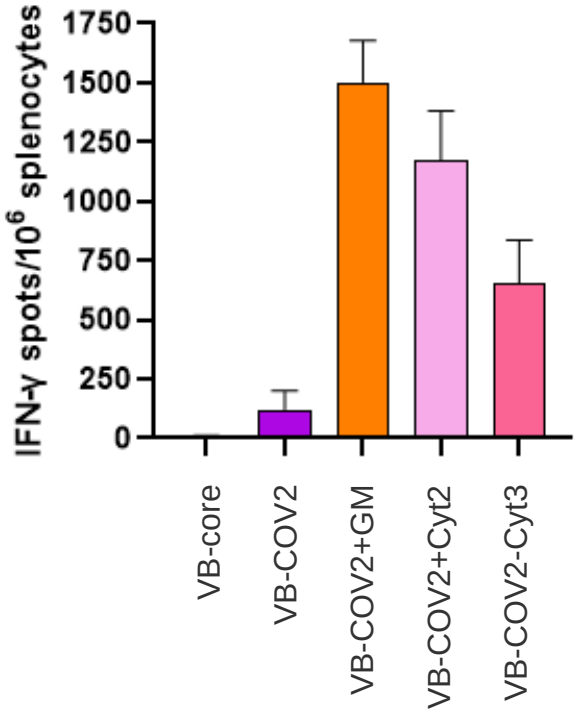

Immune stimulating

## VACCINE INDUCED ANTIBODY RESPONSES




Cyt: Cytokine

## VACCINE INDUCED IFNγ T CELL RESPONSES




- Antibody responses were evaluated using end-point titer ELISA assay
- T cell responses were evaluated using in ex vivo ELISpot detecting RBD specific peptides

# 4th module summary and perspectives

**The 4th module platform allows Nykode to introduce additional new DNA codes to our vaccines with the purpose of boosting or directing the immune responses**

- 4th module DNA codes do not impact production of the Vaccibody protein
- 4th module encoded cytokines boost anti-tumor T cell responses leading to increased anti-tumor activity
- 4th module encoded cytokines boost SARS-COV2 vaccine induced antibody and T cell responses
- Additional 5th and 6th module can be added to further boost and/or direct the immune responses


**The perspectives for the 4th module platform are tremendous and reaches outside of immune stimulatory vaccines**

**Nykode will continue to explore the potential of additional immune modulatory polypeptides and combinations of these**

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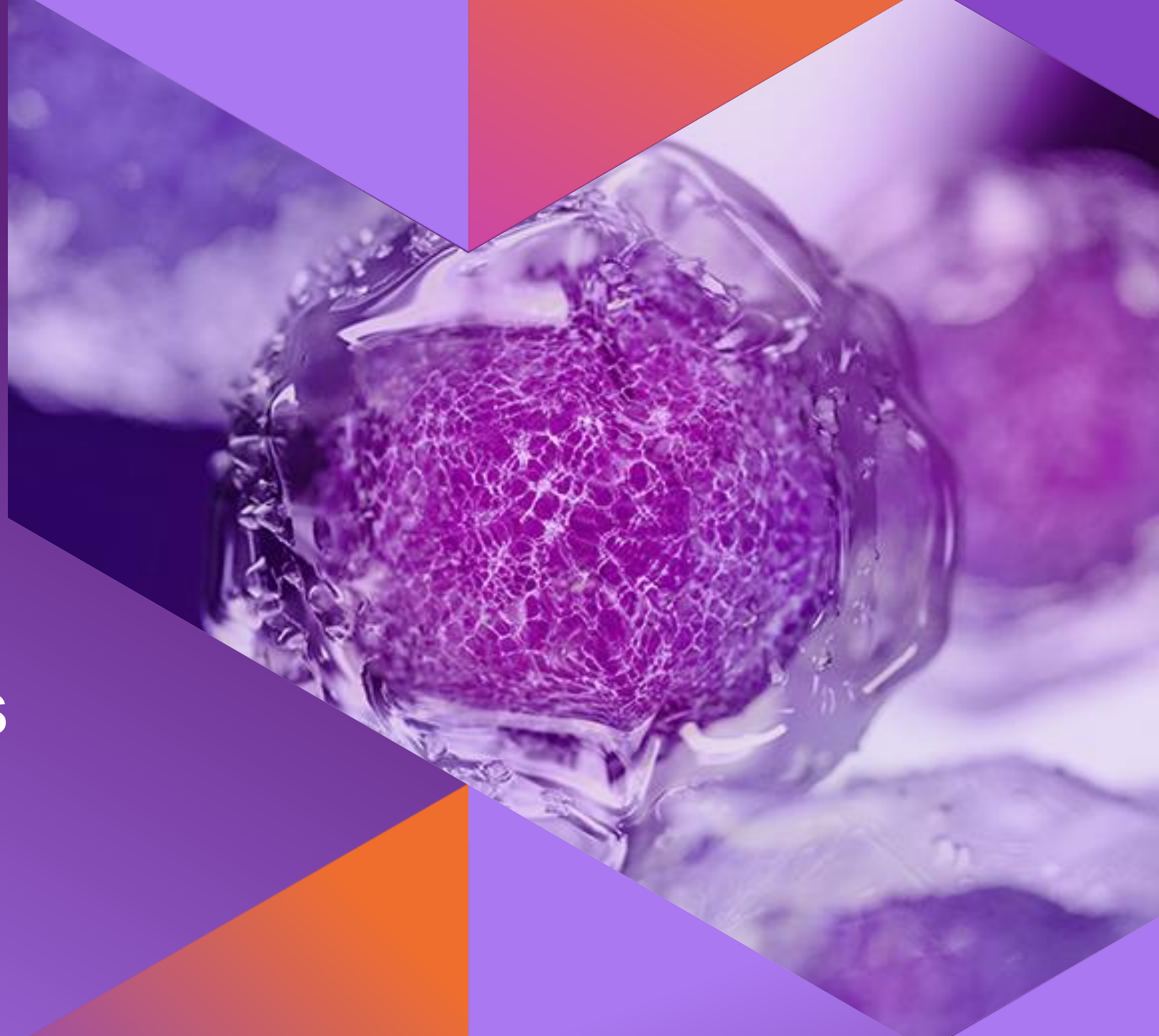
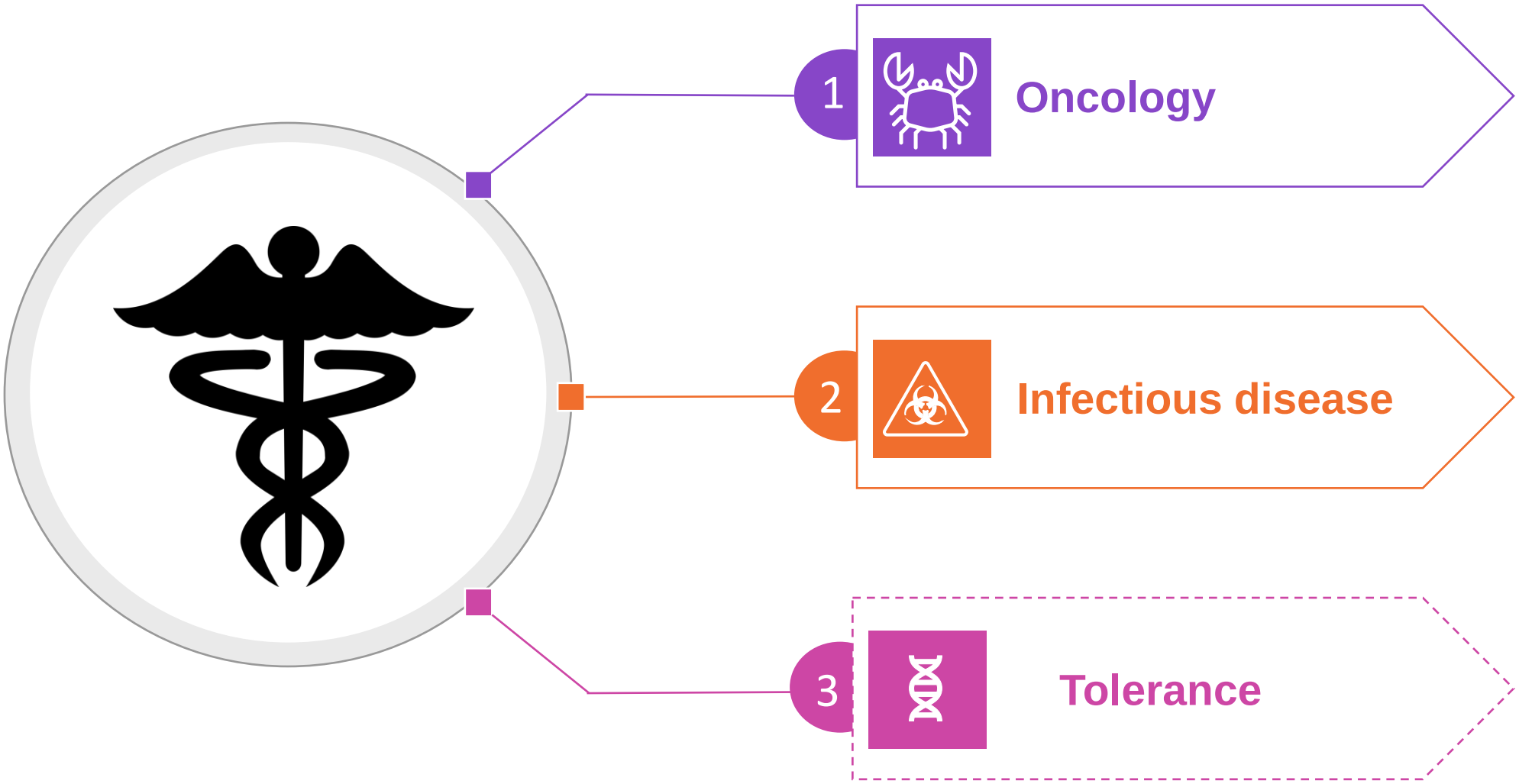
# Tolerizing vaccines



# Two key therapeutic areas and a third for future growth



# Preambles for tolerizing vaccines

Antigen-specific tolerization for the treatment of auto-immune diseases has the potential to blunt autoimmunity without compromising normal immune function

Various approaches have been pursued including delivery of auto-immune antigens by means of DNA, peptides or proteins

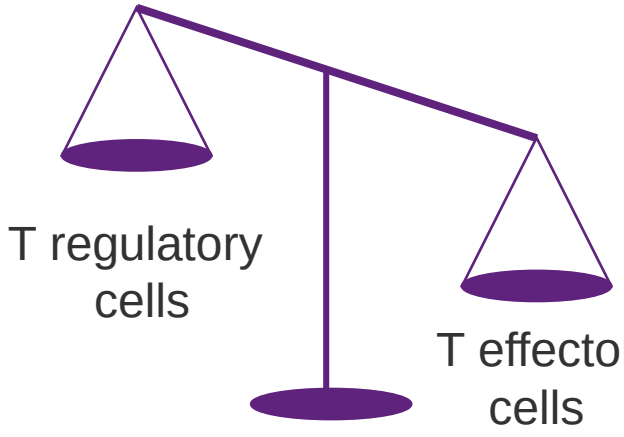
Clinical results so far, however, have been disappointing

An effective therapeutic designed to elicit tolerogenic antigen presenting cells (APCs) will need to achieve two major objectives

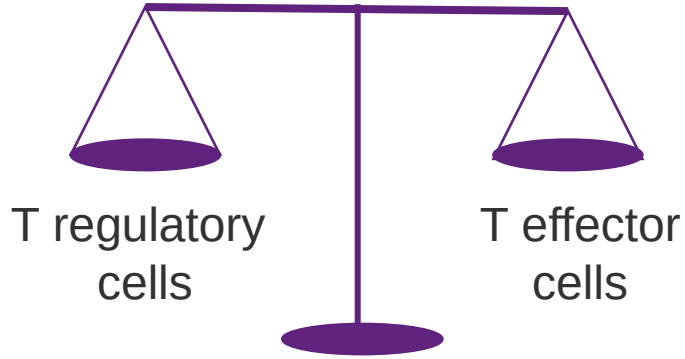
1. Deliver a disease appropriate “self-antigen” to the correct population of APCs
2. Modulate the phenotype of these APCs to present the right signals to T cells to induce tolerogenic outcomes

Significant opportunities within autoimmune diseases, allergies and allogeneic transplantation

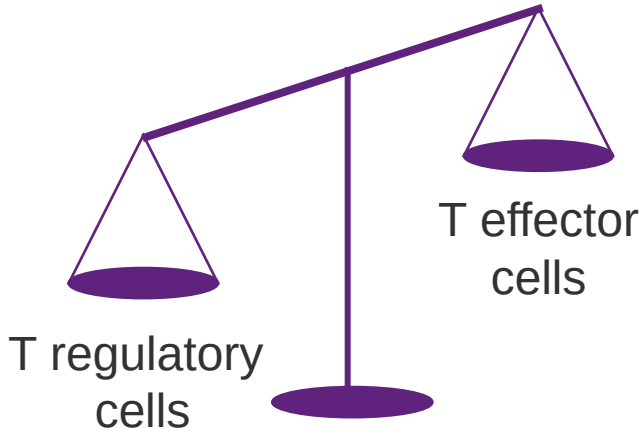
# Shifting the balance of the immune system




Disruption of Balance
**Autoimmune disorders**




Balanced immune system
**Normal situation**

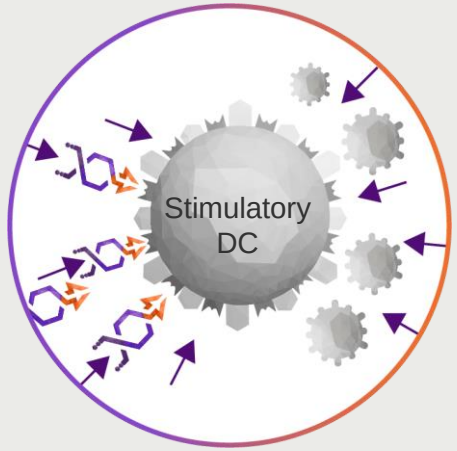


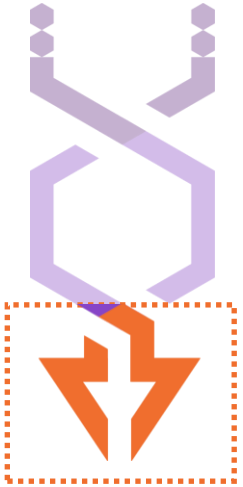

Disruption of Balance
**Cancer**

Tolerizing vaccines should shift the balance back towards normal by increasing the amount of antigen specific T regulatory cells

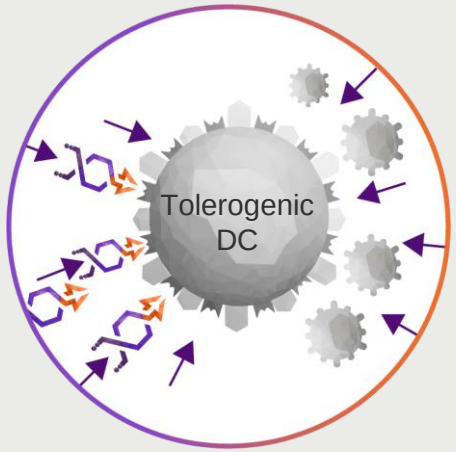
# Nykode's platform technology offers unique possibilities to explore Ag-specific immune tolerance

## CANCER AND INFECTIOUS DISEASE




## AUTOIMMUNITY, ALLERGY ETC



# Multiple sclerosis as model system


## Multiple sclerosis (MS)

- Chronic autoimmune disease of the central nervous system (CNS), where the myelinated axons in the CNS are destroyed

## Animal model system

- Experimental autoimmune encephalomyelitis (EAE) is a clinically relevant animal model of MS
- Myelin oligodendrocyte glycoprotein (MOG) is a myelin transmembrane protein exclusively expressed by oligodendrocytes within the CNS
- MOG35–55 is a potent immunogen in mice, which presents clinically in the form of a chronic progressive disease course (when co-administered with adjuvant)

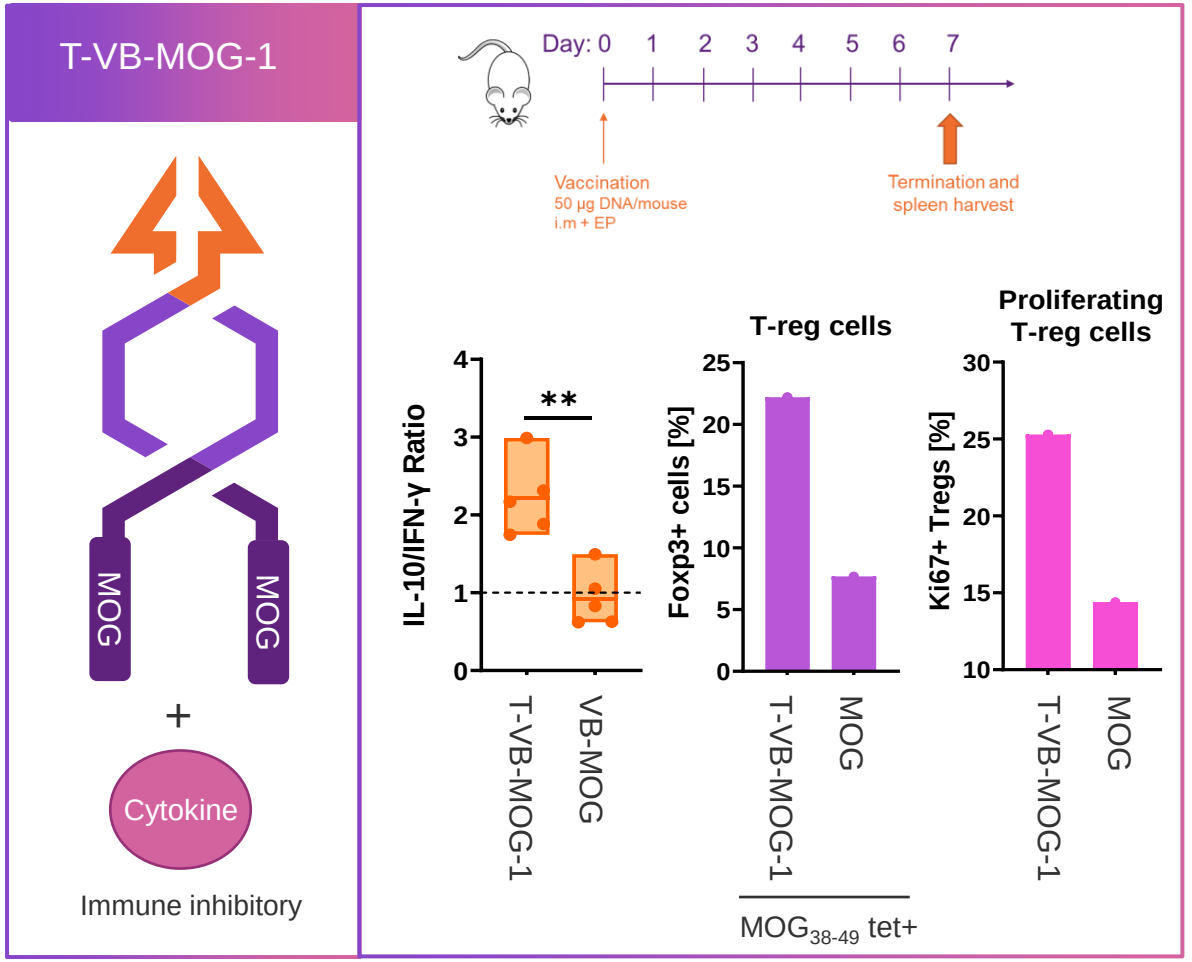
# Exploratory vaccine construct induces proliferation of MOG specific T regulatory cells

## Tolerizing vaccine design

- Targeting specific receptor on tolerizing antigen presenting cells
- MOG immunogen
- 4th module immune inhibitory cytokine

## Key results

- Increase in the IL10 and IFNγ ratio compared to standard vaccibody
- Increase in MOG specific T regulatory cells
- Increase in T regulatory cell proliferation



# What is next for tolerizing vaccines?

**Initial data with the various tolerizing vaccine constructs are encouraging**

- Increases in antigen specific T regulatory cells
- A shift in the cytokine balance towards an immune suppressive profile

**Patent applications filed to protect the overall concepts**

**Additional experimental work is required to identify the optimal combination of targeting unit and immune inhibitory 4$^{th}$ module**

- Prevention of disease in relevant animal models

**In parallel define potential first indication for a first tolerizing vaccine project**

# 05 Business development strategy

# Nykode has entered 3 key partnership deals with top-tier biopharma partners since Q4 2020

Genentech
A Member of the Roche Group

2020: Out-licensing individualized cancer vaccine at clinical stage to leverage Genentech's knowledge and capabilities to accelerate program to market

Adaptive biotechnologies

2021: In-licensing clinically validated antigens to accelerate vaccine development in infectious diseases

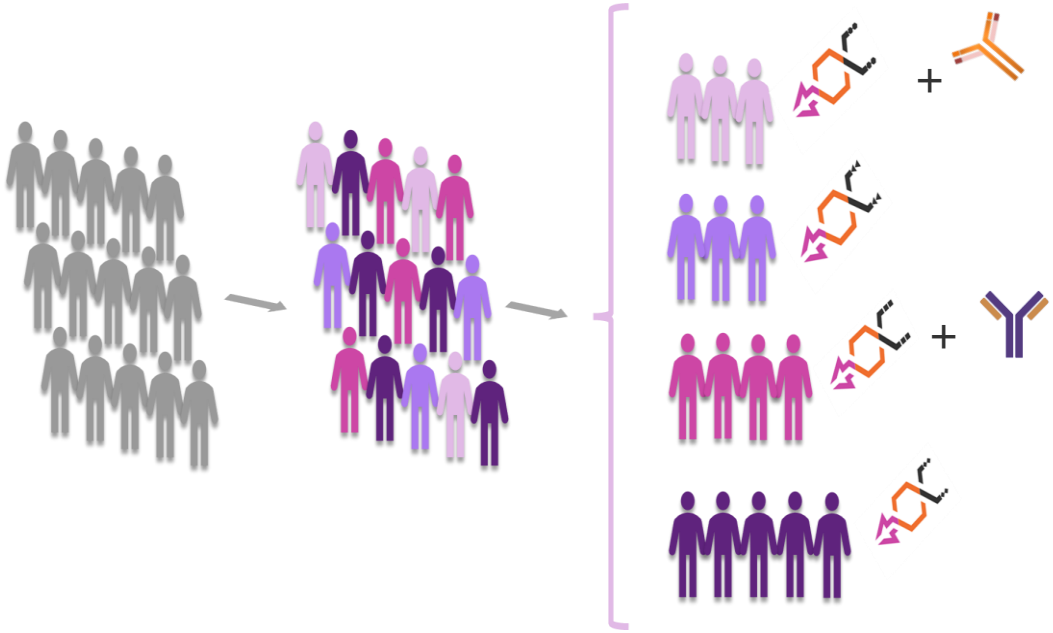
REGENERON

2021: Out-licensing to develop novel selected off-the-shelf vaccines with shared antigen design contribution and leveraging Regeneron's capabilities to accelerate broad clinical development

- VALIDATION OF NYKODE'S PLATFORM AS THE VACCINE PLATFORM OF CHOICE
- MORE THAN $1.64 BILLION PLUS ROYALTIES
- ACCELERATION OF LICENSED PROGRAMS
- ACCELERATION OF COMPANY GROWTH AND EXECUTION OF INTERNAL PROGRAMS

# Nykode's business development strategy

**MAXIMIZING VALUE BY STRENGTHENING THE PLATFORM AND ACCELERATE PRODUCTS THROUGH PARTNERSHIPS**



Antigen expression profiling

Shared antigen expression in subpopulations

Multiple off the shelf vaccines and other therapeutic products

Seek partners accessing

- Antigens
- Combination therapies
- Technologies

Seek partners with expertise that accelerate our programs

**ADAPTED STRATEGICALLY TO MATURATION OF THE COMPANY AND OUR PIPELINE**

# 06 Capital Markets Strategy, Financials and upcoming events

# Capital Markets Strategy

## UPLIFT ON OSLO STOCK EXCHANGE

- Initiated process for transfer of listing of shares from Euronext Growth to the main market of the **Oslo Stock Exchange**
- Facilitating a potential increase in liquidity of shares and access to broader shareholder base
- Expected timing Q2 2022

## POTENTIAL INTERNATIONAL LISTING

- Continues to explore a potential listing on **Nasdaq Global Markets in the U.S.** over the longer term

# Strong financial foundation for achieving our vision

- Financially well positioned to grow and execute the Company's strategy over the next years
- Strong balance sheet
  - YE 2021 liquidity of $228 million
  - Milestone payment of $20 million for initiation of Phase 1b trial in 2H 2021 received 1Q 2022

# Upcoming Catalysts

| | 2022 Key Priorities | Program | Indication | Partnerships | Milestones |
|---|---|---|---|---|---|
| **Wholly-Owned Candidates*** | | | | | |
| **Oncology** | • Advance internal oncology programs including cervical cancer program<br>• Expand into additional indications for VB10.16 | VB10.16 (off-the-shelf) | HPV16+ cervical cancer | | ✓ Phase 2 interim data<br>• Updated development strategy<br>• Updated Phase 2 data (1H 2023) |
| | | Internal programs | Undisclosed | | |
| **Infectious Disease** | • Advance COVID-19 vaccines<br>• Expand into additional high-priority disease areas | VB10.COV2 | SARS-CoV-2 | Adaptive | • Phase 1 key results measuring T cell and antibody responses in previously vaccinated subjects (2H 2022) |
| | | Internal programs | Undisclosed | | |
| **Manufacturing** | • Enhance control of manufacturing capacity and capability | | | | • Update on manufacturing strategy |
| **Technology** | • Leverage technology platform | | | | ✓ Present preclinical data from second-generation Vaccibody platform at AACR (1H 2022) |

# Q&A

## Unlocking the future of medicine

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