nykode therapeutics

Nykode is announcing positive interim results from Phase 2 trial with VB10.16 in combination with atezolizumab in advanced cervical cancer

May 9, 2022

Forward-looking statement

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A number of material factors could cause actual results and developments to differ materially from those expressed or implied by these forward-looking statements.

Positive interim results from VB C-02 – Executive Summary

- VB10.16 in combination with atezolizumab showed durable responses with a very high disease control rate (DCR) of 64% in heavily pre-treated advanced cervical cancer patients
- Anti-tumor efficacy was observed in both PD-L1 positive and negative patients, with 27% overall response rate (ORR) and 77% DCR in PD-L1 positive patients and 17% ORR and DCR 58% in PD-L1 negative patients
- DCR of 71% was observed in patients with non-inflamed tumors, including both immune desert and T cell excluded tumors
- HPV16-specific IFN-γ T cell responses were associated with clinical efficacy
- Complete clearance of HPV16 ctDNA was significantly correlated with clinical outcomes
- VB10.16 in combination with atezolizumab is well-tolerated and has a safety profile comparable to CPI monotherapy

Together these findings indicate a differentiated anti-tumor response pattern of the combination treatment compared to checkpoint inhibitor monotherapy

Today’s presenters from Nykode management

International management team with solid drug development experience

MICHAEL ENGSIG

CEO

M.Sc. Biochemistry, G.D.Bus.Admin.

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

- Takeda and Nycomed
- PPD
- KLIFO

AGNETE B. FREDRIKSEN

Chief Innovation & Strategy Officer

M.Sc. Molecular Biology, Ph.D. Immunology

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

- Co-founder Vaccibody/Nykode
- Served as President & CSO 2007-2021

SIRI TORHAUG

Chief Medical Officer

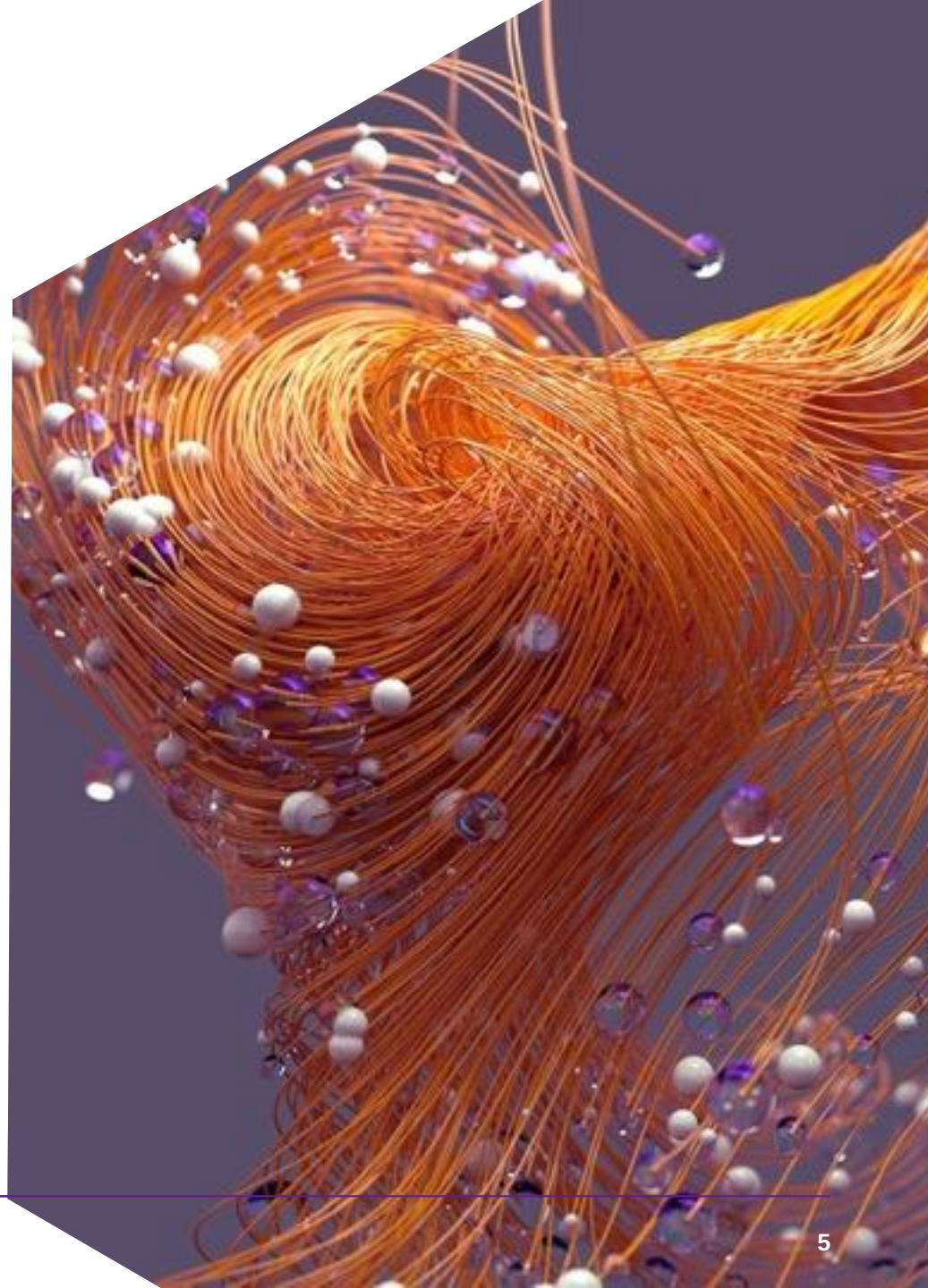
MD, Oncology specialist

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

- Oslo university hospital
- Novartis
- AstraZeneca

Overview

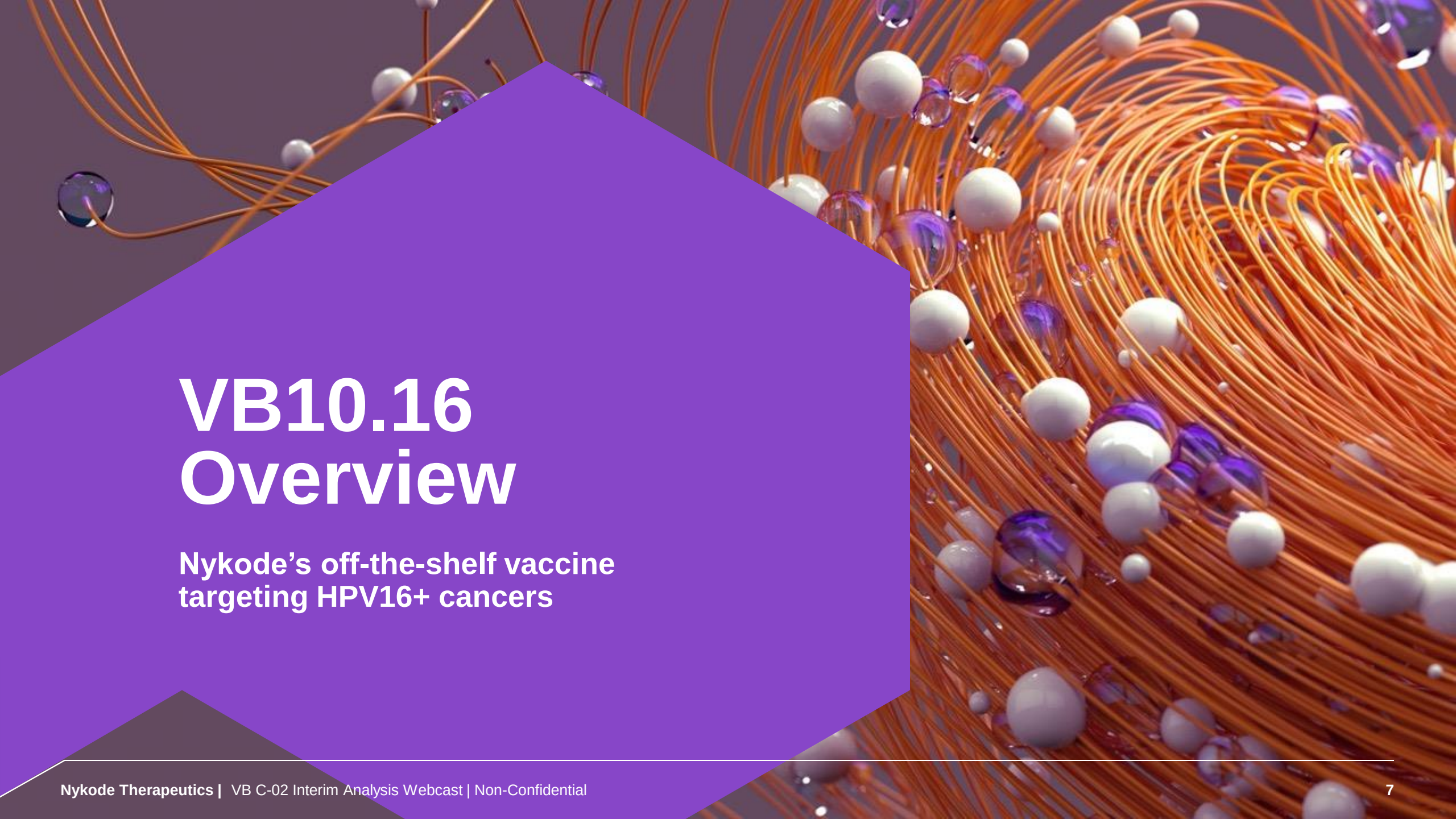
- Proprietary Vaccibody™ immunotherapy platform uniquely targeting Antigen Presenting Cells (APCs) for a potent, broad and lasting immune response
- Pipeline of oncology and infectious disease vaccines includes partnered programs and wholly-owned clinical candidates
- Potentially more than $1.64 billion in upfront and milestone payments plus royalties from top-tier biopharma partners
- Wholly-owned programs include
  - cervical cancer candidate in Phase 2
  - next generation COVID vaccine for variants of concern in Phase 1/2
- Well capitalized and multiple significant catalysts in near-to-medium term



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



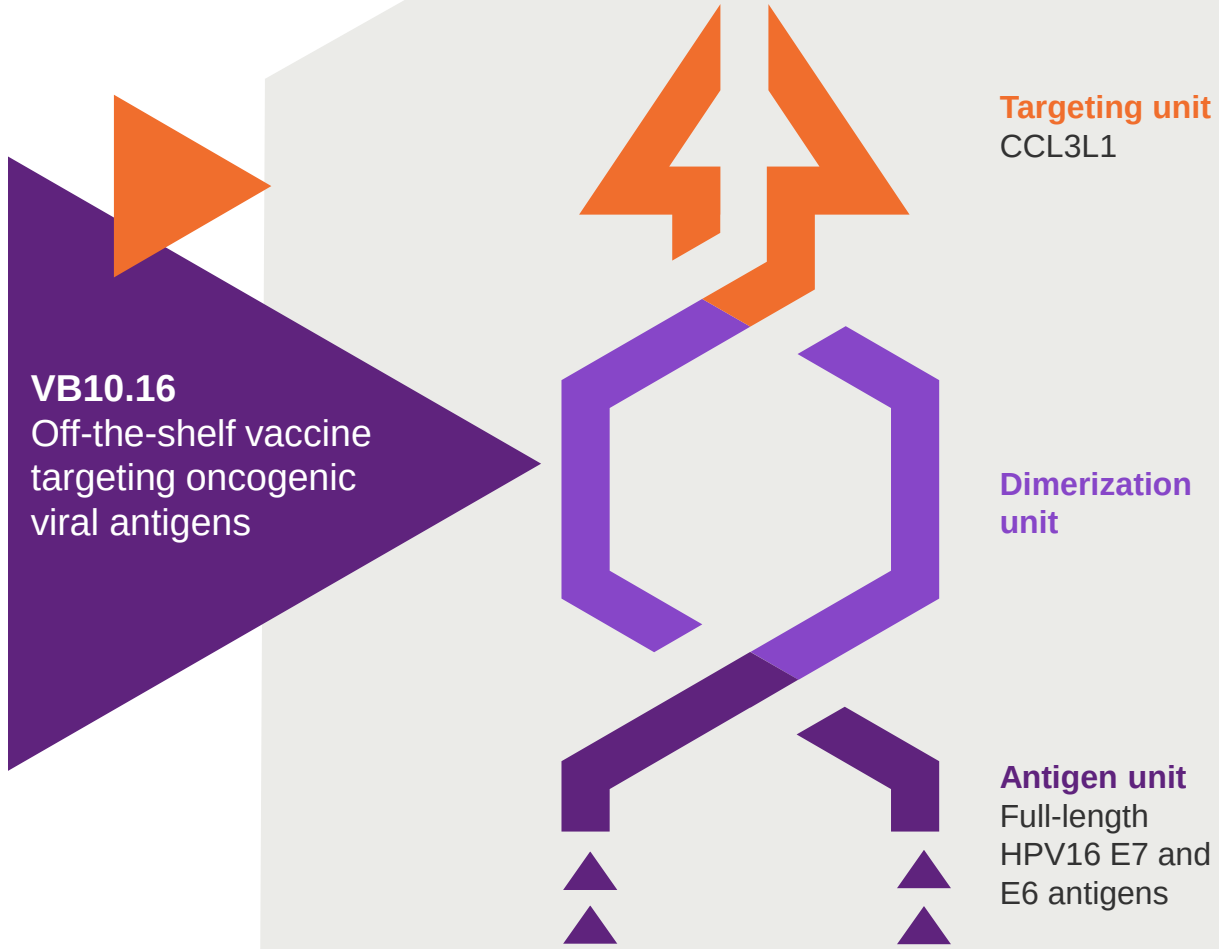
VB10.16 Overview

Nykode’s off-the-shelf vaccine targeting HPV16+ cancers

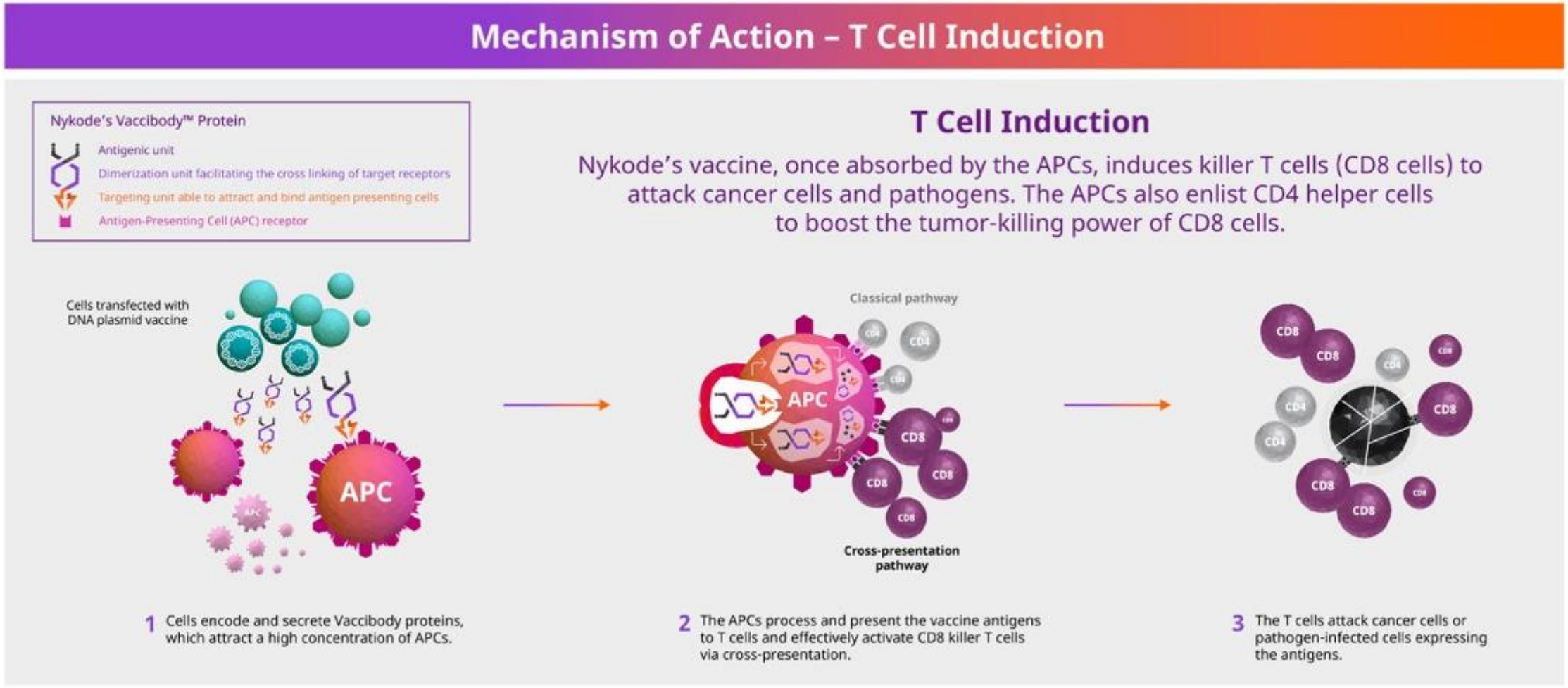
VB10.16: Therapeutic HPV vaccine

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

- Finalized VB C-01 Phase 1/2a study investigating VB10.16 monotherapy in HPV16+ precancerous cervical lesions
- Ongoing VB C-02 Phase 2 study investigating VB10.16 in combination with atezolizumab in advanced cervical cancer
- Nykode is exploring the commercial potential of VB10.16 for the treatment of additional HPV driven cancer indications
- Wholly-owned by Nykode

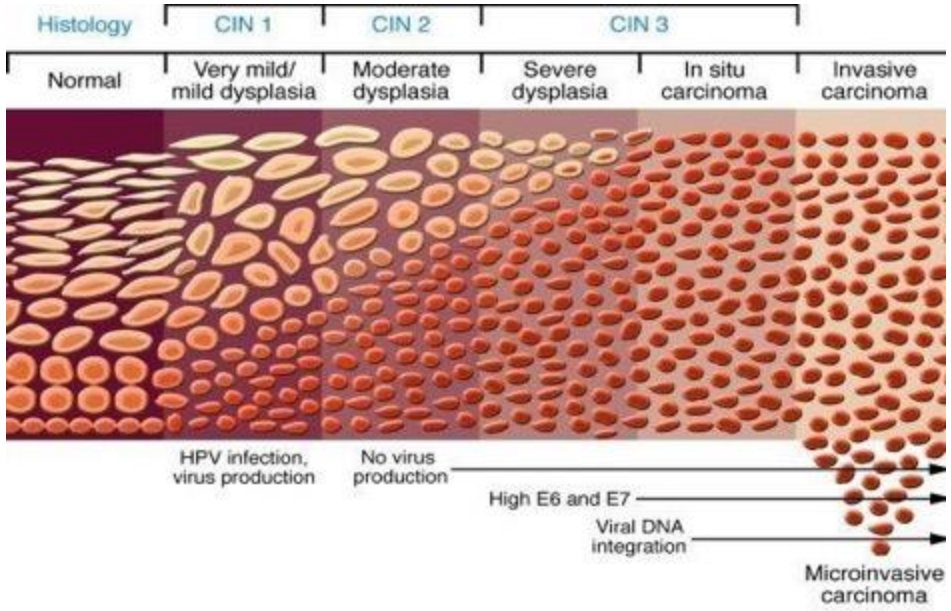


Unique APC-Targeting Vaccine Platform Induces a Rapid, Robust and Long-Lasting CD8 T Cell Response



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



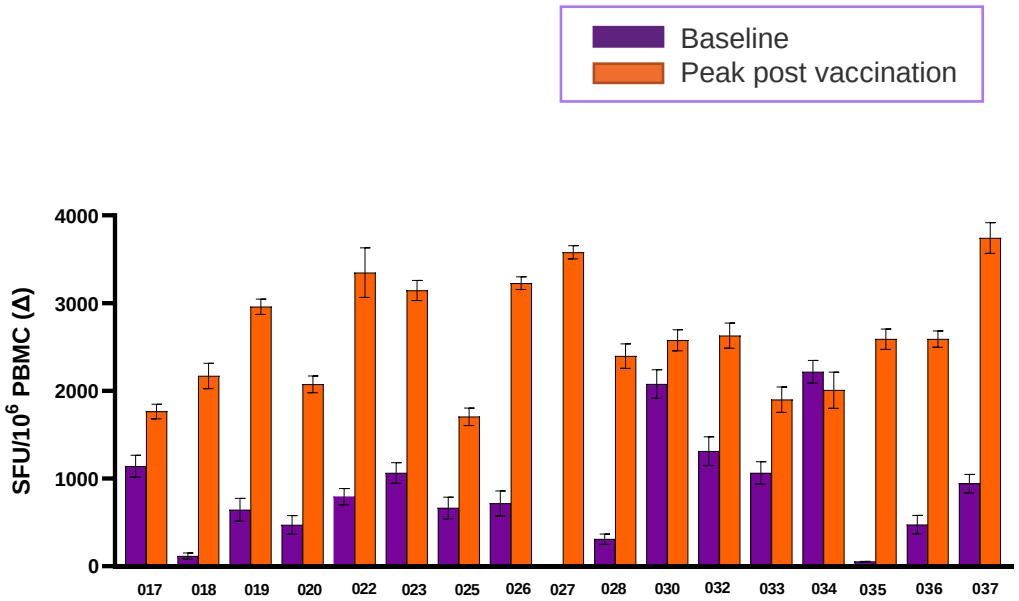
Lowy et al. 2006

VB10.16 monotherapy in pre-cancerous cervical lesions:

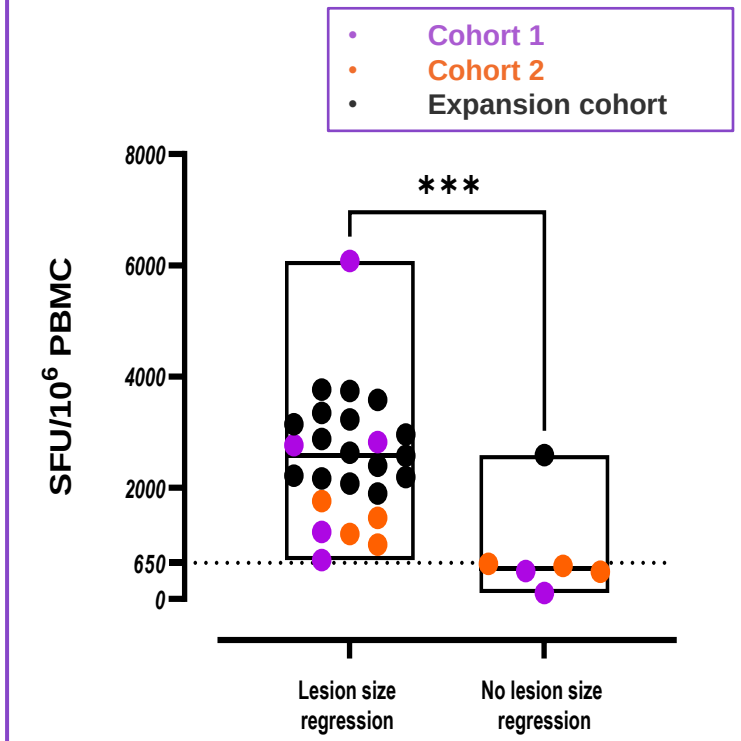
Strong HPV16-specific T cell responses induced post vaccination correlated with lesion size regression

- 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 RESPONSES IN ALL SUBJECTS IN THE EXPANSION COHORT



LESION SIZE REGRESSION CORRELATES WITH HPV-16 SPECIFIC RESPONSES

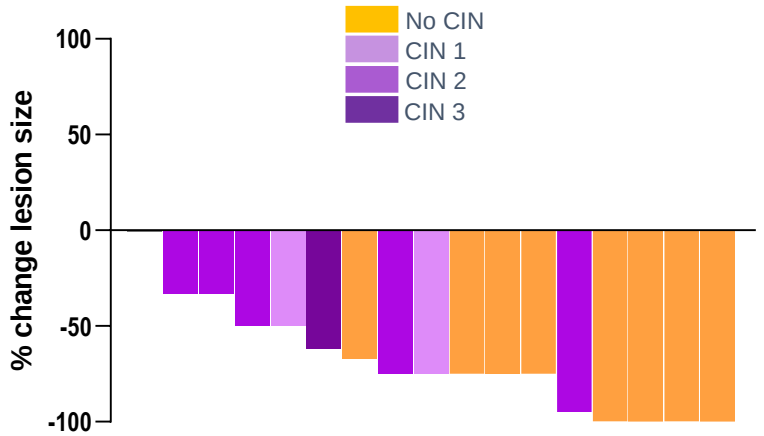


VB10.16 monotherapy in pre-cancerous cervical lesions:

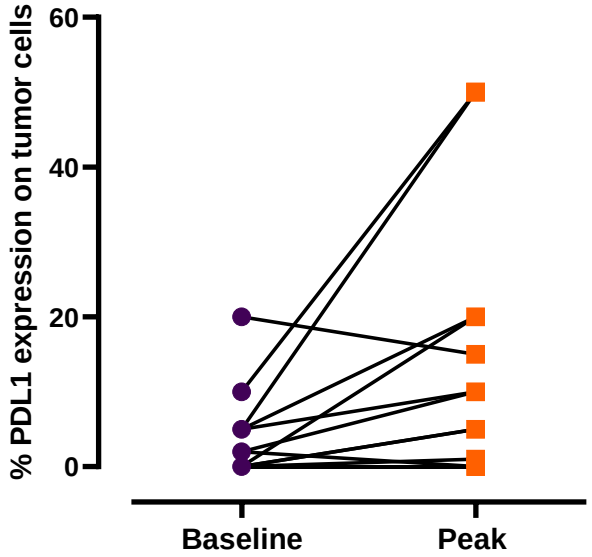
Lesion size regression and upregulations of PD-L1 observed in the majority of subjects

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

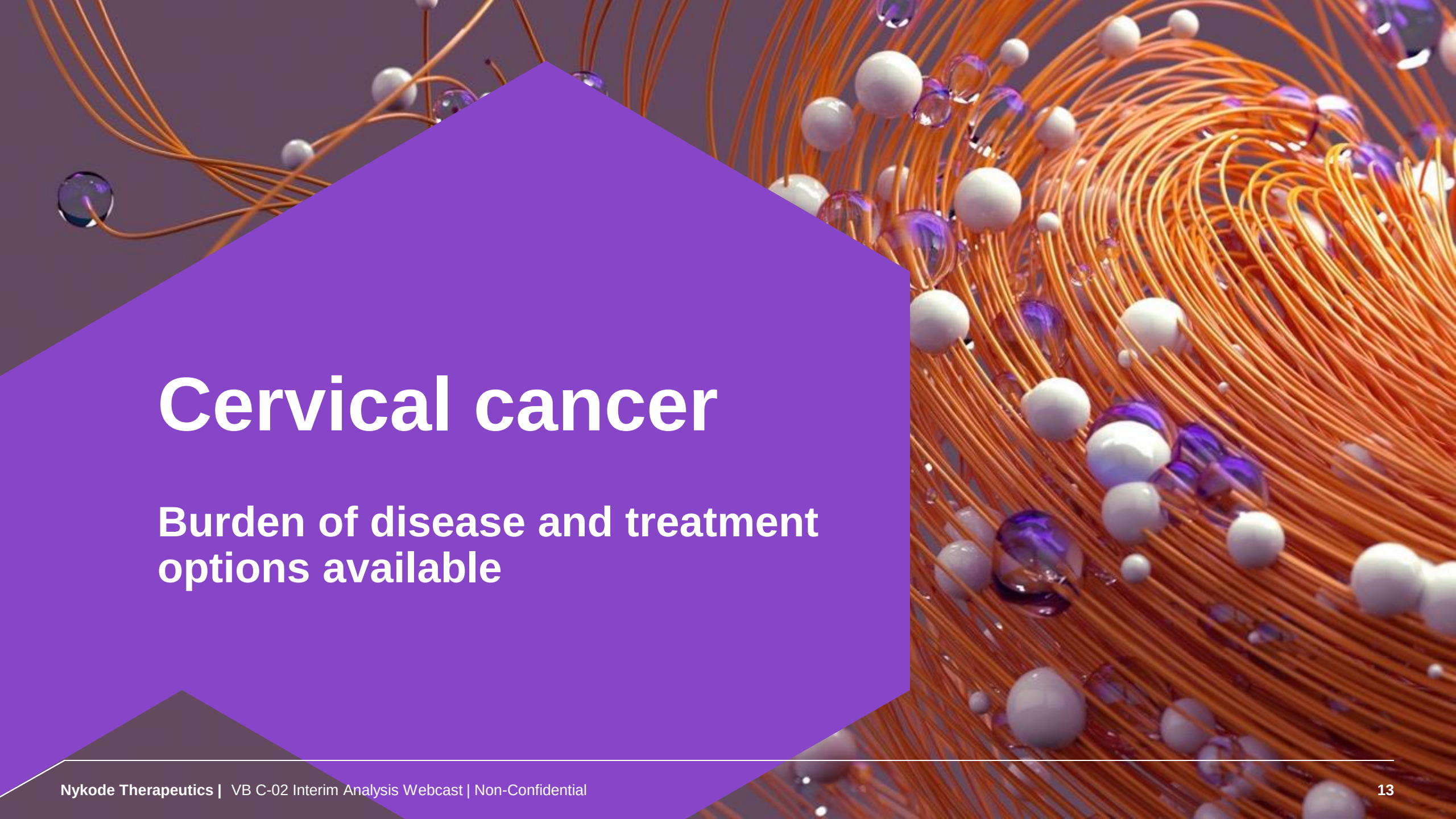
LESION SIZE REDUCTION AND CIN REGRESSION



UPREGULATION OF PD-L1 POST VACCINATION



Peak indicate PD-L1 expression at 16 or 24 weeks after first vaccination



Cervical cancer

Burden of disease and treatment options available

Cervical cancer

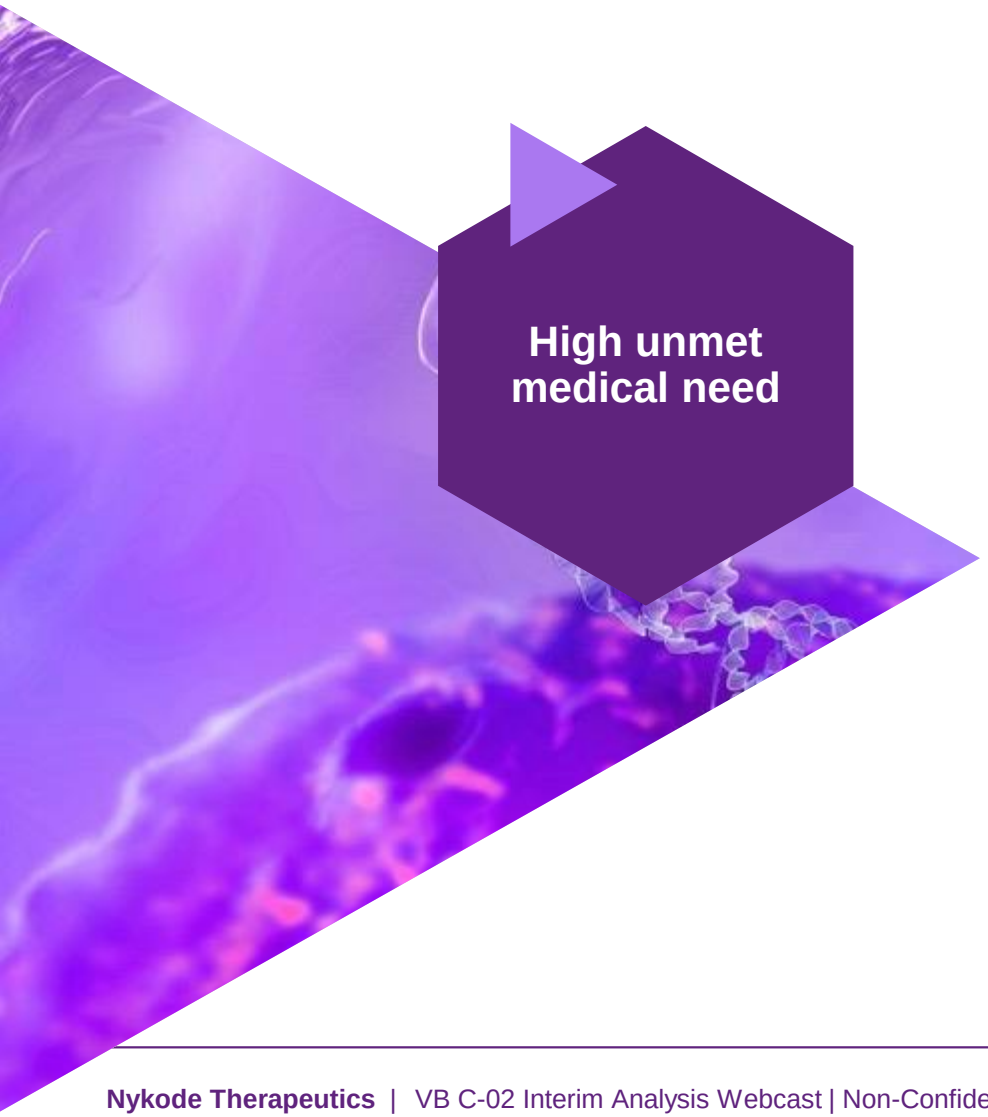
A leading cause of cancer death in women worldwide

- 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

Advanced cervical cancer

Limited treatment options after progression on first-line treatment



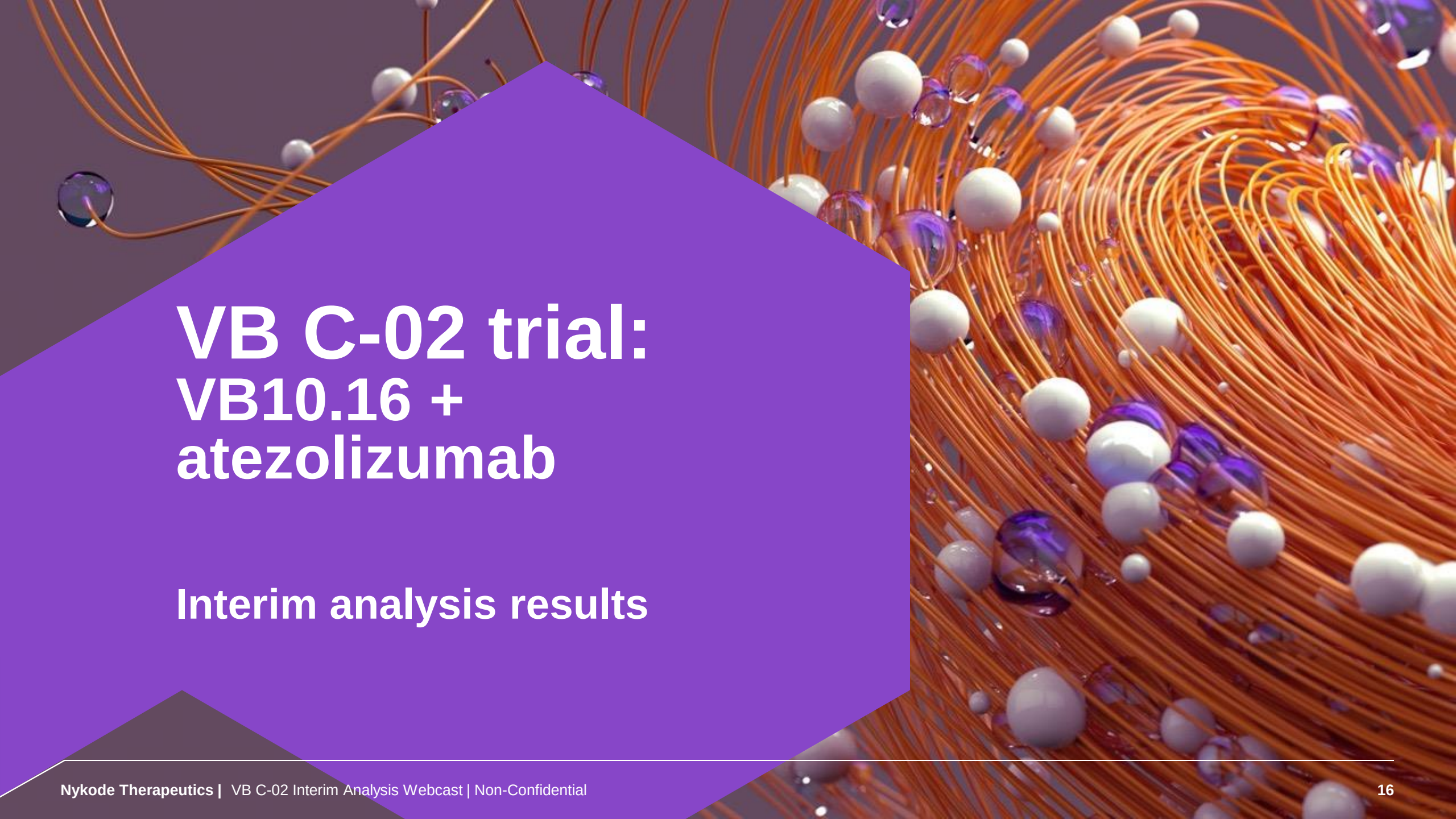
Pembrolizumab is the only anti–PD-1 agent approved in the US as second-line therapy for PD-L1 positive patients with recurrent or metastatic cervical cancer

- 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

Chung et al. 2019/2021; ESMO 2017.



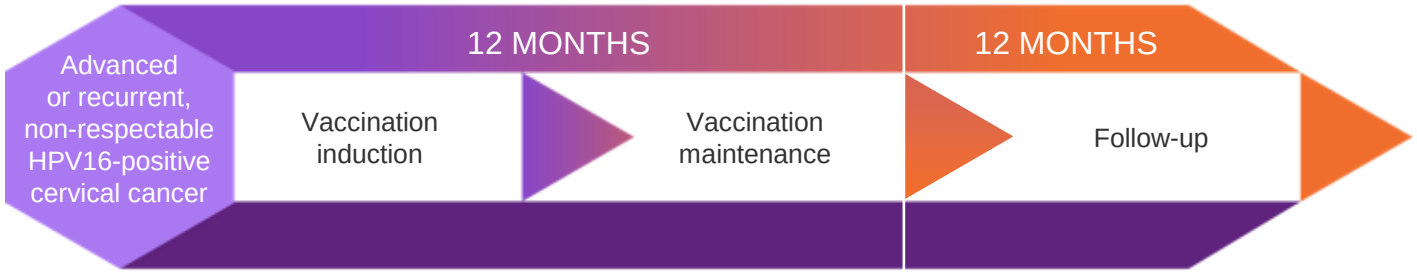
VB C-02 trial:
VB10.16 + atezolizumab

Interim analysis results

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

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

- Objectives: safety/tolerability, immunogenicity and efficacy
- Primary endpoints: incidence/severity of AEs, ORR (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)
- Last Patient First dose: 16 Feb 2022



Interim analysis

Number of patients included in the interim analysis

Population	N
Enrolled patients	50
Efficacy Analysis Set (EAS) At least one available post-baseline scan at cut off date*	39
Completed Treatment	*6*
Discontinued	*21*
Ongoing	*12*
Safety Analysis Set (SAS) 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

VB 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 *SD+*	17 (44%) *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*

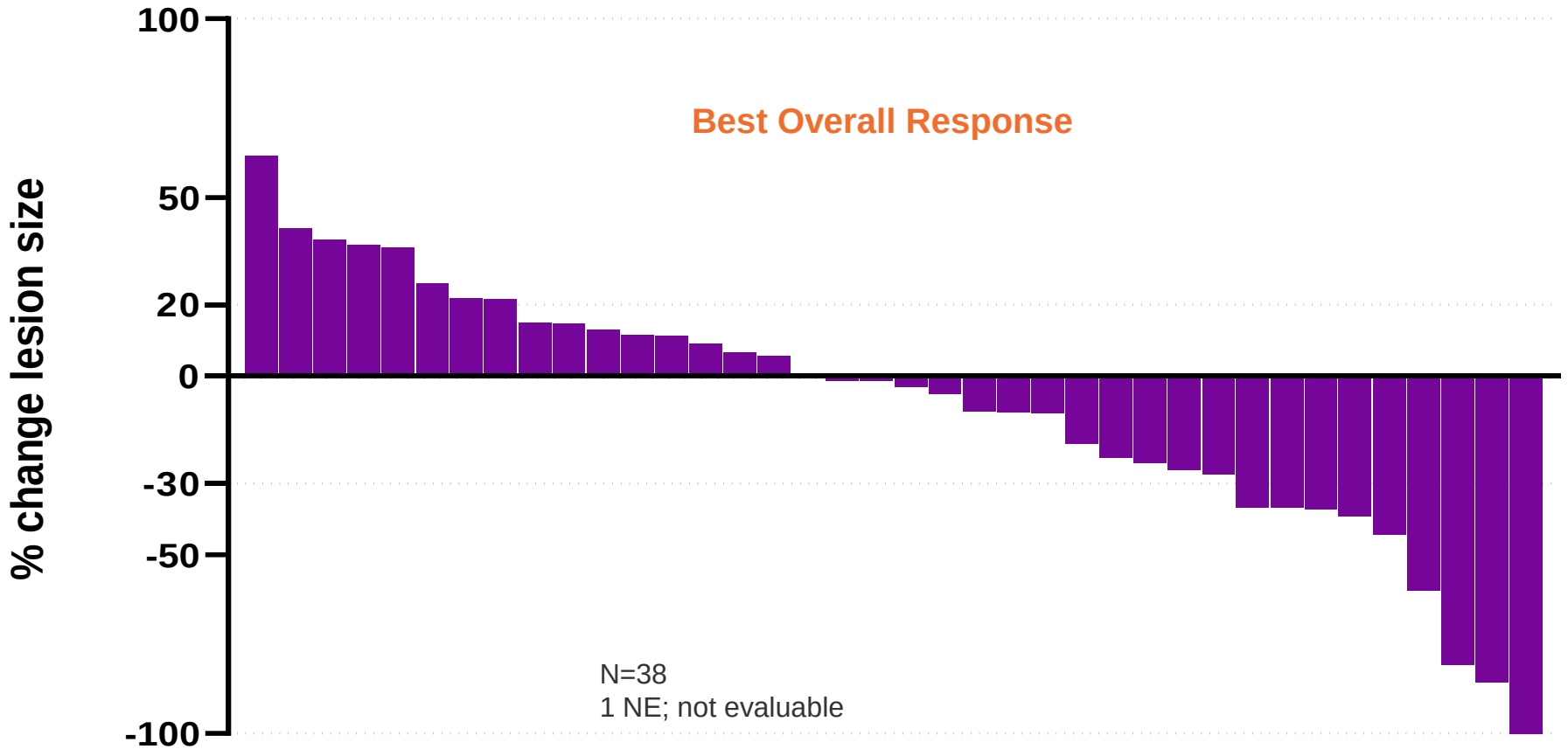
ORR = 21% (8/39 patients)
PD-L1 positive* = 27% (6/22 patients)
PD-L1 negative = 17% (2/12 patients)

DCR = 64% (25/39 patients)
PD-L1 positive = 77% (17/22 patients)
PD-L1 negative = 58% (7/12 patients)

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

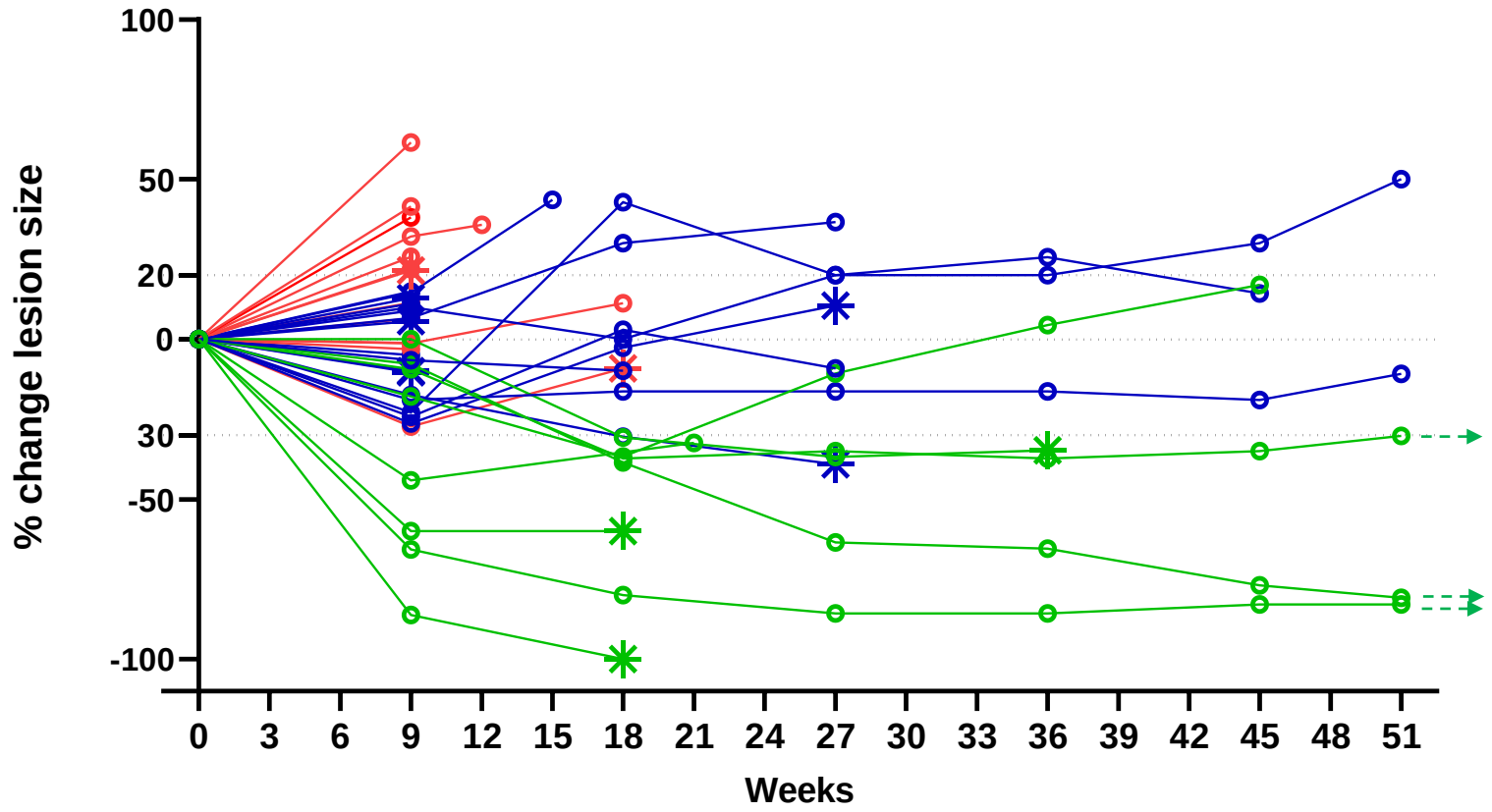
- *PD-L1 status at baseline was available in 34 patients*
- *1 PD-L1 negative patient was NE (RECIST)*

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



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

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



Complete/Partial Response
Stable Disease
Progressive Disease

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

✱ 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)

Safety and tolerability

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

TRAEs considered related to VB10.16

System Organ Class 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)	-	-

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 seven 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.

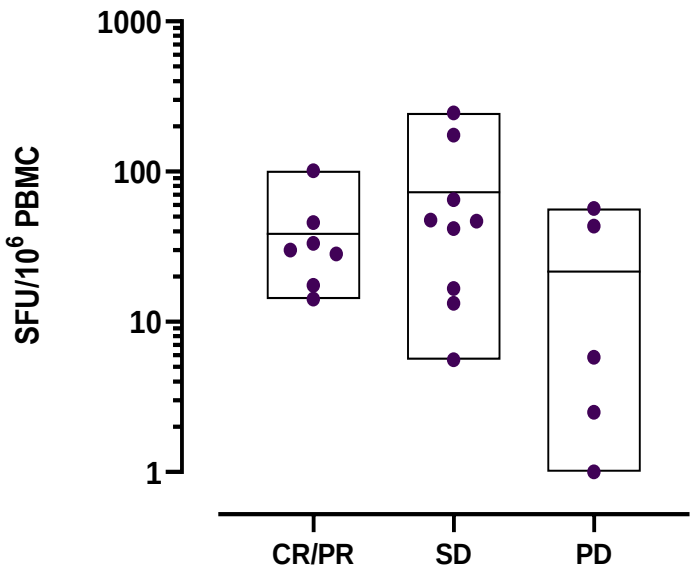
50 patients were included in the safety population for the interim analysis. Median number of VB10.16 doses given was 5 (range 1-11).

Strong HPV16-specific T cell responses were associated with clinical response in advanced cervical cancer patients

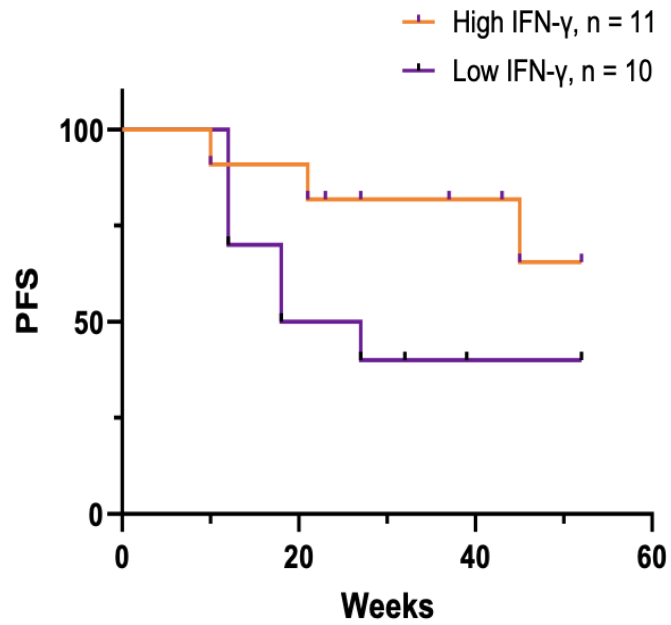
A strong HPV16-specific IFN-γ T cell response was associated with clinical response indicating HPV-specific T cells are important for clinical efficacy in advanced cervical cancer

Supported by data presented from VB C-01 clinical trial where a strong significant correlation was demonstrated between HPV16-specific T cell responses and clinical responses in a pre-cancerous setting

T CELL VS BEST OVERALL RESPONSE



PROGRESSION FREE SURVIVAL IN HIGH/LOW T CELL RESPONDERS



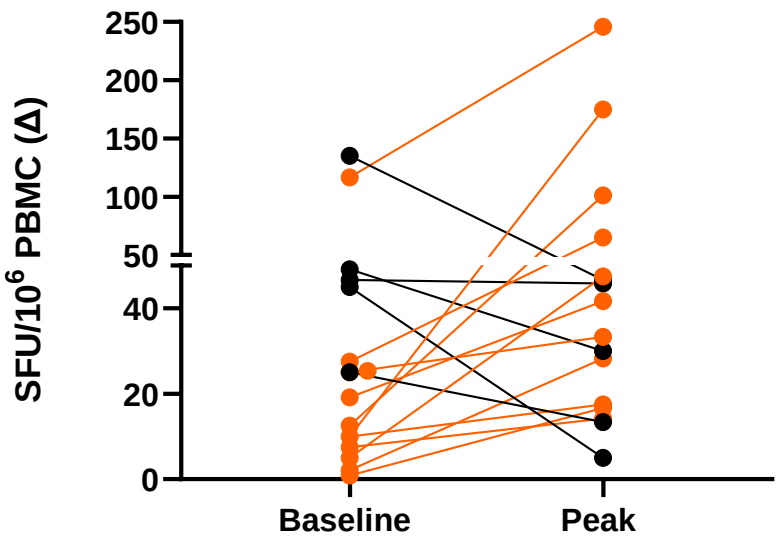
- IFN-γ T cell responses were evaluated in 21 subjects
- T cell responses were evaluated in *ex vivo* ELISpot detecting HPV16 E6 and E7 antigens separately

HPV16-specific T cell responses were increased in patients achieving disease control

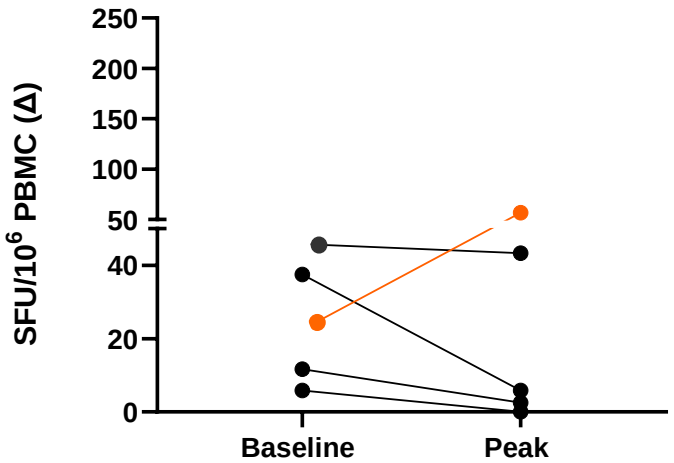
Increased HPV16-specific T cell responses in post vaccination samples observed in the majority of patients with disease control

Indicating a clinically relevant T cell response induced post vaccination with VB10.16 in combination with atezolizumab

IFNγ T CELL RESPONSE IN PATIENTS WITH DISEASE CONTROL



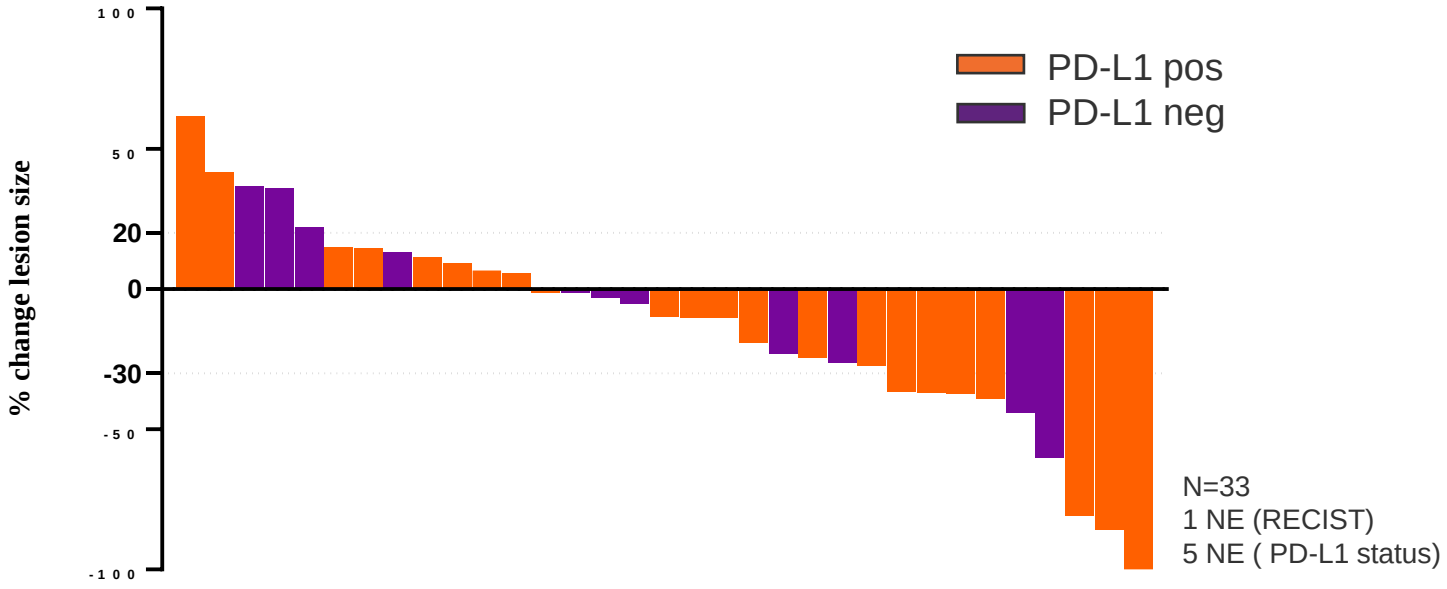
IFNγ T CELL RESPONSE IN PATIENTS WITH PD



- IFN-γ T cell responses were evaluated in 21 subjects. T cell responses were detected in *ex vivo* ELISpot detecting HPV16 E6 and E7 antigens.
- Peak response post vaccination compared to baseline is shown per patient
- 3 baseline samples were collected 7 days after first vaccination to replace pre-vaccination samples lost in shipment

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

Tumor regression in PD-L1 +/-



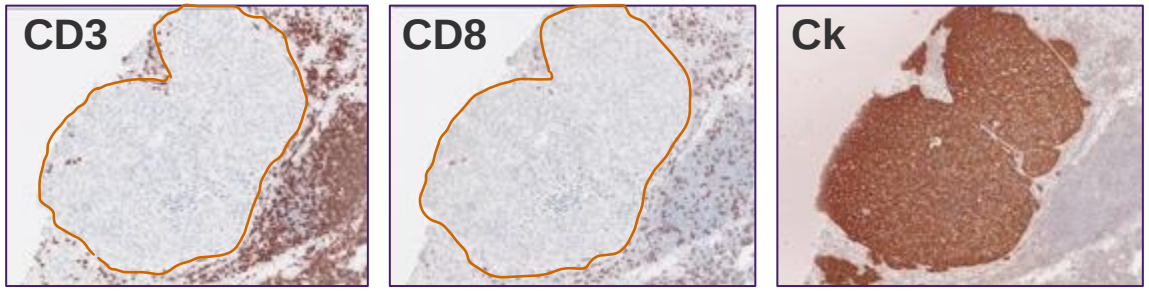
PD-L1 status	ORR (n/N)	DCR (n/N)
Positive (TIC 1-2)	**27%** (6/22)	**77%** (17/22)
Negative (TIC 0)	**17%** (2/12)	**58%** (7/12)

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

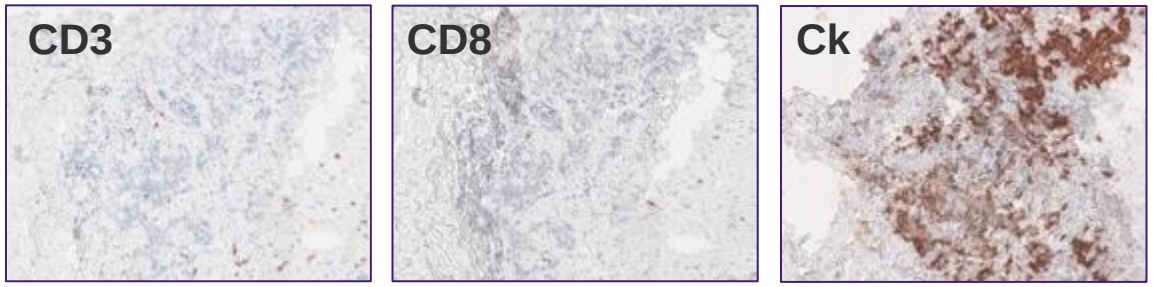
- PD-L1 was scored by TIC (Tumor and immune cell) scoring using Ventana SP263 platform (Roche Diagnostics)
- PD-L1 status at baseline was available in 34 patients, 1 PD-L1 negative, was NE for RECIST

Disease control achieved in patients with non-inflamed tumors at baseline

T cell excluded tumor



Immune Desert



10 of 14 patients with non-inflamed tumor immune status at baseline achieved disease control on combination treatment

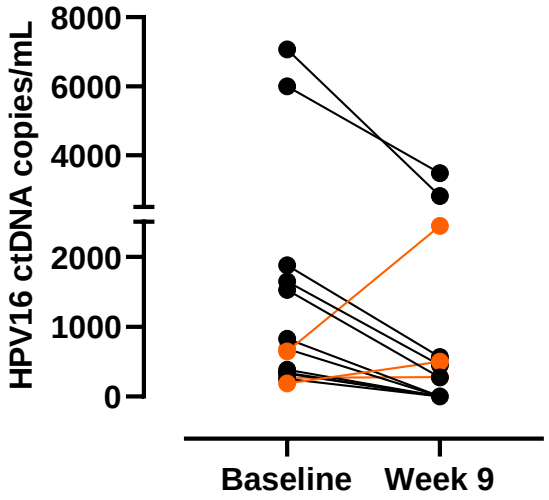
	DCR
Non-inflamed tumors	10 of 14 (71%)
T cell excluded	5 (36%)
Immune desert	5 (36%)

Patients with non-inflamed tumor at baseline, generally unresponsive to CPI monotherapy, show disease control on the combination treatment

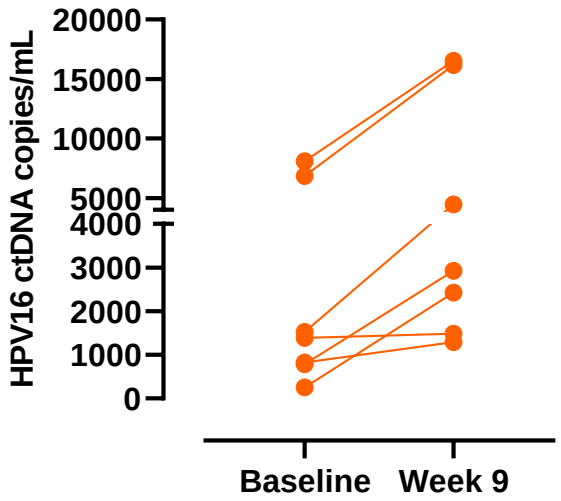
Galon, J & Bruni, D. Nat Reviews Drug Discovery 2019
Trujillo, J. A., et al. *Cancer immunology research*, 2018

Reduced HPV16 ctDNA correlated with clinical response

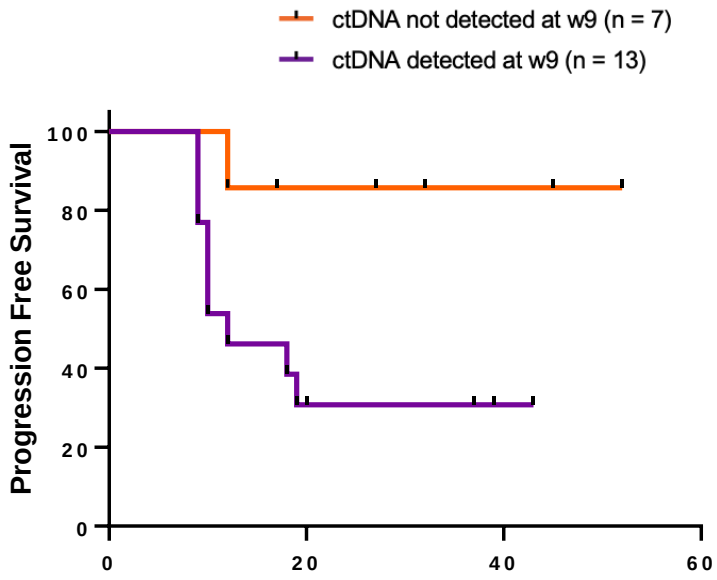
HPV16 ctDNA IN PATIENTS WITH DISEASE CONTROL



HPV16 ctDNA IN PATIENTS WITH PD



PROGRESSION FREE SUVIVAL



HPV16 ctDNA can serve as an early marker of response to HPV16-specific treatments in cervical cancer

Complete clearance of HPV16 ctDNA was significantly associated with disease control and prolonged PFS

Patients with increasing ctDNA at week 9 was generally associated with lack of response

- Only patients with HPV16 ctDNA at baseline are shown, 1 patient discont. due to AE and is not included in PFS curve
- HPV16 ctDNA analysed by ddPCR

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

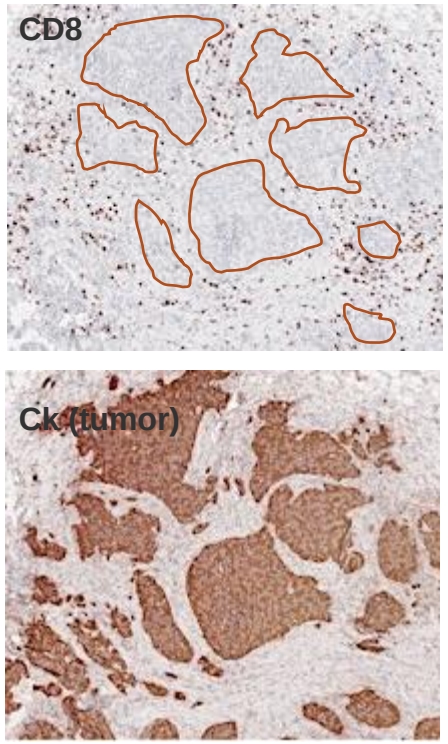
Tumor response status
Partial Response at Week 9 and ongoing response

HPV16 specific T cell response
Increased post vaccination

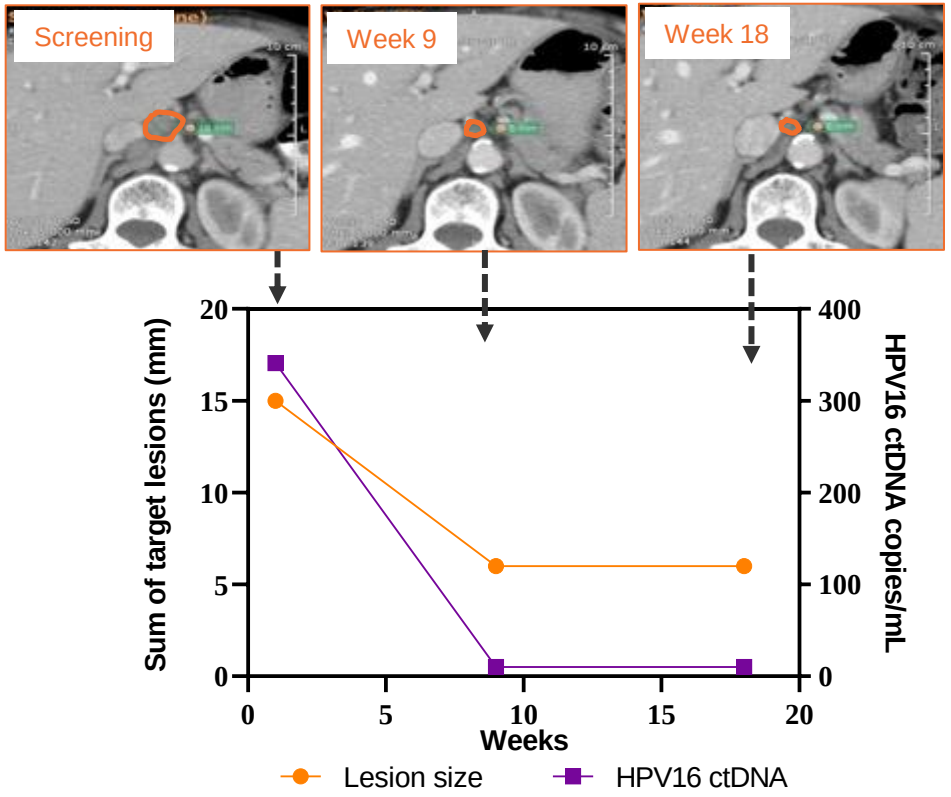
Tumor microenvironment at baseline
T cell excluded and PD-L1 negative

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

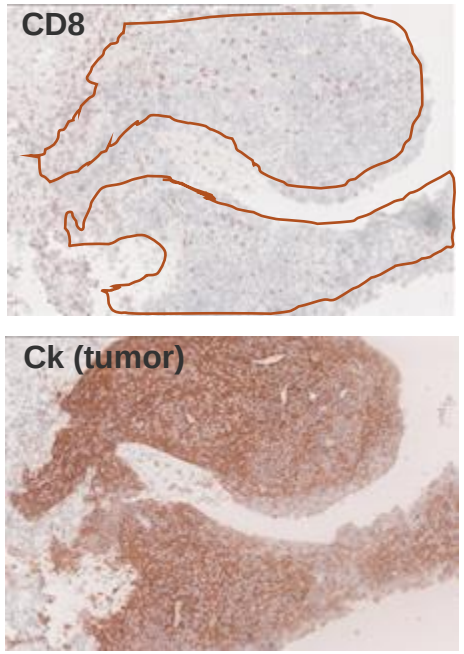
Clinical status
Completed study treatment (48 weeks) with no signs of progression at last follow-up scan

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

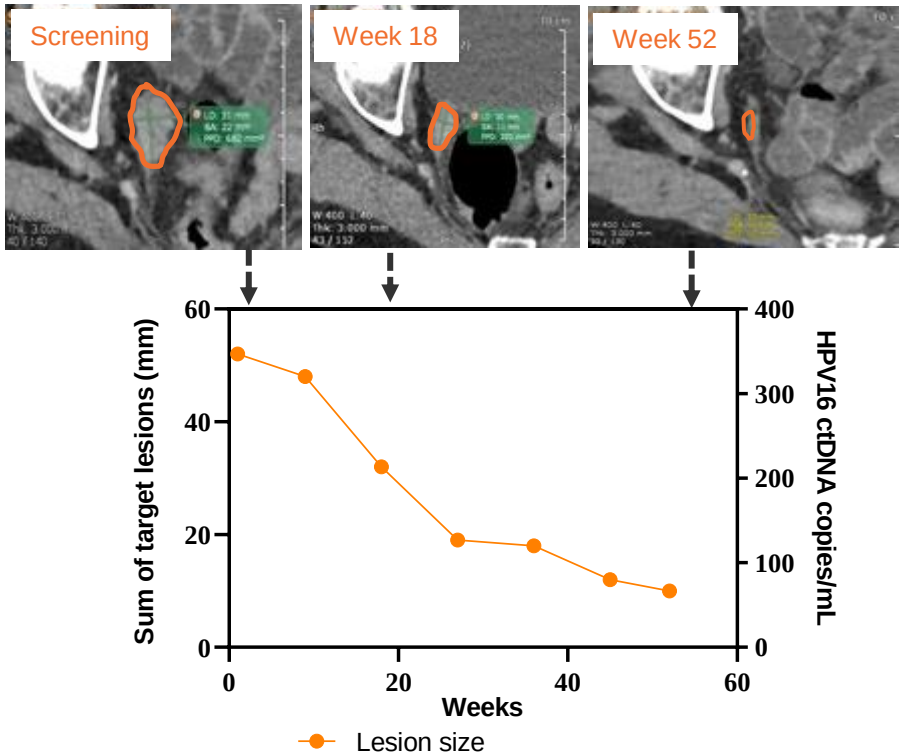
HPV16 specific T cell response
Increased post vaccination

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

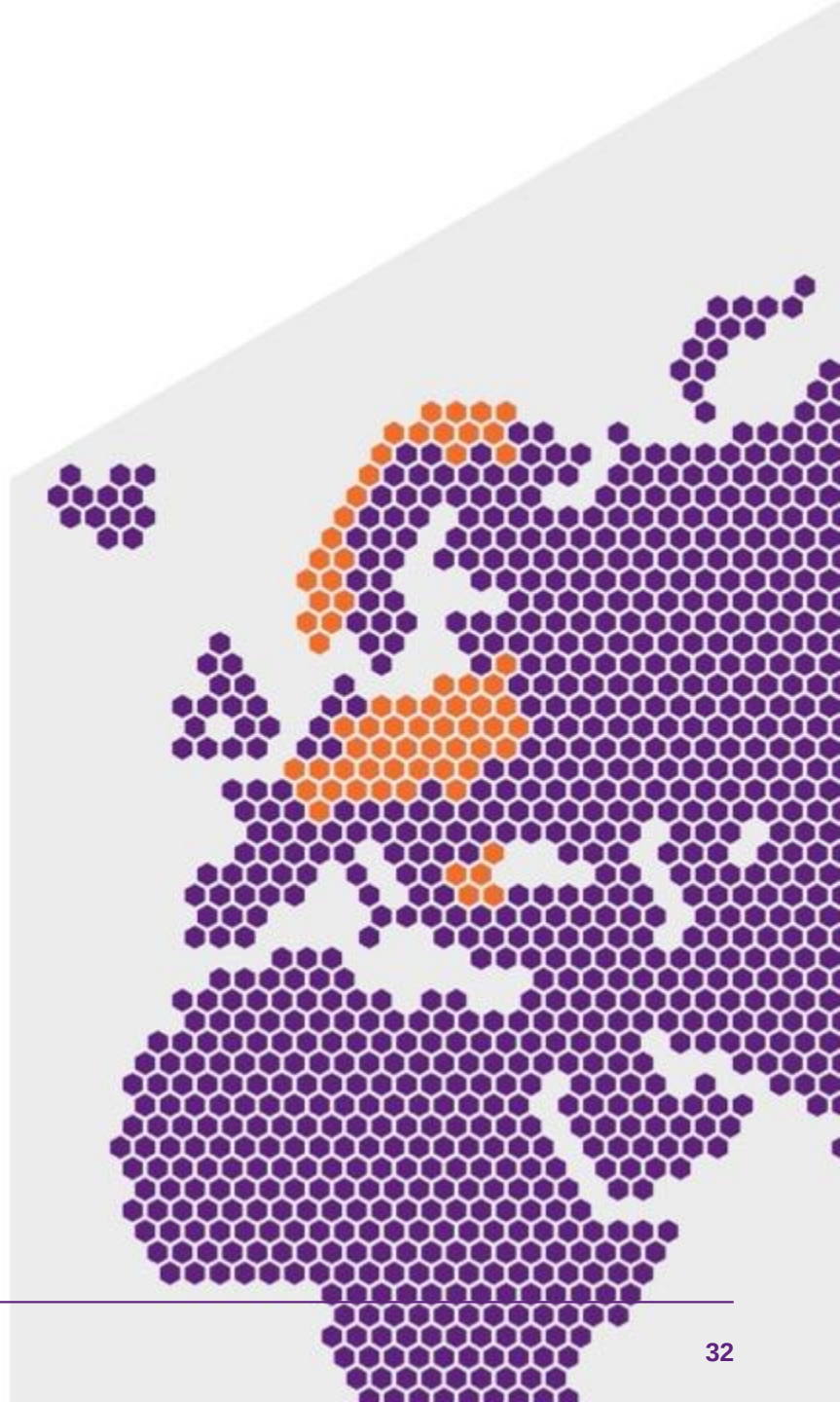
- VB10.16 in combination with atezolizumab showed promising efficacy in heavily pre-treated patients with advanced HPV16+ cervical cancer who have a high unmet medical need
- VB10.16 in combination with atezolizumab showed durable responses with a very high DCR in advanced cervical cancer patients
- 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

Acknowledgement

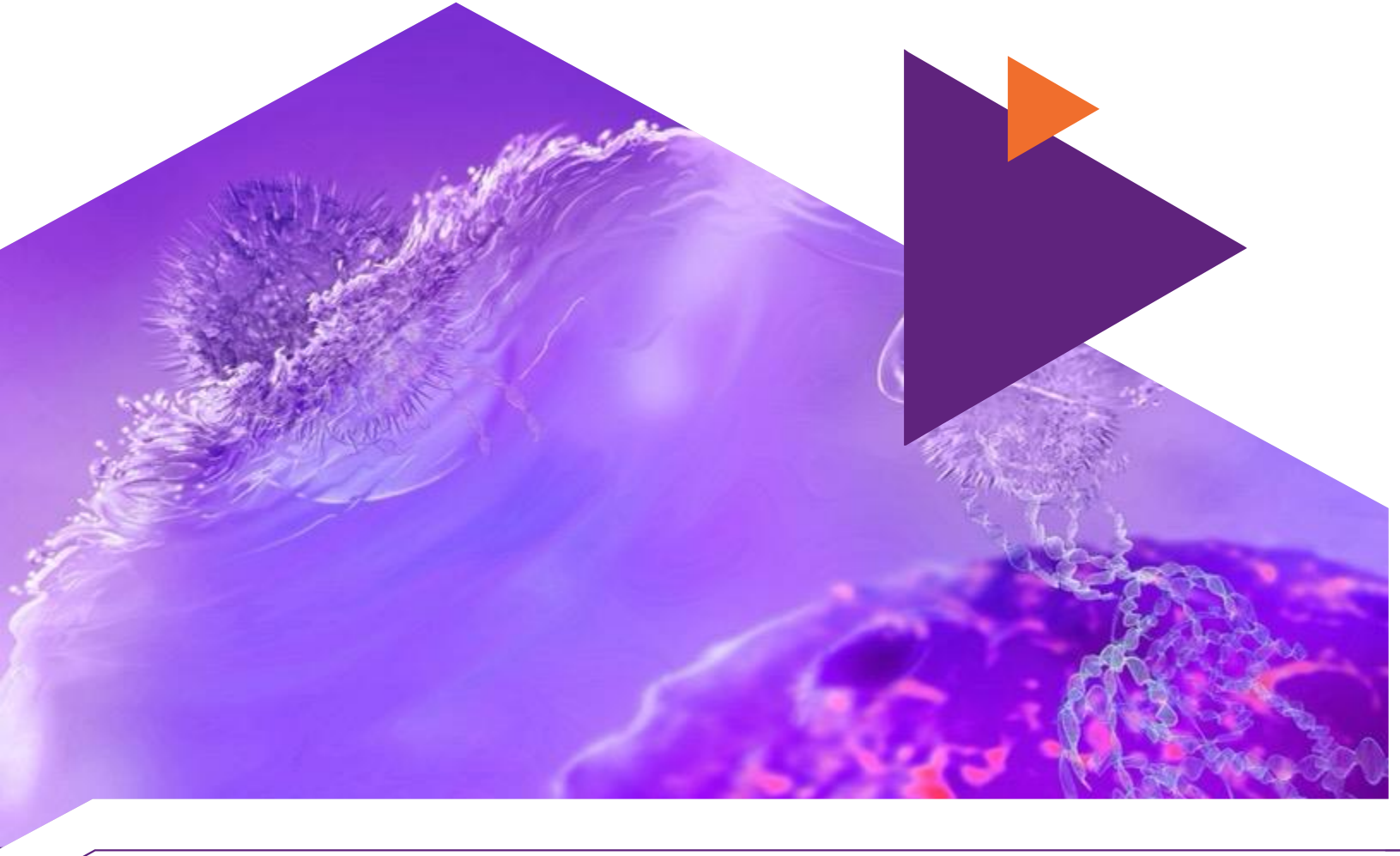
We would like to thank the patients, their families as well as investigators for their participation in the trial

Atezolizumab was supplied by Roche



Financials and upcoming events

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 • Expand into additional indications for VB10.16	VB10.16 (off-the-shelf)	HPV16+ cervical cancer		✓ Phase 2 interim data • Update on VB10.16 development strategy • Updated Phase 2 data (1H 2023)
		Internal programs	Undisclosed		
Infectious Disease	• Advance COVID-19 vaccines • 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)

Invite to Capital Markets Day

May 12, 2022

2.00-4.00 p.m. CET
(8.00-10.00 a.m. ET)

TOPICS OF DISCUSSION

- Pipeline update - Overview of Nykode's product candidate pipeline with a focus on the VB C-02 interim analysis
- Research update - Deep dive into Nykode's research and the ongoing technology projects
- Capital markets strategy update, including potential uplisting to the main market of Oslo Stock Exchange (Oslo Børs)

Physical attendance requires registration. To register for the in-person event, please send an email to ctran@nykode.com before May 11 at 3.00 p.m. CET.

Location: Forum Auditorium, Oslo Science Park, Gaustadalléen 21, 0349 Oslo, Norway

Conference call dial in numbers:
PIN Code for all countries: 755176

US: +1 646-787-0157	UK: +44-203-7696819	CH: +41-22-5017540
DE: +49-30-21789327	FR: +33-1-81221259	BE: +32-2-6810135
NL: +31-20-3690737	LU: +352-20-301626	DK: +45 78768490
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Q&A

UNLOCKING THE FUTURE OF MEDICINE

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