nykode therapeutics

Interim analysis of VB10.NEO a fully individualized cancer vaccine and VB10.16 an off the shelf cancer vaccine targeting HPV16

October 26, 2022

Neoantigen-Based Therapies Summit

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.

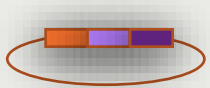
A number of material factors could cause actual results and developments to differ materially from those expressed or implied by these forward-looking statements.

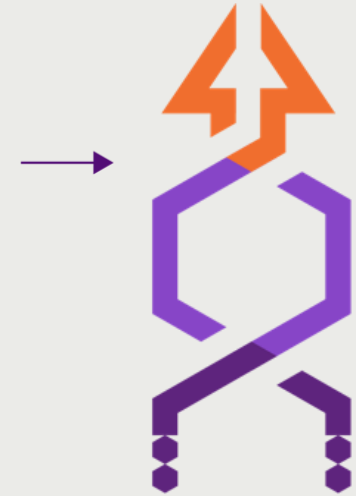
Unique Antigen Presenting Cell (APC) targeted vaccine technology for cancer and infectious disease

MODULAR VACCINE INCLUDES THREE DISTINCT COMPONENTS

Vaccibody vaccines can be delivered through DNA, mRNA, viral vectors or as fusion protein

DNA plasmid encoding Vaccibody





- **Targeting unit** to attract and bind APCs
  Ability to change the targeting unit enables different immune response profiles that can be tailored to specific diseases*
- **Dimerization unit** for crosslinking targeted receptors on the surface of the APC to facilitate strong binding
- **Antigenic unit** presents globular antigens and T cell epitopes expressed in cancer, viruses, bacteria, parasites and autoimmune disease

*Targeting unit can consist of natural ligands, including cytokines/chemokines; bacterial proteins; scFv from mAb binding

Vaccine induces a rapid, robust and long-lasting CD8 T cell response against cancer cells

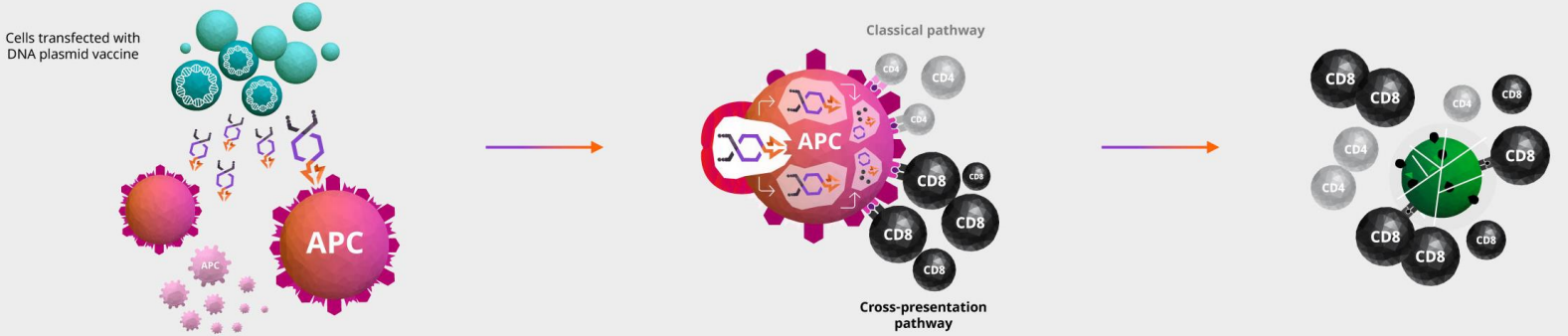
Mechanism of Action – T Cell Induction

Nykode's Vaccibody™ Protein

- Antigenic unit
- Dimerization unit facilitating the cross linking of target receptors
- Targeting unit able to attract and bind antigen presenting cells
- Antigen-Presenting Cell (APC) receptor

T Cell Induction

Nykode's vaccine, once absorbed by the APCs, induces killer T cells (CD8 cells) to attack cancer cells and pathogens. The APCs also enlist CD4 helper cells to boost the tumor-killing power of CD8 cells.



1 Cells encode and secrete Vaccibody proteins, which attract a high concentration of APCs.

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

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

VB10.NEO: Nykode's individualized cancer vaccine

Targeting antigen presenting cell

Proprietary neoantigen selection method

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

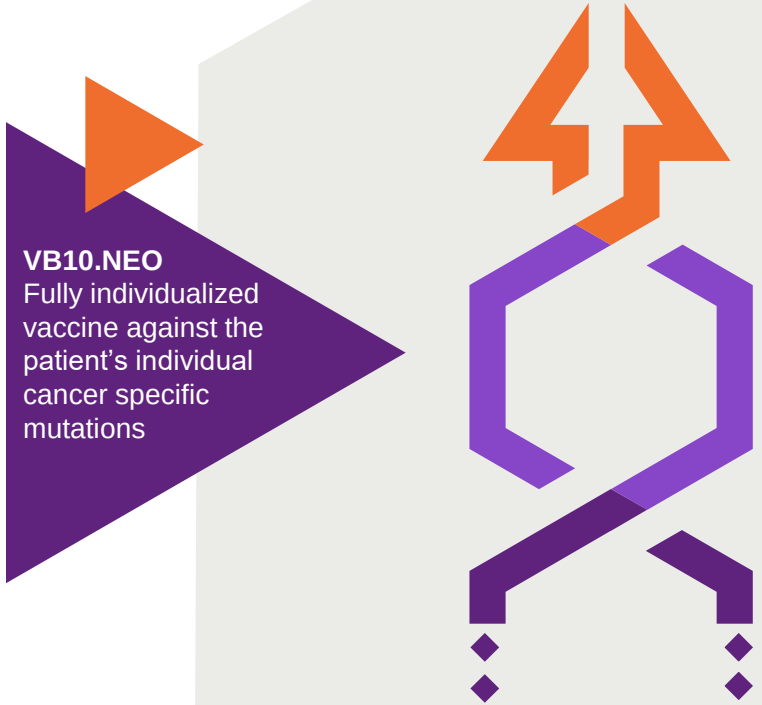
Promising immunogenicity data

- Phase I/IIa in 22 patients with melanoma, NSCLC, SCCHN, RCC or urothelial cancer

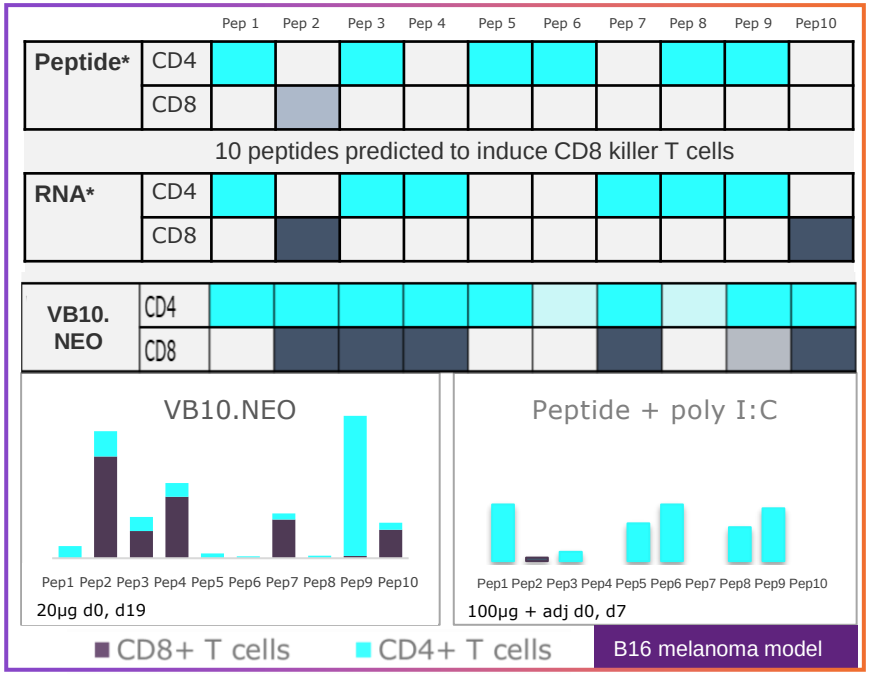
Delivered as DNA plasmid

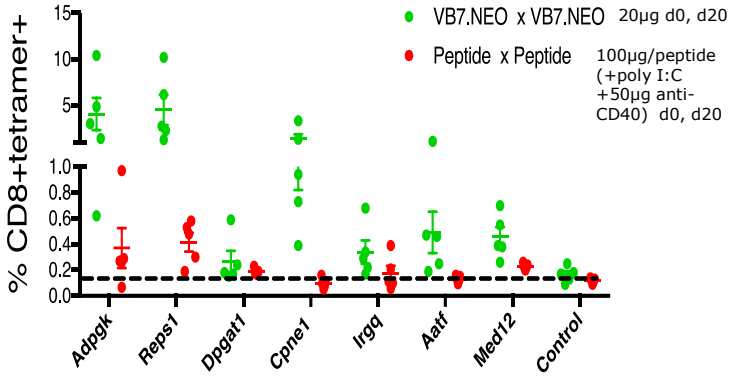
- Flexible, rapid and cost-effective manufacturing. 100% manufacturing success rate

Exclusively out-licensed to Roche and Genentech, 2020



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





Genentech
A Member of the Roche Group

MC38 colon carcinoma

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

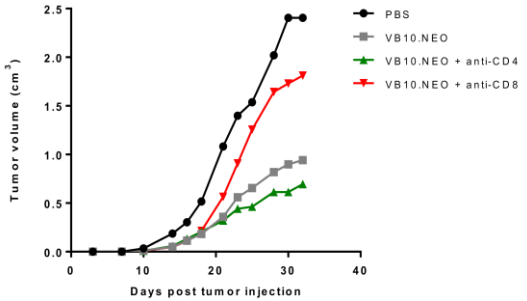
*Castle et al., 2012 and Kreiter et al., 2015

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

Neoepitope-specific CD8 T cells are essential for tumour protection

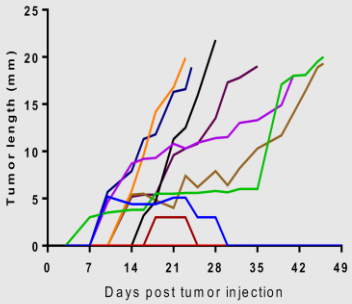
CT26 colon carcinoma model

AVERAGE, ALL GROUPS

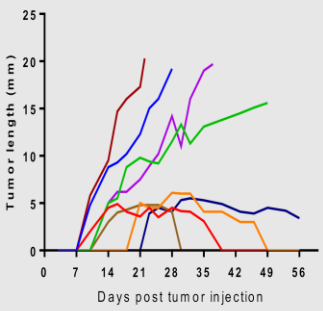


INDIVIDUAL GROWTH CURVES

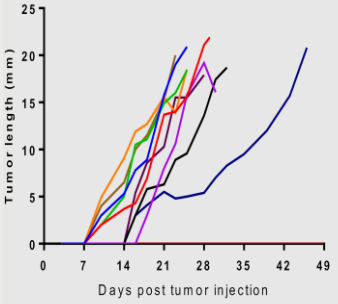
VB10.NEO



VB10.NEO, CD4 depleted



VB10.NEO, CD8 depleted



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

VB N-01 Trial overview

An open-label first-in-human phase 1/2a study to evaluate safety, feasibility and efficacy of multiple dosing with individualised VB10.NEO or VB10.NEO and bempegaldesleukin (NKTR-214) immunotherapy in patients with locally advanced or metastatic melanoma, NSCLC, clear renal cell carcinoma, urothelial cancer or squamous cell carcinoma of head and neck, who did not reach complete responses with current standard of care immune checkpoint blockade

Tumor types/ arms and main incl. criteria per CTP v. 5-7

1. Malignant Melanoma (Must be on- or initiate CPI at baseline)

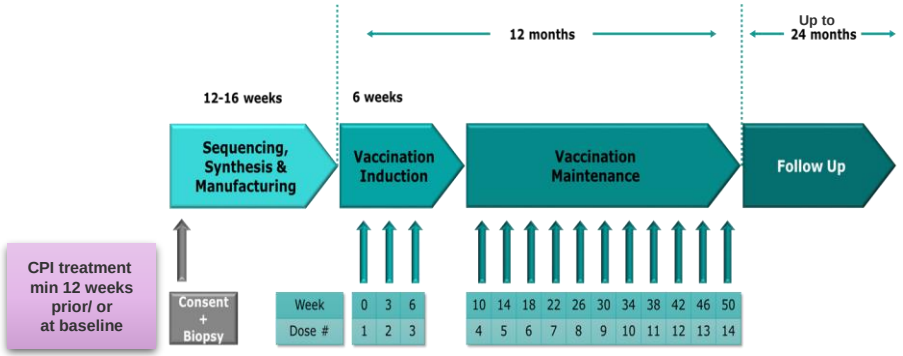
2. Non-Small Cell Lung Cancer (must have been on CPI for at least 12 wks before screening and must be on CPI as part of anti-cancer treatment)

3. Renal Cell Carcinoma (must have been on CPI for at least 12 wks before screening and must be on CPI as part of anti-cancer treatment)

4. Urothelial Cancer (must have been on CPI for at least 12 wks before screening and must be on CPI as part of anti-cancer treatment)

5. Squamous Cell Carcinoma of the head and neck (SCCHN) (Must be on- or initiate CPI at baseline)

Treatment schedule



VB N-01 – Population and baseline characteristics

VB N-01 included a population with various pre-treated and advanced cancer types

Population*	N
VB10.NEO dosed patients (safety population)	41
Completed VB10.NEO treatment	17
Discontinued VB10.NEO treatment	24
Due to Adverse reaction	*1*
Ongoing VB10.NEO treatment	0

**Cut off date is 20 May 2022*

Median number of vaccines given is 11 (range 1-15)

Median duration in the trial is 54 weeks (range 1-155 weeks)

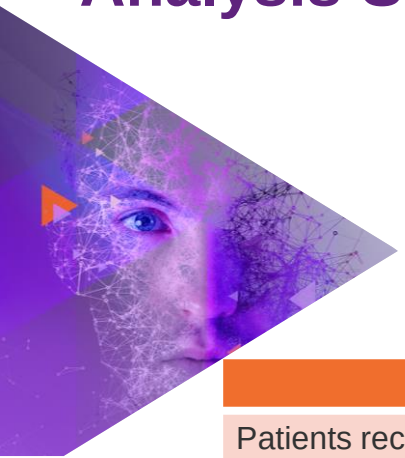
Characteristic	N (%)
Mean Age (range)	62.6 yrs (33-81 ys)
Median Age	62.0 yrs
Ethnicity	
White	41 (100%)
Gender	
Female	16 (39%)
Male	25 (61%)
ECOG	
0	24 (58.5%)
1	17 (41.5%)
PD-L1 status at baseline	
Positive	7 (21%)
Negative	0 (0%)
Missing/unknown	27 (79%)
Cancer type	
Head and neck cancer	14
Non-small cell lung cancer	5
Renal cell carcinoma	10
Melanoma	8
Urothelial carcinoma	4
Metastatic disease	
Y	37 (90%)
N	4 (10%)

Characteristic	N (%)
Prior systemic treatment lines	
1	10 (24%)
2	20 (49%)
3	7 (17%)
4	4 (10%)
Prior surgery	
Y	29 (70%)
N	12 (30%)
Prior radiotherapy	
Prior	23 (56%)
During trial	10 (24%)
Chemotherapy	
Prior	22 (54%)
Concomitant	8 (19.5%)
Other immunotherapy (non-CPI)	
Prior	
Concomitant	3 (7.3%)
	0 (0%)
CPI therapy	
Prior	41 (100%)
Concomitant	33 (80.4%)
Targeted therapy	
Prior	19 (46%)
Concomitant	10 (24%)

Safety and Tolerability
VB10.NEO was generally well-tolerated

- **VB10.NEO was generally safe and well-tolerated in patients with solid tumors when administered in combination with various background therapies.**
- *The most common AEs reported were fatigue (34%) and diarrhoea (27%).*
- *56% of patients experienced a serious adverse event. In one case (somnolence) this was considered related to VB10.NEO.*
- *24% had AE of grade 3 or higher related to VB10.NEO. The most common gr 3 AE related to VB10.NEO was hypertension (15%).*
- *One AE of grade 4 (increased amylase) was considered possibly related to VB10.NEO.*
- *12% of patients had a potential immune-mediated adverse event, when using the narrow MedDRA search term.*
- **The observed adverse events are generally consistent with the known safety profiles of the background therapies with various CPIs, chemotherapy, as well as other targeted cancer therapies with no overt signs of add-on toxicity.**

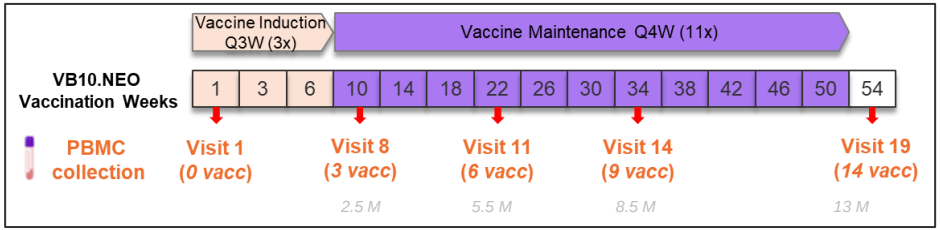
Immunogenicity Evaluable Analysis Set (IEAS)



	# pts
Patients received ≥ 1 dose VB10.NEO	41
IEAS	34
Included in current interim analysis	22
Completed ELISpot analysis	17

All patients enrolled into VB N-01 who have completed at least 4 vaccinations ***and*** provided at least 1 post baseline PBMC sample for immunogenicity assessment (n=34)

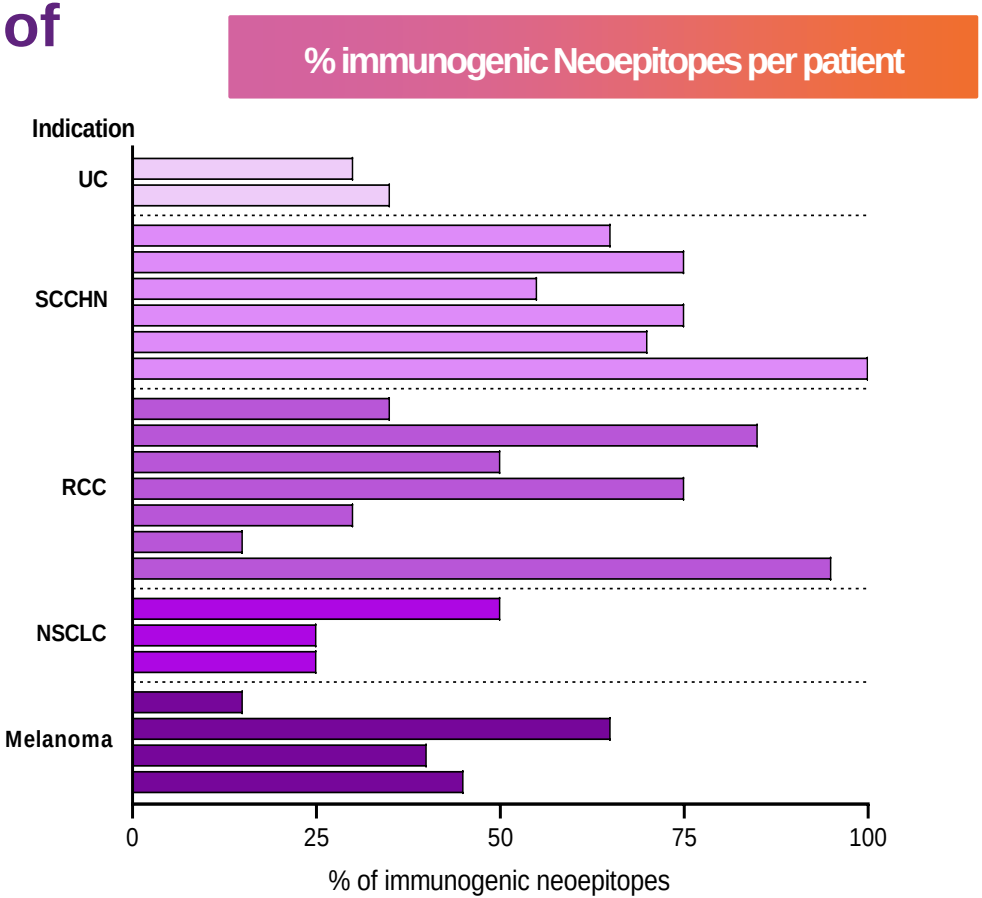
- Immunogenicity assessed after 3, 6, 9 and 14 vaccinations
- Patients in Arm 5b (n=6) who received bempegaldesleukin according to protocol are *not* included
- Patients having received concomitant treatments with immunosuppressive properties (i.e. everolimus, lenvatinib, prednisolone) are included



T-cell responses to majority of selected neoepitopes

All patients across five indications showed a response to at least one neoepitope

On average, 53% of selected neoepitopes were immunogenic, ranging from 3 to all 20 neoepitopes in the VB10.NEO vaccine demonstrating a broad response

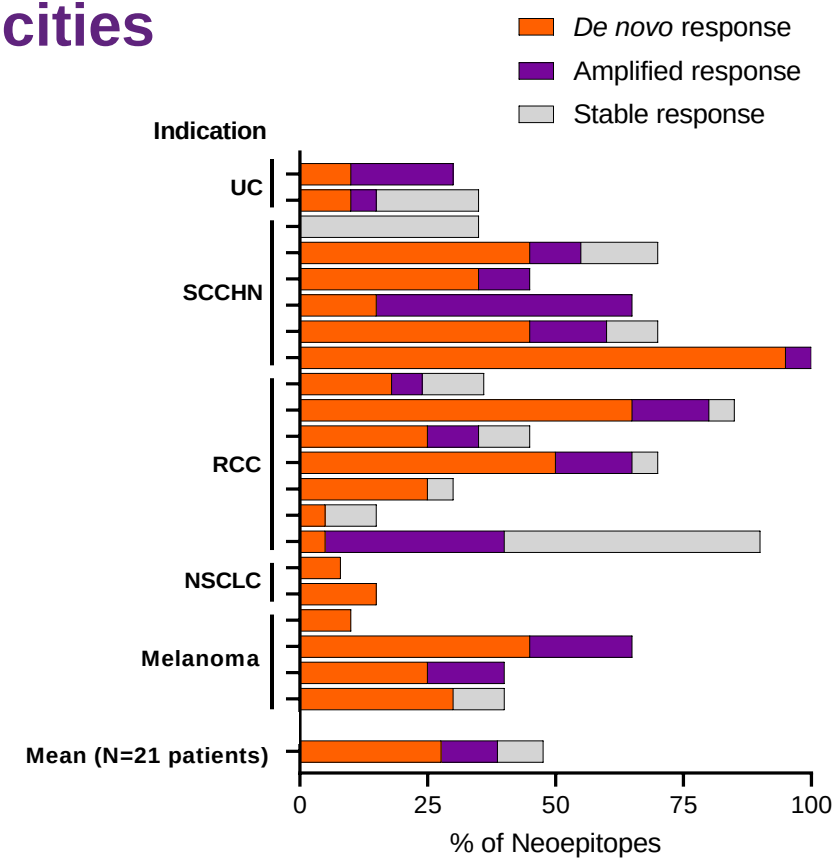


VB10.NEO amplify pre-existing T-cell responses and induce novel T-cell specificities

Expansion of both pre-existing and novel T-cell responses in most patients

- 20/21 (95%) *de novo* expanded
- 14/21 amplification of pre-existing

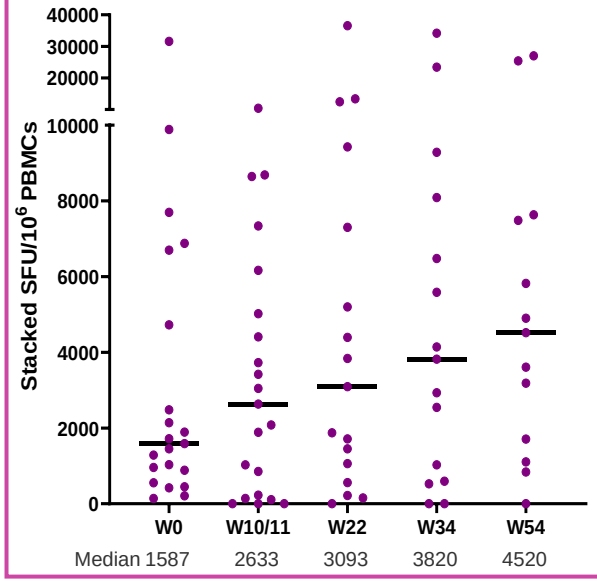
Neoepitopes immunogenic at baseline and not expanded in post-vaccination samples (stable) were observed in 12/21 samples



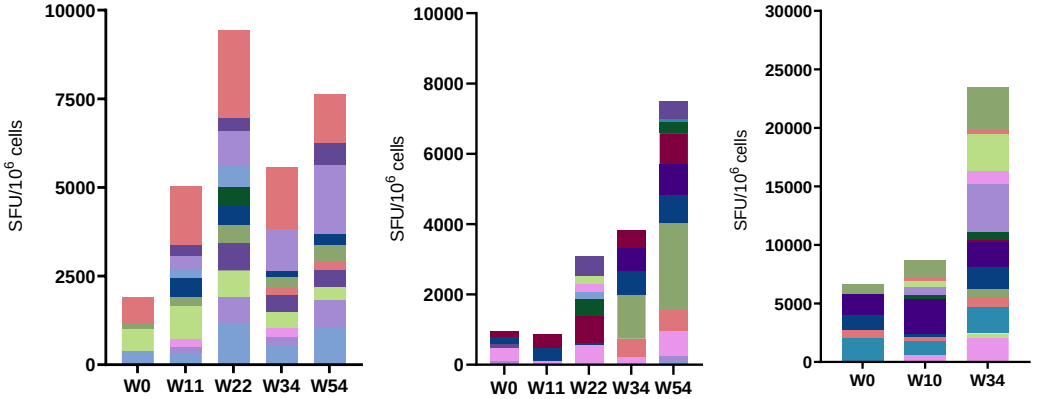
Analysis reported for patients with available PBMC, data missing for 1 or more neoepitopes for 1 patient (N=21)

Multiple vaccinations boost the breadth and magnitude of the immune response

The magnitude of IFNγ T cell response is increased with multiple vaccinations



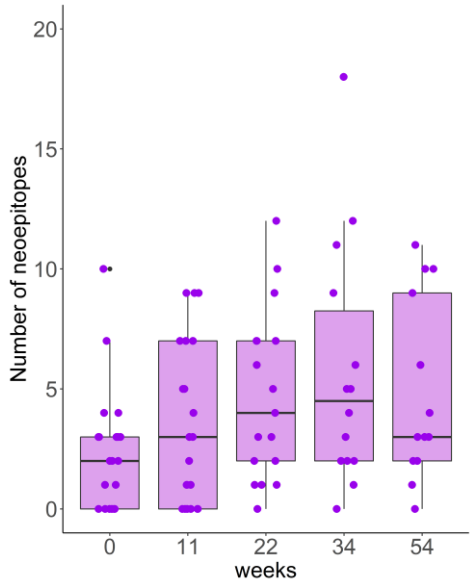
Increased magnitude of response to VB10.NEO was observed as shown in selected patients



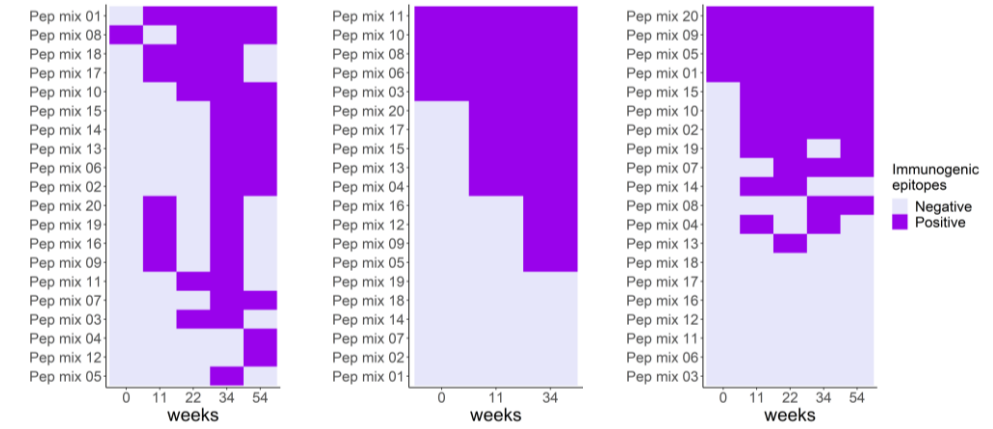
Breadth and magnitude show stacked IFNγ T-cell response to all immunogenic neoepitopes

Repeated vaccinations boost the breadth of the immune response

The number of vaccine-induced immunogenic neoepitopes is increased with multiple vaccinations



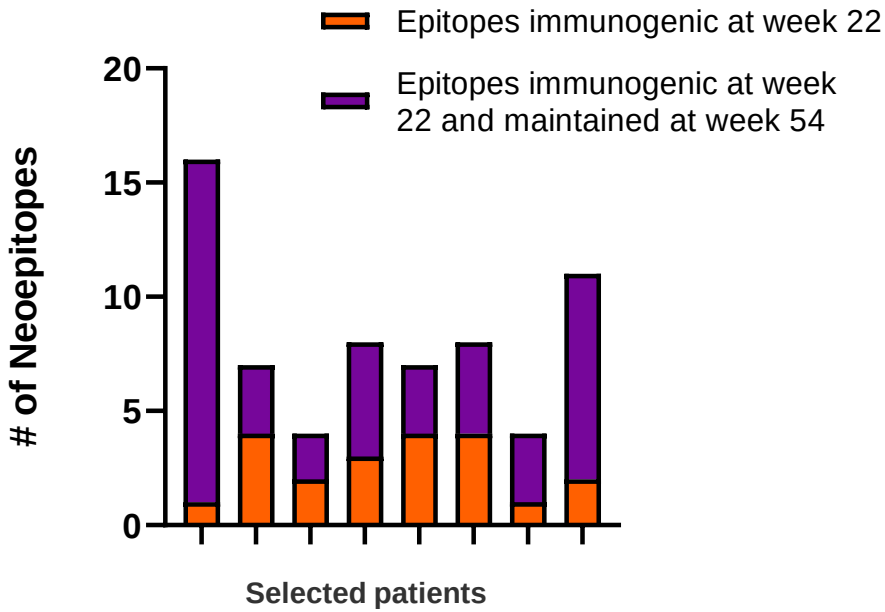
The number of neoepitopes being immunogenic increased with multiple vaccinations, as shown in selected patients



Responses were detected from week 11 and maintained up to one year

Most T-cell responses detected at week 22 were maintained for at least one year

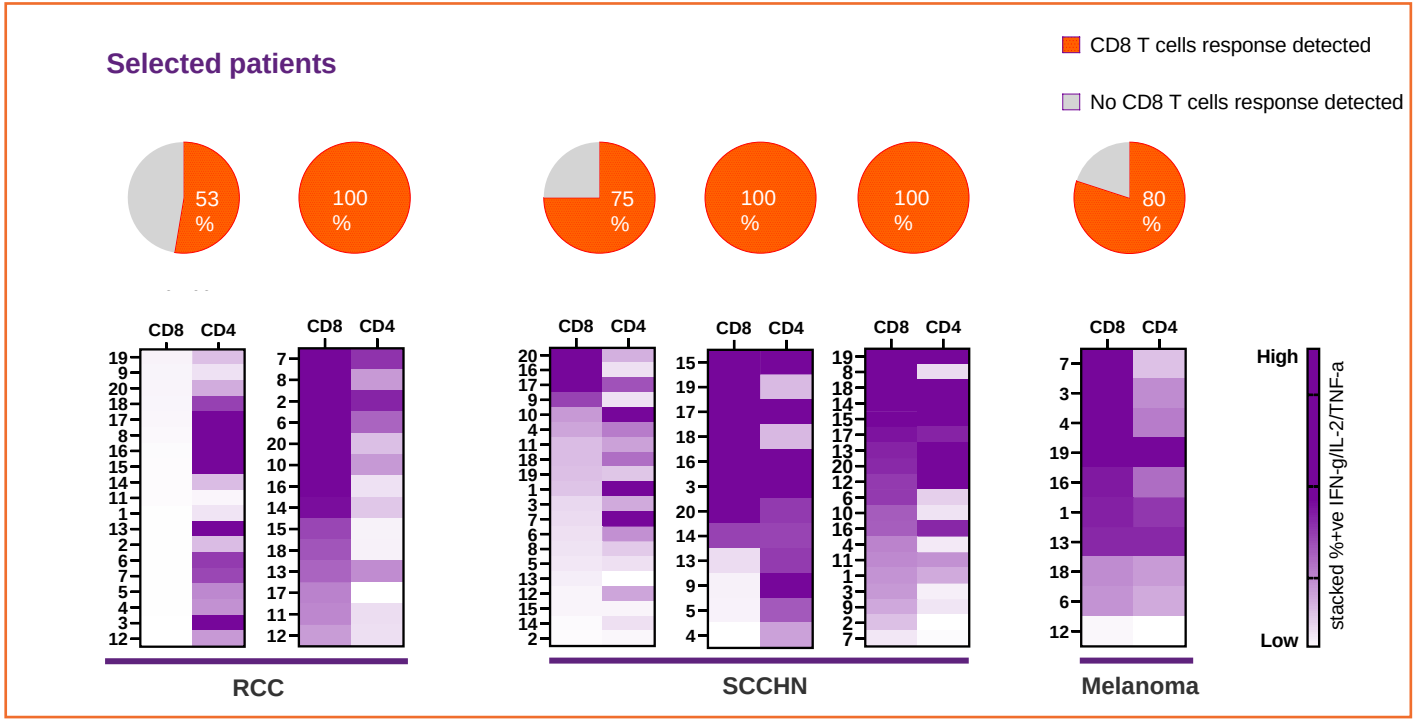
Responses to 68% of neoepitopes were maintained for at least one year



Preliminary immune phenotyping shows that the majority of neoepitopes activates CD8 T cells

T cell responses are characterized by both CD8 and CD4 T cells

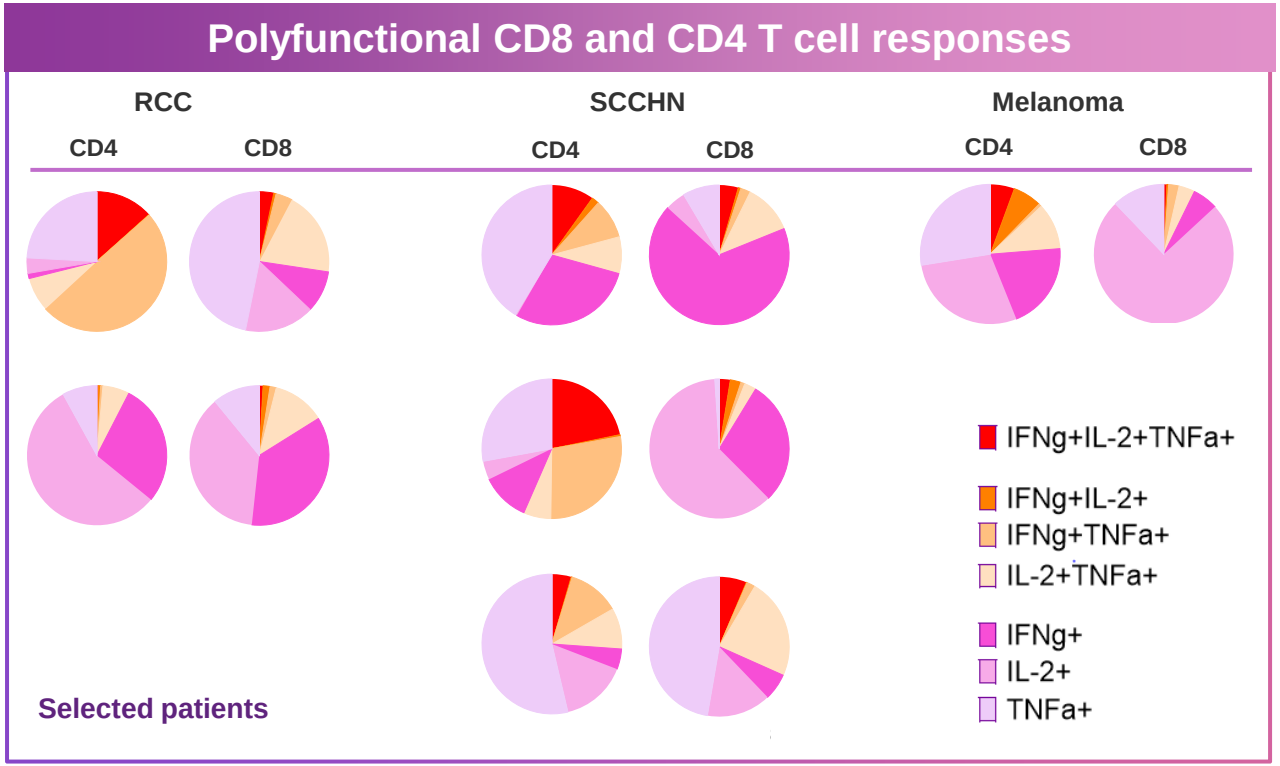
The majority of tested neoepitopes activated functional CD8 T cells in all subjects analyzed



CD8 response defined as ≥ 0.2% above DMSO background.
Phenotyping was performed by IVS ICS using PBMC from week 22 for 6 subjects. Number indicate neoepitope in VB10.NEO

Neoepitope-reactive CD8 and CD4 T cells are polyfunctional

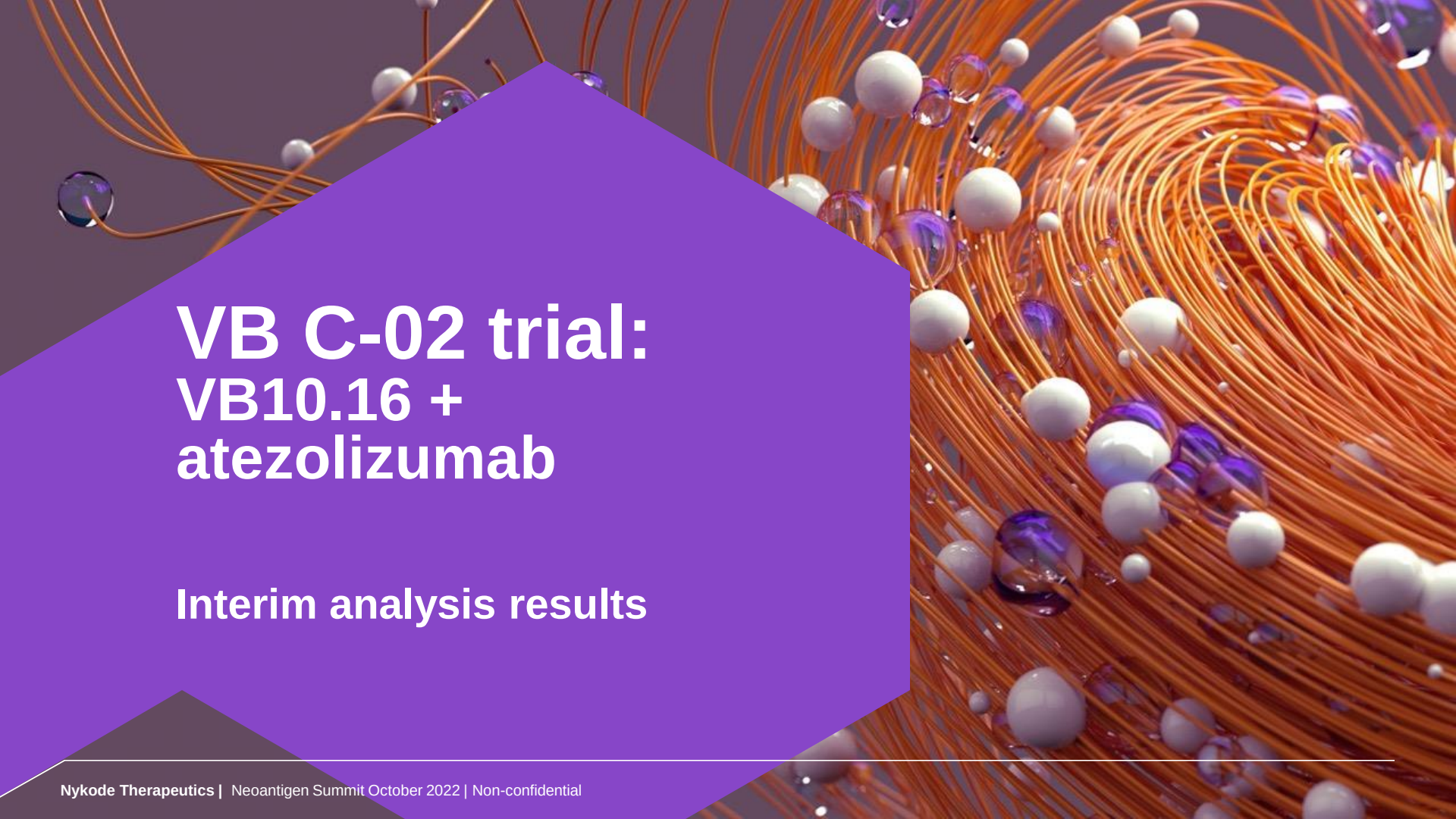
The majority of the neoepitopes induced a polyfunctional T cell response characterized by a Th1/Tc1 cytokine profile



Preliminary data from 7 subjects analysed by IVS ICS using PBMC from week 22

VB N-01: Summary

- **VB10.NEO was generally safe and well-tolerated in patients with solid tumors**
- **A broad T-cell response was observed in the majority of patients, inducing expansion of both novel and pre-existing T cells**
- **Breadth and magnitude of immune response increased upon multiple vaccinations**
- **Most T-cell responses detected at week 22 were maintained for at least one year**
- **VB10.NEO induced polyfunctional CD8 and CD4 T-cells**



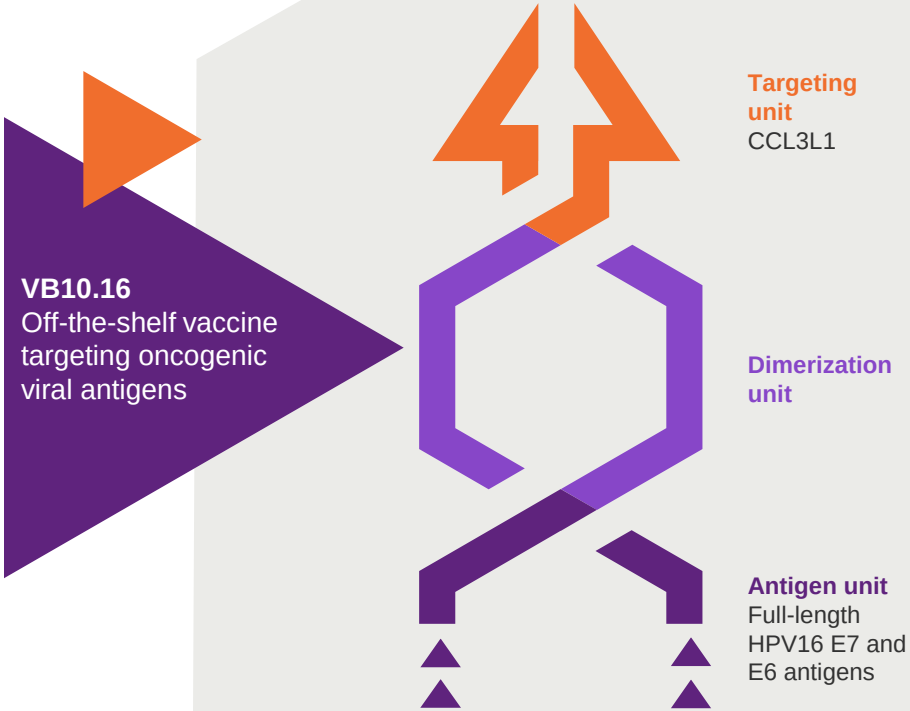
VB C-02 trial:
VB10.16 + atezolizumab

Interim analysis results

VB10.16: Therapeutic HPV vaccine

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

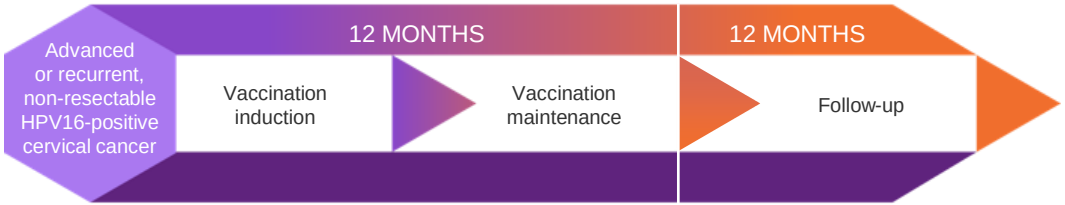
- Finalized VB C-01 Phase 1/2a study investigating VB10.16 monotherapy in HPV16+ precancerous cervical lesions
- Ongoing VB C-02 Phase 2 study investigating VB10.16 in combination with atezolizumab in advanced cervical cancer
- Nykode is exploring the commercial potential of VB10.16 for the treatment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



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



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*

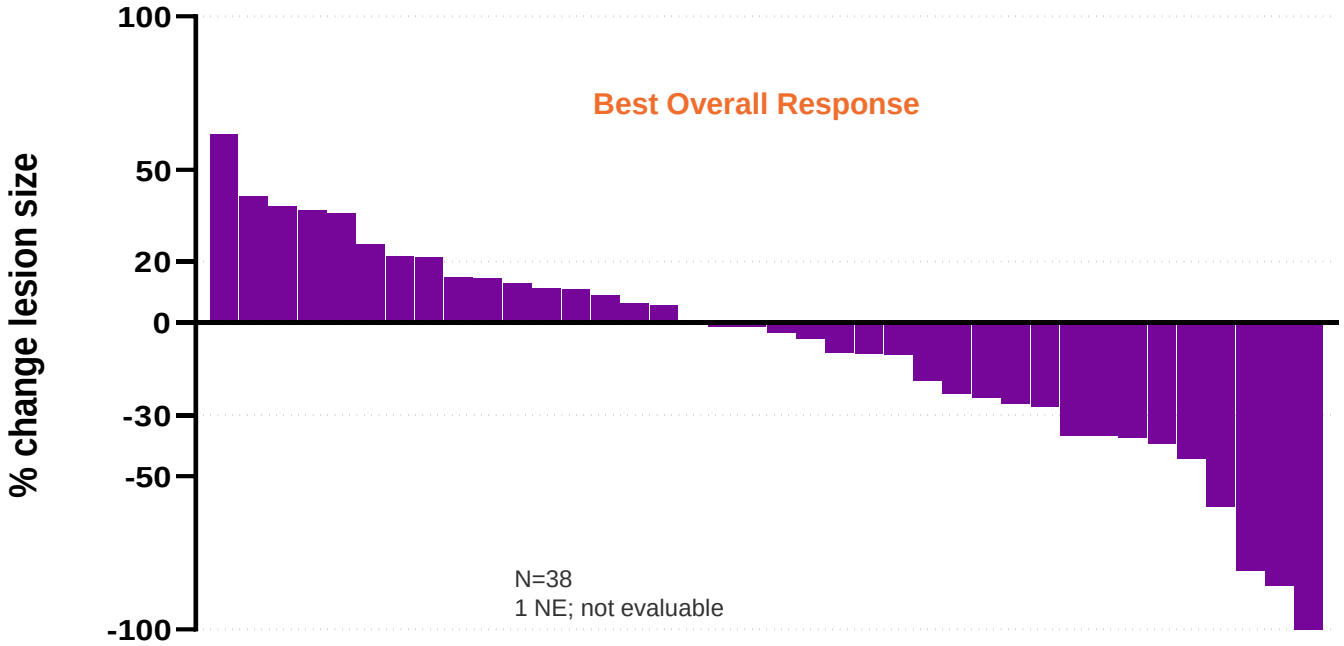
ORR = 21% (8/39 patients)
PD-L1 positive* = 27% (6/22 patients)
PD-L1 negative = 17% (2/12 patients)

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)

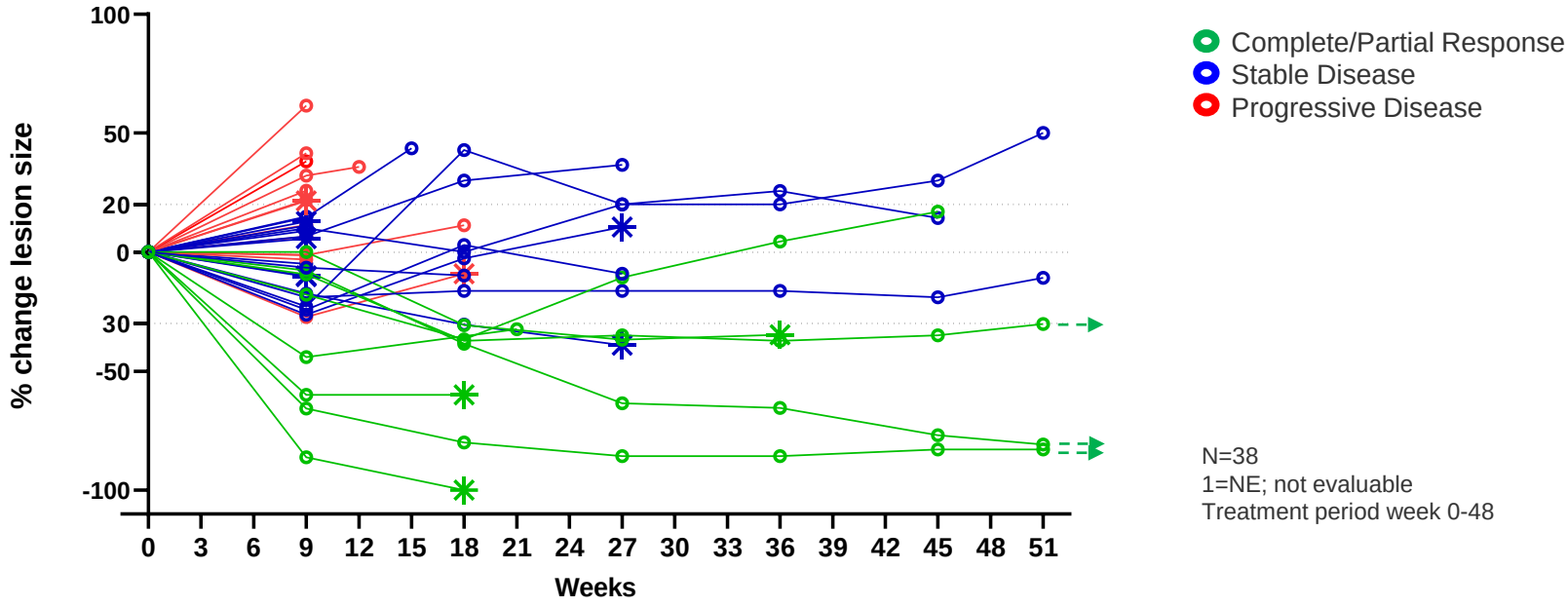
- *PD-L1 status at baseline was available in 34 patients*
- *1 PD-L1 negative patient was NE (RECIST)*

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



✱ 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

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.

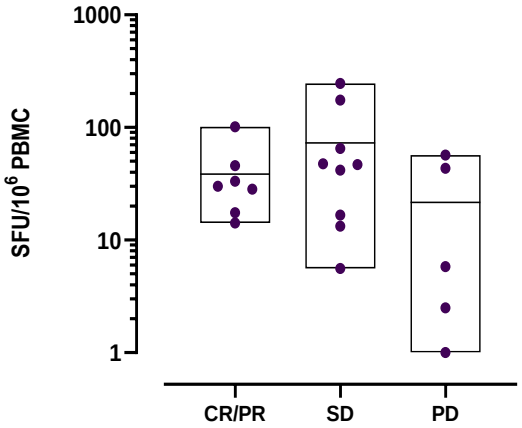
50 patients were included in the safety population for the interim analysis. Median number of VB10.16 doses given was 5 (range 1-11).

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

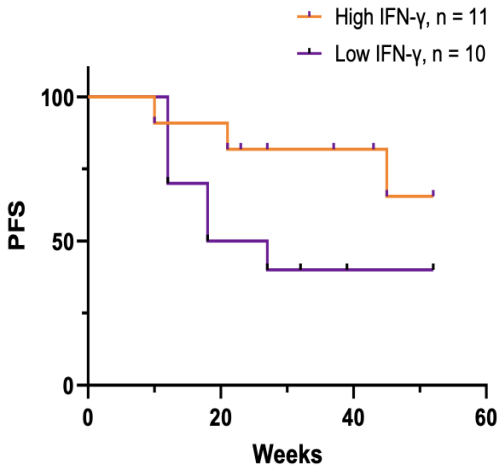
A strong HPV16-specific IFN-γ T cell response was associated with clinical response indicating HPV-specific T cells are important for clinical efficacy in advanced cervical cancer

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



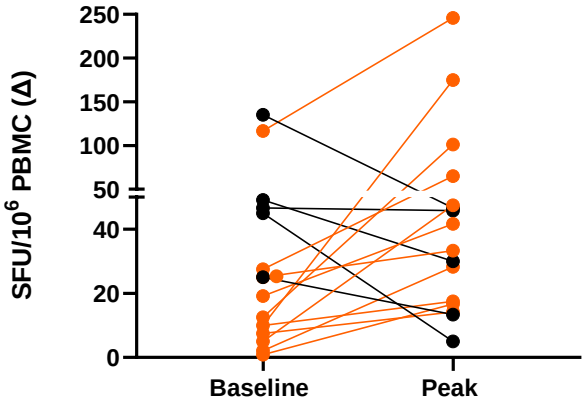
- IFN-γ T cell responses were evaluated in 21 subjects
- T cell responses were evaluated in *ex vivo* ELISpot detecting HPV16 E6 and E7 antigens separately

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

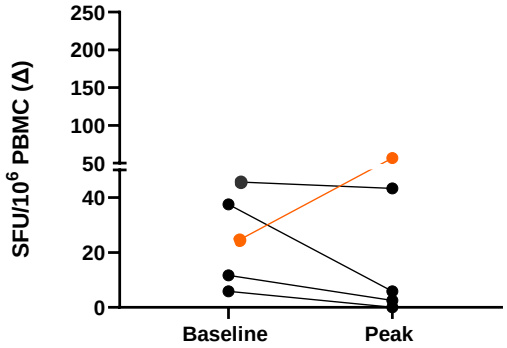
Increased HPV16-specific T cell responses in post vaccination samples observed in the majority of patients with disease control

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



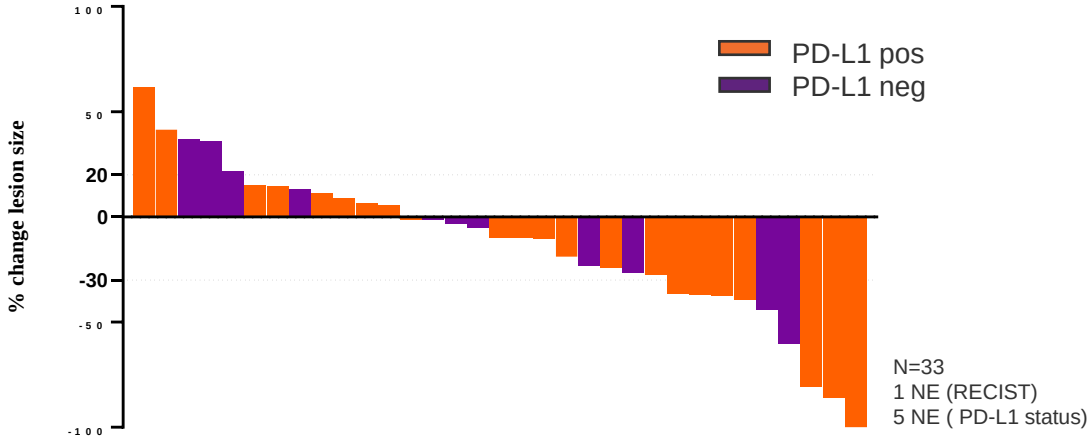
IFNγ T CELL RESPONSE IN PATIENTS WITH PD



- 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 +/-



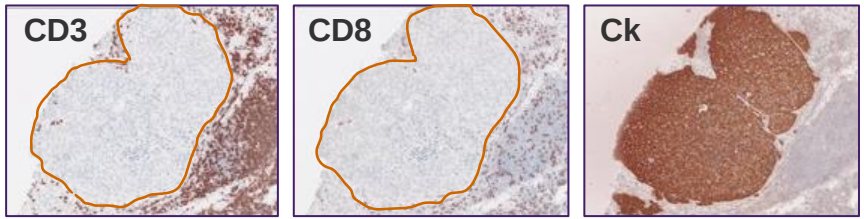
PD-L1 status	ORR (n/N)	DCR (n/N)
Positive (TIC 1-2)	**27%** (6/22)	**77%** (17/22)
Negative (TIC 0)	**17%** (2/12)	**58%** (7/12)

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

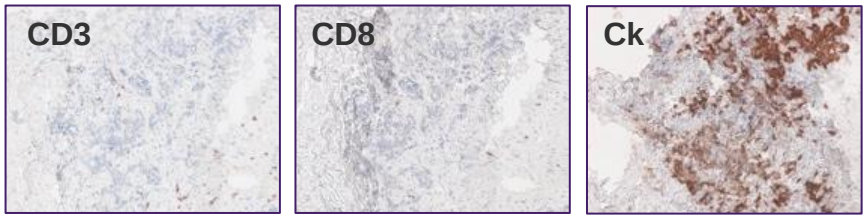
- PD-L1 was scored by TIC (Tumor and immune cell) scoring using Ventana SP263 platform (Roche Diagnostics)
- PD-L1 status at baseline was available in 34 patients, 1 PD-L1 negative, was NE for RECIST

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

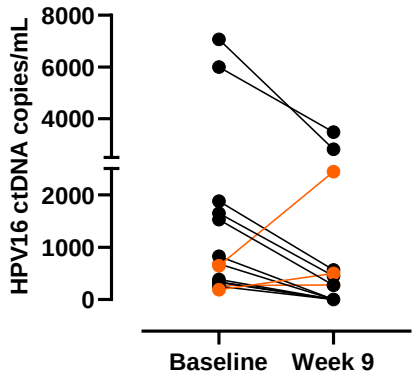
	DCR
Non-inflamed tumors	10 of 14 (71%)
T cell excluded	5 (36%)
Immune desert	5 (36%)

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

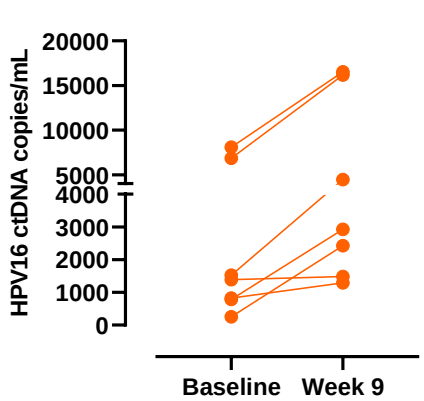
Galon, J & Bruni, D. Nat Reviews Drug Discovery 2019
Trujillo, J. A., et al. *Cancer immunology research*, 2018

Reduced HPV16 ctDNA correlated with clinical response

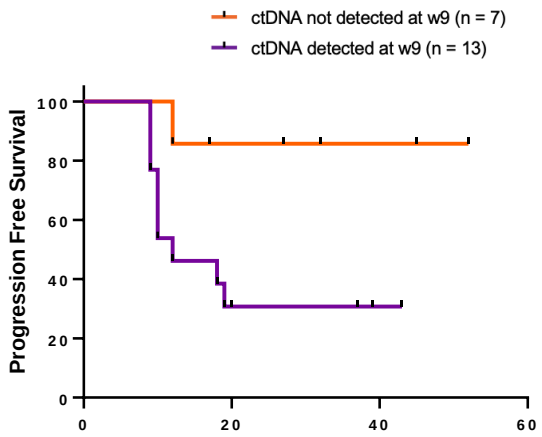
HPV16 ctDNA IN PATIENTS WITH DISEASE CONTROL



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

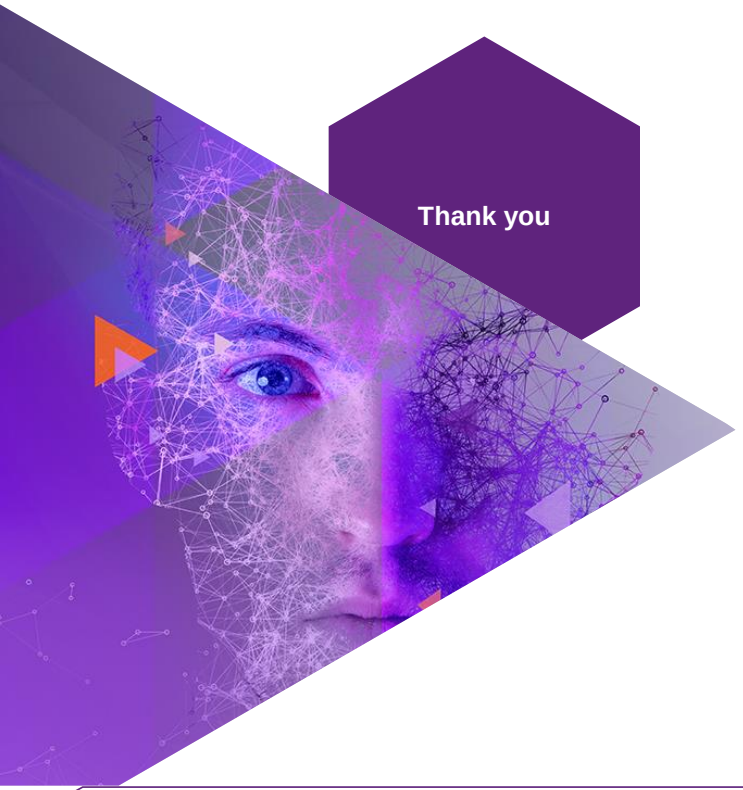
- Only patients with HPV16 ctDNA at baseline are shown, 1 patient discont. due to AE and is not included in PFS curve
- HPV16 ctDNA analysed by ddPCR

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 in the VB C-02 trial

VB10.NEO is exclusively out-licensed to Genentech

UNLOCKING THE FUTURE OF MEDICINE