



Viral Vector Based Immunotherapies

Corporate Presentation

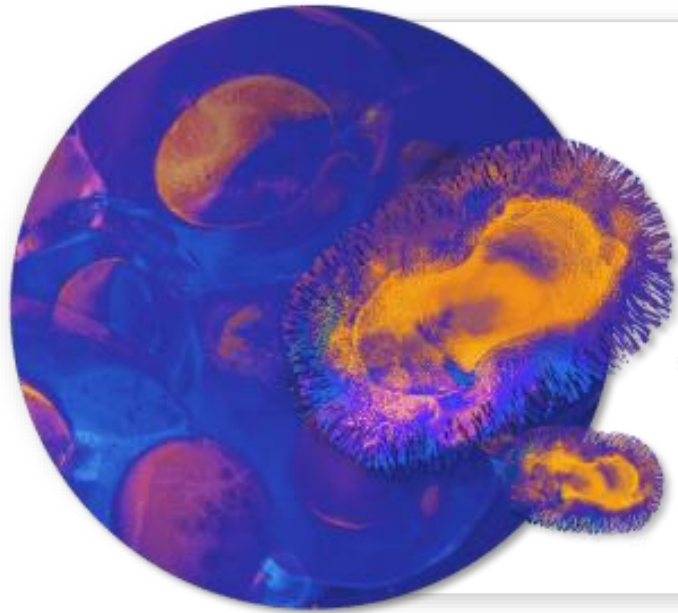
May 25, 2023



Disclaimer

This presentation contains forward-looking statements, which are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated. There can be no guarantee that (i) the results of pre-clinical work and prior clinical trials will be predictive of the results of the clinical trials currently under way, (ii) regulatory authorities will agree with the Company's further development plans for its therapies, or (iii) the Company will find development and commercialization partners for its therapies in a timely manner and on satisfactory terms and conditions, if at all. The occurrence of any of these risks could have a significant negative outcome for the Company's activities, perspectives, financial situation, results and development.

For a discussion of risks and uncertainties which could cause the Company's actual results, financial condition, performance or achievements to differ from those contained in the forward-looking statements, please refer to the Risk Factors ("Facteurs de Risques") section of the Universal Registration Document, available on the AMF website (<http://www.amf-france.org>) or on Transgene's website (www.transgene.fr). Forward-looking statements speak only as of the date on which they are made and Transgene undertakes no obligation to update these forward-looking statements, even if new information becomes available in the future.



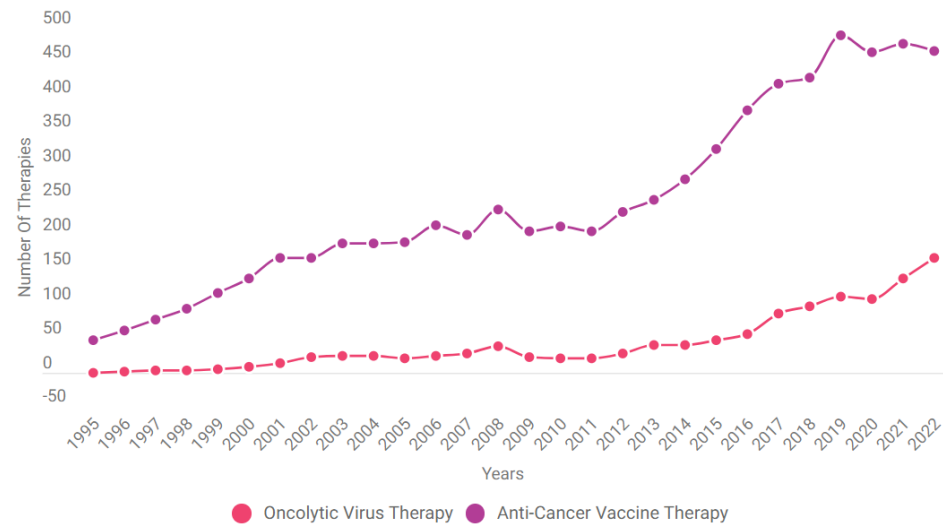
Leader in viral vector-based immunotherapies
designed to transform
the standard of care of solid tumors

Transgene is Focused on Two Exciting Areas of Immunotherapy Therapeutic Cancer Vaccines (TCVs) and Oncolytic Viruses (OVs) on the Rise

In Vivo
Pharma Intelligence

A Promising Future For Oncolytic Viruses As Cancer Immunotherapies

**Exhibit 1: Oncolytic Virus Therapy And Anti-Cancer Vaccine Therapy
Trends, 1995–2022**



Note: annual snapshots are taken each May

The Washington Post
Democracy Dies in Darkness

Getting closer to a vaccine for cancer

BIOTECH
FIERCE

Oncolytic viruses show
promise in cancer-killing
combos

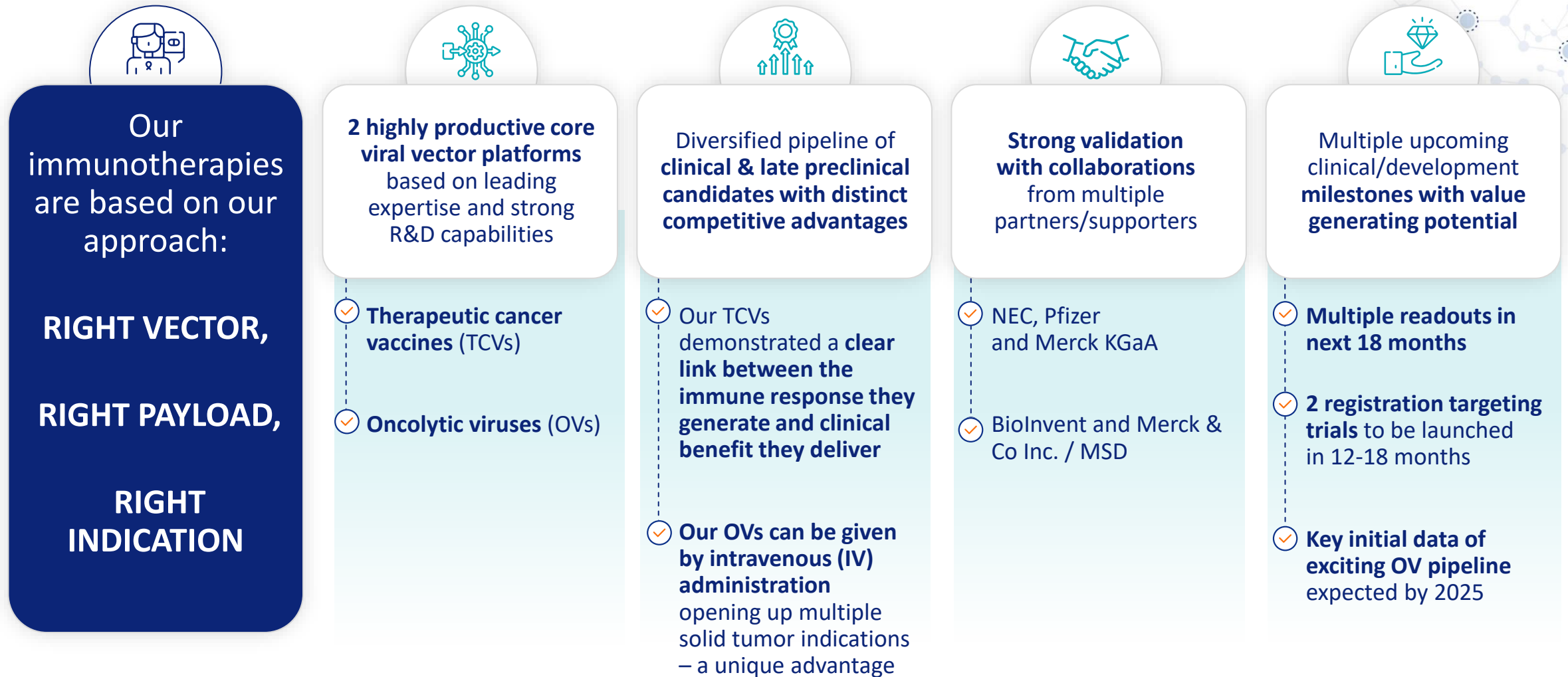
CANCER
RESEARCH
UK

Hiding in plain sight: How we can use immune cells to deliver cancer-killing
viruses to tumours

GEN
Genetic Engineering
& Biotechnology News

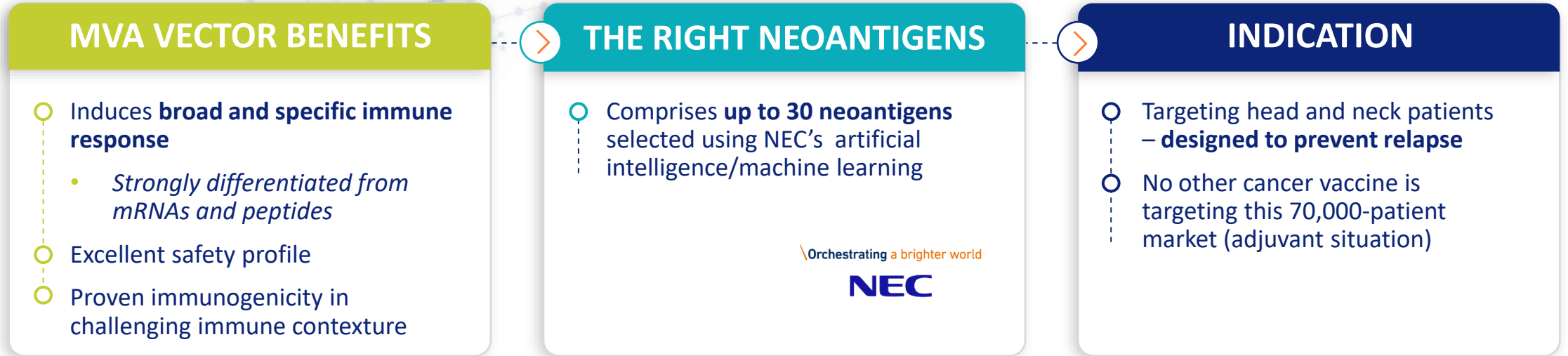
Viral Vector Production Evolves to Meet
Surging Demand

Transgene – a Global Player in Next Generation Cancer Immunotherapies



Harnessing Innovation to Deliver Much Improved Cancer Vaccines

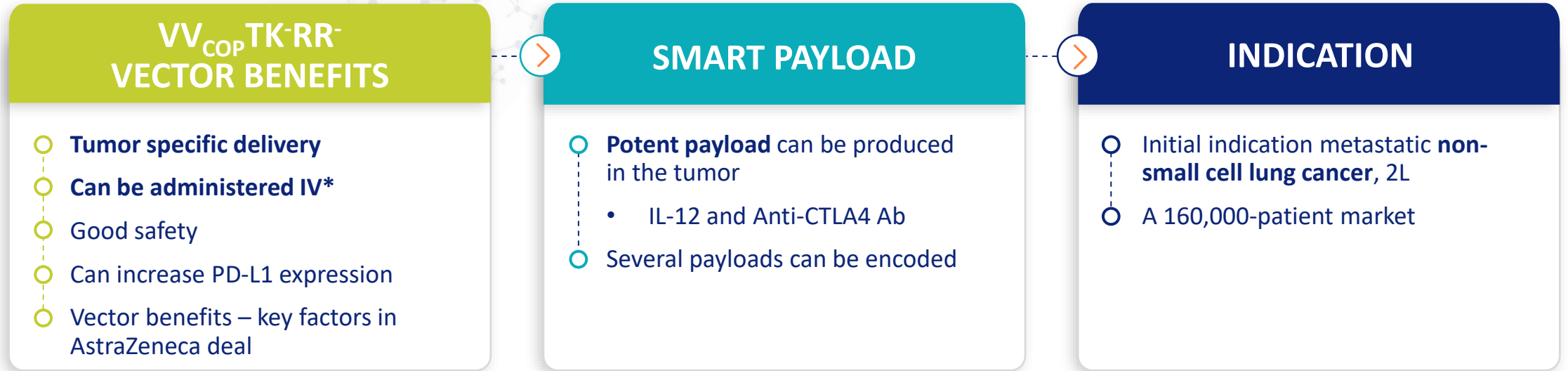
TG4050 – a Novel Individualized Cancer Immunotherapy Designed for Success



Immune responses linked to clinical benefits
Potential registrational trial to begin H2 2023

Harnessing Innovation to Realize the Significant Potential of OV^s

TG6050 a Powerful Off-The-Shelf Cancer Immunotherapy Designed for Success








invirio

**Generated a multi armed IV OV
that can potentially be an industry
leading product for solid tumors**

* IV: intravenous administration

Advancing a Diversified Immunotherapy Portfolio

From Off-the-Shelf Treatments to Patient Tailored Therapies

Product	Target/transgene	Indication	Collaboration	Preclinical	Phase I	Phase II
THERAPEUTIC CANCER VACCINE (TCVs) ➔ MVA						
TG4001	HPV16 E6 – E7	Anogenital HPV+ cancers		<div></div>	<div></div>	<div>Potential registrational trial in preparation</div>
	TG4050	30 neoantigens		<div></div>	<div></div>	<div>Potential registrational trial to start in H2 2023</div>
		Ovarian cancer		<div></div>	<div></div>	
ONCOLYTIC VIRUS (OVs) ➔ VV _{COP} TK ⁻ RR ⁻						
	TG6050	IL-12 + Anti-CTLA4		<div></div>	<div></div>	
	BT-001	Anti-CTLA4 + GM-CSF		<div></div>	<div></div>	
	TG6002	5-FU chemotherapy		Gastro-intestinal cancers (IV*)	<div></div>	<div></div>
Colorectal cancer (IHA*)			<div></div>	<div></div>		

Recent Achievements are Solid Basis for Multiple Readouts in Next 18 Months

The Viral Vector Experts in Immuno-Oncology

TG4050 | Neoantigen vaccine



- ✓ Promising data as single agent (adjuvant setting)
 - ➔ June 2023 | Updated data to be presented (head and neck)
 - ➔ H2 2023 | Potential registrational Phase II trial expected to start
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TG4001 | HPV16 cancers

- ✓ Positive Interim Analysis Results based on PFS
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invirio | Oncolytic Viruses Platform

- ✓ PoC of IV administration
 - ➔ Expand the potential of our technologies through existing and new partnerships, and proprietary development

TG6050 (IV) | IL12 + anti-CTLA4

- ✓ Positive data demonstrating IV feasibility of Invir.IO® backbone
 - ➔ H2 2024 | Phase I trial completion

BT-001 (IT) | Anti-CTLA4 + GM-CSF

- ✓ Positive Phase I part A data (single agent)
 - ➔ H2 2023 | Start Ph. I part B (combination w. pembrolizumab)

Transgene – 2028 Snapshot – Significant Value Created

Two Approved Products Targeting Sizeable Market Opportunities with Clear Clinical Benefits

• **TG4001**

Conditional approval for first indication targeting a ~\$1 bn market opportunity

Limited competition

Ongoing trials in additional indications

• **TG4050**

Conditional approval for first indication:

Head and Neck cancer (adjuvant)

~\$1+ bn market opportunity

No other cancer vaccines targeting this indication

Potential registrational trial to start in H2 2023

• **TG6050**

Delivered high value clinical data in initial indication when given IV

NSCLC 2L: ~\$1.5+ bn market opportunity

Broader clinical development plan to be implemented



Generated several additional new cancer vaccines and IV OV candidates based on right vector, right payload, right indication approach

Further strengthened our viral vector and payload engineering technology platforms

Source: Company estimates



Cancer Therapeutic Vaccines

Potent immunotherapies
to induce specific antitumor immune responses
and improve patient outcome



Therapeutic Cancer Vaccines - Educate the Immune System to Destroy Cancer Cells

MVA-based vaccines activate T cells through several mechanisms

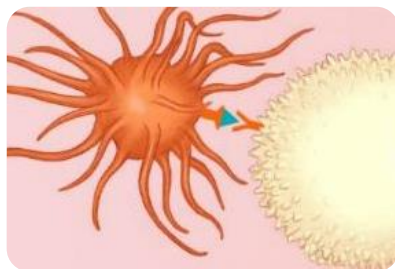
SIGNAL ACTIVATION

Infected cells will **express vaccine antigens** that will be uptaken by APCs



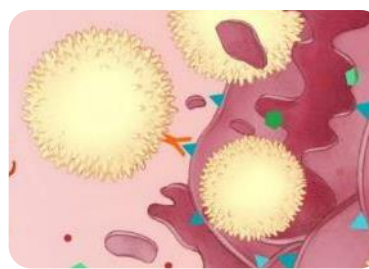
IMMUNE AMPLIFICATION

APCs **boost specific antitumoral T cells**



CANCER CELL KILLING

T cells **attack** tumor cells



Strongly differentiated from mRNAs and peptide approaches

Induction of broad immune responses to induce antitumor activity

- Priming of innate immunity
- Development of an active adaptive response – Increase of effector subgroups of CD4 and CD8 T-cells

Tumor-specific antigens and neoantigens can be used to target a broad range of solid tumors

Compelling clinical evidence obtained

- Good safety profile
- Strong immune responses to antigen/neoantigen payloads
- Signs of clinical benefit for patients
 - As single agent in maintenance setting
 - In combination with ICI in advanced setting

myvac® - TG4050 | Individualized Neoantigen Cancer Vaccine

Taking the Treatment of Each Patient's Tumor to a New Level

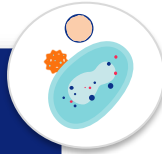
MVA viral vector: a powerful platform for vaccine development

Strongly immunogenic vector

- Demonstrated capability to express **complex antigen structures** and have them presented by APCs
- Ability to elicit **strong, durable and specific** immune response
- Established safety profile

Optimal neoantigen display

- **VacDesignR™** for **optimal design of the recombinant cassettes**
- Selection of **best promoter sequences**



one patient • one genome
• one vaccine



Artificial Intelligence to identify up to 30 potent neoantigens

- NEC's machine learning environment based on multiple parameters **to classify most immunogenic neoantigens** from whole tumor genome analysis*
 - **Takes in account multiple parameters**
- **NEC covers 50% of the development cost of TG4050**

NEC



First clinical data has already shown remarkable induction of immune responses against chosen neoantigens and **signs of patient benefit**



[Click here](#)

● TG4050 is already Showing the Potential To Manage Patients with High-Risk of Recurrence or Molecular Relapse



one patient • one genome
• one vaccine

Goal

to extend remission
period in high-risk patients
after initial cancer surgery

**TMB: tumor mutational burden*

To **induce specific T cell response**
in patients in clinical remission but with high risk of relapse

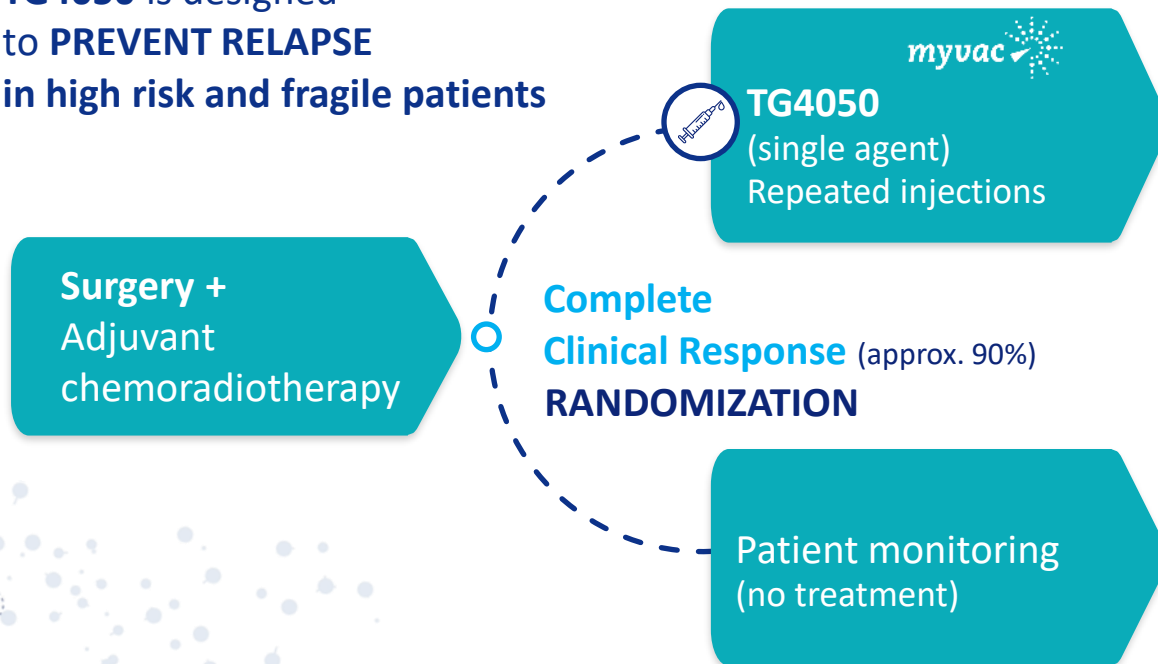
Two ongoing clinical trials – **Head & Neck and Ovarian cancers**
TG4050 given **as single agent**

- **Positive initial data** (safety, immunogenicity, first signs of efficacy)
- Intend to **launch potential registrational Phase II trial in H2 2023**
- **Mid-term objective:** Establish TG4050 as the SOC in maintenance setting for patients with H&N cancers, a \$1+ bn market

Potential to address numerous solid tumors after surgery
in **adjuvant/maintenance settings W or w/o ICIs**, such as H&N, ovarian, urothelial, breast, lung cancers, ie a multi billion market

TG4050 | HPV-Negative Head and Neck Cancer - Trial after Surgery and Adjuvant Therapy

TG4050 is designed to **PREVENT RELAPSE** in high risk and fragile patients



Recurrence

12-month PFS is approx. 60% (w/o TG4050)*

Clinical situation where checkpoint blockers have failed (ie. KN412)

Randomized Phase I Trial

30 Patients (NCT: 04183166)

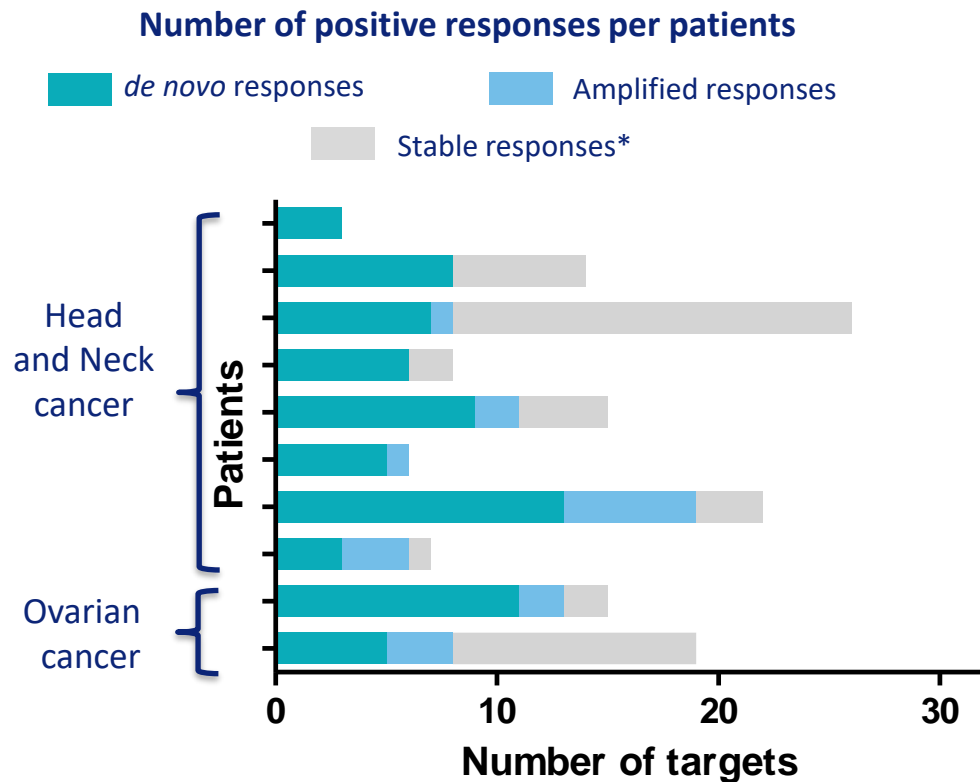
Last patient treatment expected in **H1 2023**



LEAD INVESTIGATOR: Pr. Christian Ottensmeier,
Clatterbridge Cancer Care Center, Liverpool

TG4050 – Generates an Unprecedented Rate of T Cell Response Against Tumor Specific Epitopes

Induction of multiple T cell responses in all treated patients



Median of 9 positive responses per patient, out of 30

Responses were either **amplification of pre-existing responses** (20%) or **de novo responses** (80%) induced during vaccination

Profound remodeling of immune cells consistent with anti tumor response

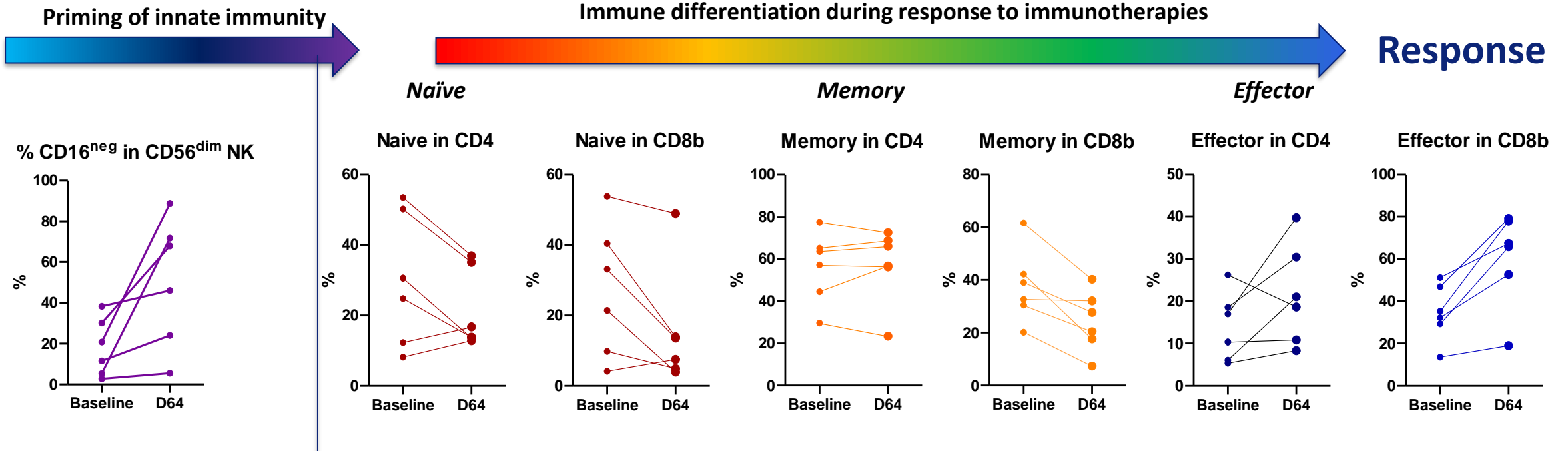
*Immunoreactive T-cells present at baseline but not amplified by vaccine.



Source: Lalanne et al, "Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OvC) and head and neck squamous cell carcinoma (HNSCC)" [AACR 2023](#), April 18, 2023, Poster presentation

Profound Remodelling of Immune Cells consistent with Anti Tumor Response

Suggesting that the Vaccine Effectively Primes the Immune System



AACR ANNUAL MEETING
American Association for Cancer Research
2022 New Orleans

Source: Block et al, "Phase I trials of personalized cancer vaccine TG4050 in surgically treated high-risk head and neck squamous cell carcinoma (HNSCC) and relapsing ovarian cancer (OvC) patients" [AACR 2022](#), April 12, 2022, Poster presentation

- ✓ **Priming of innate immunity:** Loss of CD16 on CD56^{dim} NK cells suggests **ongoing antitumor activity**
- ✓ **Maturation and differentiation of CD4 and CD8 into effector cells** – Consistent with the **development of an active adaptive response**
- **Effector subgroups of CD4 and CD8 T-cells are increased**
- Consistent with **decrease in naive and memory CD4 and CD8 T-cell** over treatment

Extremely Promising First Signals of Clinical Activity

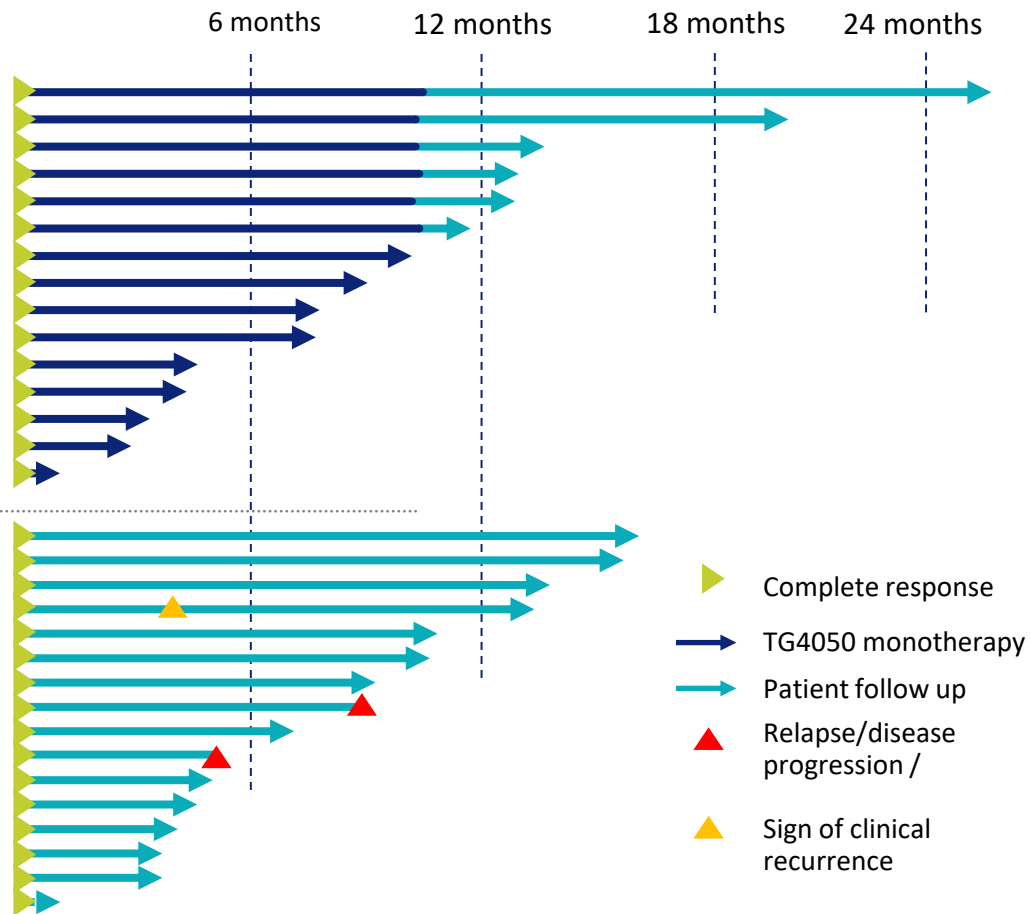
Repeated injections of single agent TG4050 in patients with minimal residual disease

Head & Neck Cancer Trial

32 patients randomized – March 2023

Arm A:
TG4050
single agent

Arm B:
Control arm



No related SAEs
Good safety profile

All 16 treated patients are stable

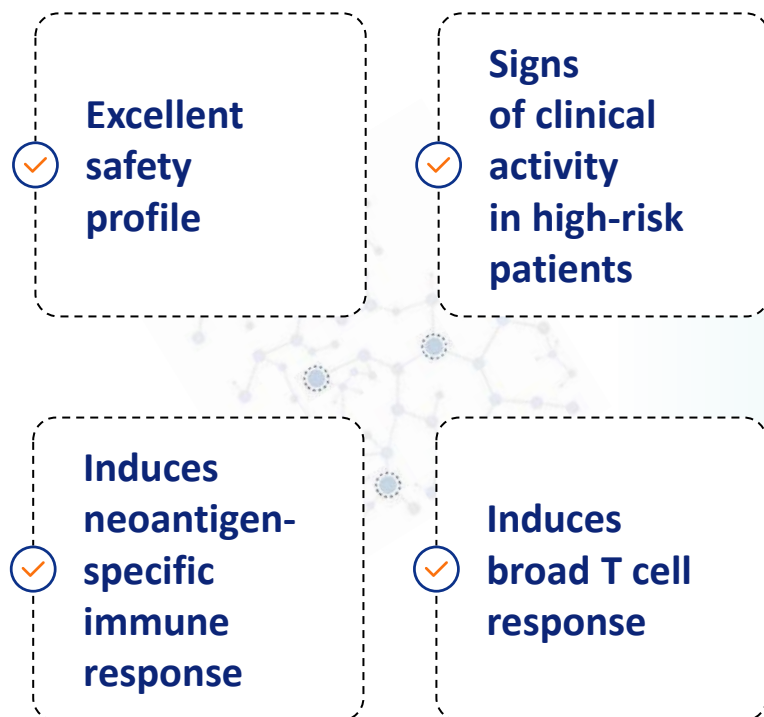
**Only patients
in the control arm
have relapsed**

Trial fully enrolled



Source: Lalanee et al, "Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OvC) and head and neck squamous cell carcinoma (HNSCC)" [AACR 2023](#), April 18, 2023, Poster presentation

TG4050 | Exciting First Data Justifies our Ambitious Development Plan



Updated data to be presented at **ASCO 2023**



Intend to launch potential registrational **Phase II trial** in H2 2023



Potential to extend remission period for high-risk patients and address a \$1+ bn market*
(head and neck cancer – adjuvant)



Potential to address other solid tumors after surgery in **adjuvant/maintenance settings w or w/o ICIs,** such as ovarian, urothelial, breast, lung cancers, ie a multi billion market

● TG4001 | Designed to Boost the Patient's Immune System against HPV-Positive Tumors



INDUCES SPECIFIC AND DURABLE T CELL RESPONSES



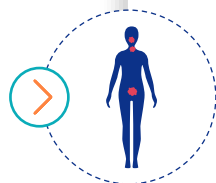
MVA virus - E6 and E7 HPV antigens + IL2
Designed to **induce specific E6 and E7 T cell response**

Unsatisfactory treatment options for advanced HPV+ cancer patients

In 2L, ORR is around 10–15% , median PFS is around 2 months and median OS is less than 11 months with ICI single agent*

○ Goal to double performance of SOC

A \$1 bn market opportunity (EU, UK, US, Japan)



MoA and first signals of efficacy demonstrated in clinic in combination with ICI

- ✓ Clinically relevant anti-tumor activity - Induces strong and long lasting, specific responses against tumors
- ✓ Excellent safety profile - Good combination candidate
- ✓ In hard-to-treat HPV cancer patients, has induced
 - Increase of CD3, CD8 infiltrates
 - Increase of PD-L1 expression
 - Shifts cold tumours into hot tumors, in combination with ICIs

ORR: objective response rate (RECIST 1.1); m PFS: median progression-free survival; m OS: median overall survival; SOC: standard of care

*Estimates based on the following trials: • Anal 2L: NCI9673 (Nivolumab, Phase II) ^[ref]; KN028 + KN158 ^[ref] (pooled analysis: Phase Ib KN028 and Phase II KN158); CARACAS (Phase II) ^[ref] • Cervical 2L: KN158 (Phase II) ^[ref] • Cervical, vaginal vulvar 2L: CM 358 (Phase II) ^[ref]

TG4001 + Avelumab (Single Arm Ph. Ib/II) | Increased Benefit and Long-Lasting Responses

Landmark Data Compare Favorably to ICIs in Monotherapy and Competitive Landscape

Increased ORR and durable responses n=25

- ORR: 32%
- mPFS: 5.6 months
- mOS: 13.3 months
- Good safety profile

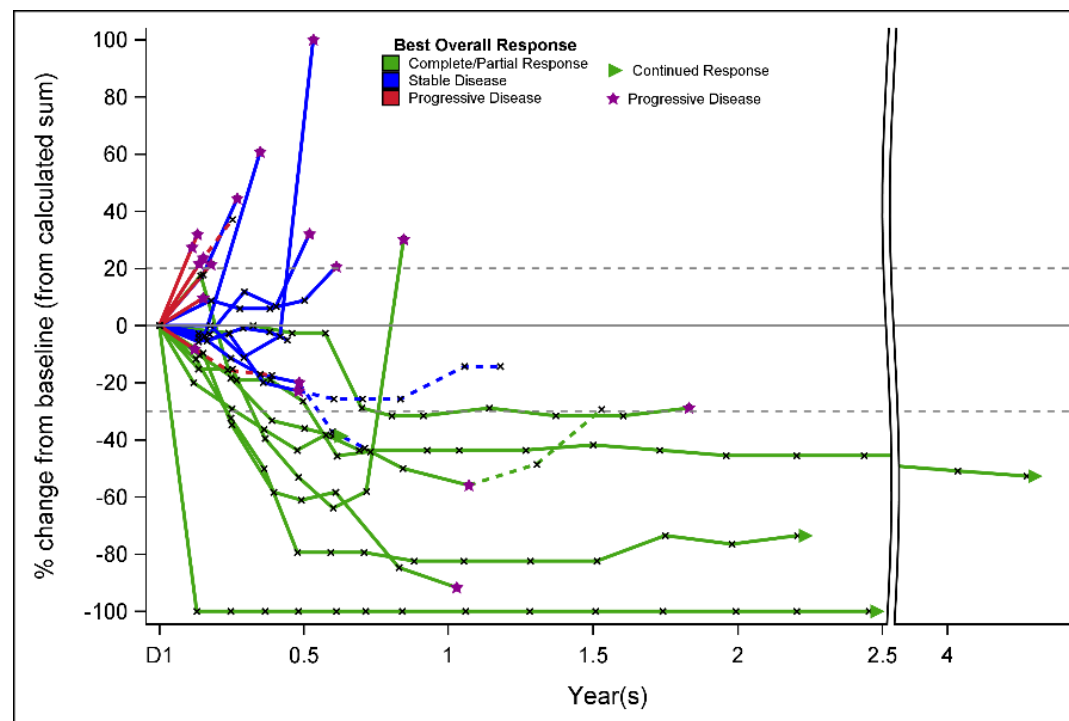
1 COMPLETE RESPONSE

Patient with anal cancer and peritoneal extension that all disappeared – still followed in the trial

7 PARTIAL RESPONSES

9 STABLE DISEASES

Long lasting responses in metastatic patients without liver metastases - Aug. 2022

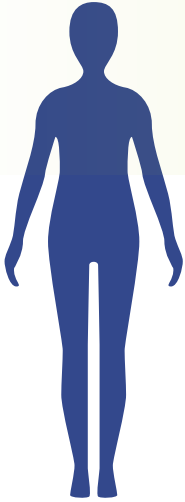


Compares favorably to ICIs in monotherapy and competitive landscape

Clinical collaboration
for avelumab free supply



TG4001 | Current Randomized Controlled Phase II Trial to Deliver Final Data in 2024



Patients with HPV16-positive anogenital cancer *incl. cervical, vulvar, vaginal, penile and anal cancers*

- With recurrent/metastatic disease
- Treated in 1st line or in 2nd line (with a maximum of 1 prior systemic chemotherapy vs 2 allowed in Phase Ib/II trial)
- Without previous exposure to cancer immunotherapy
- Without liver metastasis at baseline
- Including all levels of PD-L1 expression

Patients with
recurrent/metastatic disease

Randomized
(1:1)

Arm A

TG4001 + avelumab

Arm B

Avelumab single agent

POSITIVE INTERIM ANALYSIS RESULTS

(November 2022)

- ✓ First efficacy signals observed
- ✓ Good safety profile
- ✓ Trial to enroll up to 120 Patients (NCT: 03260023)

PRIMARY ENDPOINT

- ✓ Progression-Free Survival
(RECIST 1.1)



Clinical collaboration
with

for avelumab free supply



Our Goal with TG4001: Boost Response to Immune Checkpoint Inhibitors in HPV+ Cancers

TG4001 is the only HPV vaccine developed in comparison with ICI monotherapy that has shown a benefit from MOA*

- ✓ Good safety profile
- ✓ Increased Response Rate and PFS in hard-to-treat patients
- ✓ Induces antigen-specific immune response
- ✓ Induces broad T cell response
- ✓ Long-lasting responses
- ✓ Active in PD-L1 positive and negative patients

First Randomized Phase II trial of HPV vaccine + ICI expected to read out

Immunological data to be presented at ASCO (June 2023)

Randomized Phase II data expected in 2024

Upcoming registration targeting trial in preparation, aiming for a \$1bn market opportunity

TG4001 is owned 100% by Transgene



Oncolytic Viruses

! Rapidly Generating Multiple Virus-Powered
! Off-the-Shelf Drug Candidates Targeting Solid Tumors

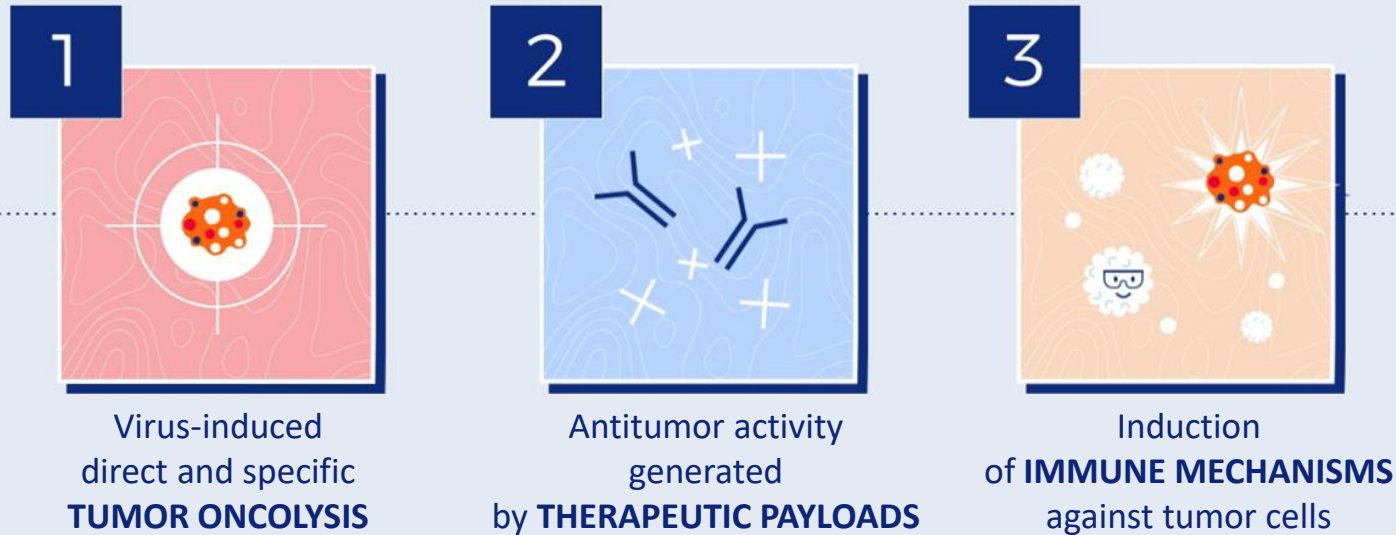
invirio



Our Oncolytic Viruses (OV) – Combined Effects of Vector, Payload and Immune Stimulation

Competitive Advantage Enhanced by our Patented Backbone VV_{cop}TK-RR⁻ - basis of our Invir.IO® Platform

Cancer cell death through multiple MOAs



Proprietary vector with multiple competitive advantages

- Encode numerous and various **payloads**
- **Multiple routes of administration** (IV, IT, locoregional) and extend OV market beyond IT administration
- Potential to target multiorgan lesions and warm up TME
- Address broad range of solid tumors



invirio

Clinical evidence obtained

- Good safety profile
- Able to reach tumors, selectively replicate and express payload, incl. via **intravenous administration**

Compelling Data Generated with TG6002 Support Intravenous (IV) Route of Administration



Goal

to target multiorgan lesions and reverse tumor resistance



To turn cold tumors into hot tumors through multi-pronged MoA

TG6002 demonstrated PoC of IV Route

- TG6002 replicates in tumor tissue without sign of widespread replication
- The payload is expressed in tumor tissue
- Long-lasting expression of the payload
- No impact of neutralizing antibodies on PK/PD data
- T cell activation, immune checkpoint receptor expression and priming of an adaptive response against tumor associated antigens*

Potential to address numerous solid tumors via multiple routes of administration, in particular intravenous administration
– strong differentiation versus other OV players

BT-001 | Patented OV Armed with Anti-CTLA4 Ab + GM-CSF

Ongoing Phase I Trial Assessing IT* Route of Administration

50/50 collaboration
with **BioInvent**

The right virus + payload

VV_{cop} TK-RR⁻ oncolytic armed with
BioInvent's potent **anti-CTLA4 Ab + GM-CSF**

- Activates and increases T-effector cells
- Treg depleting activity
- Stimulates immune cells (incl. APC)

Winner of the **2022 JITC Best Oncolytic**
and Local Immunotherapy Paper **Award**

Can be developed for
multiple cancer indications
lesions with high Treg infiltration



Positive Phase I part A readout

- Single agent **well tolerated**
- **Replicates** and **persists in tumor tissue**
- **Anti-CTLA4 expressed in the tumor**
with **no detectable systemic exposure**
- **Stable injected lesion** in **11/18 patients**
- **Tumor shrinkage** observed in two
patients

Ongoing Phase I (NCT04725331)
monotherapy and combination w. anti-PD1

➤ **Ph. I part B** (combination with
pembrolizumab) **to start in H2 2023**

Objectives: evaluate safety profile,
determine Phase II dose and indications

Collaboration with MSD
which provides pembrolizumab (KEYTRUDA®)



*IT: intratumoral administration

TG6050 administered IV | IL-12 and anti-CTLA4 Produced Directly in the Tumor

Approved Phase I Trial to Assess Systemic Route of Administration

Oncolytic armed with IL-12 and anti-CTLA4 Ab

- Triggers a powerful antitumor immune response
- Restores the immune defenses within the tumor

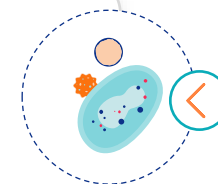
The Invir.IO® objective

- Avoid toxicity / off target thanks to selective replication of viral vector
- Ensure sufficient production of IL-12 in the tumor
- **Outstanding preclinical data (strong antitumor activity)**

Phase I trial - Indication: metastatic and PD1 failed tumors

- Advanced or metastatic NSCLC after failure with available treatment options, including anti-PD1/PD-L1 – **IV administration**
- Inclusions ongoing (NCT: 05788926)

Potential to address a \$1.5 bn opportunity



Initial goal

demonstrate potential of IV administration in “cold”, non-resectable metastatic tumors



* IV: intravenous administration **IHA: intrahepatic artery administration



Source: Marchand et al, TG6050, “An oncolytic vaccinia virus armed with interleukin 12 and anti-CTLA4 antibody induces TME remodeling and strong anti-tumoral responses” [AACR 2023](#), April 16, 2023, Poster presentation

● Invir.IO® Pipeline Will Allow us to Generate Significant Value



Backbone with highly competitive properties and potential

- Ability to safely be **administered IV**
- **Express selectively its payload in the tumor**



Rapid progress from design to start of clinic development

- Potential to generate **multiple novel oncolytics**

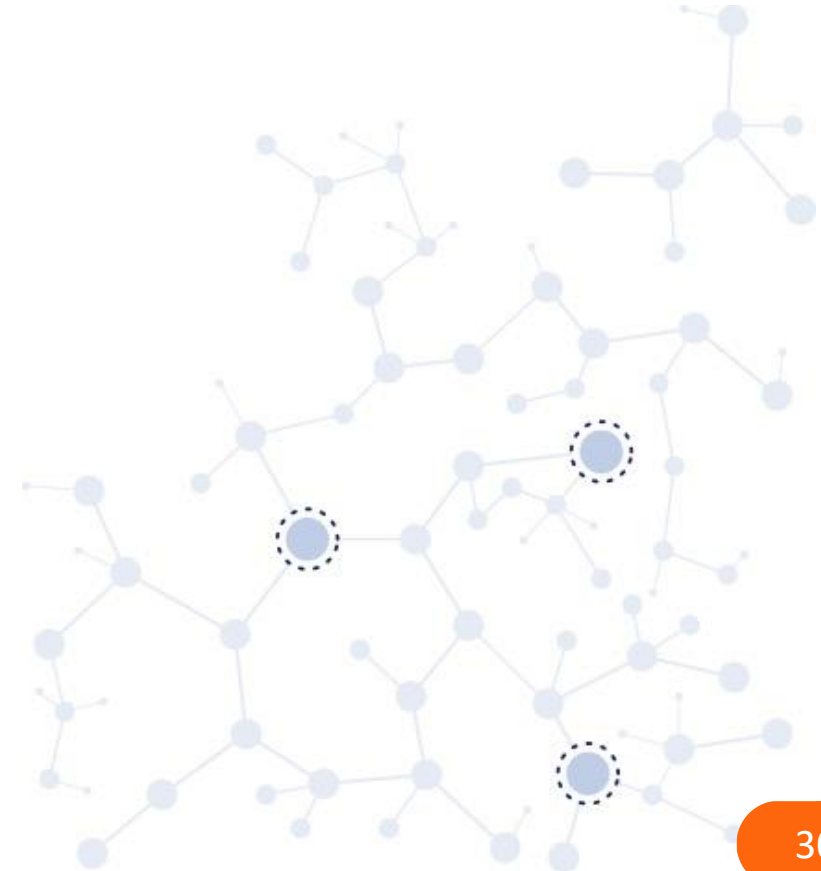
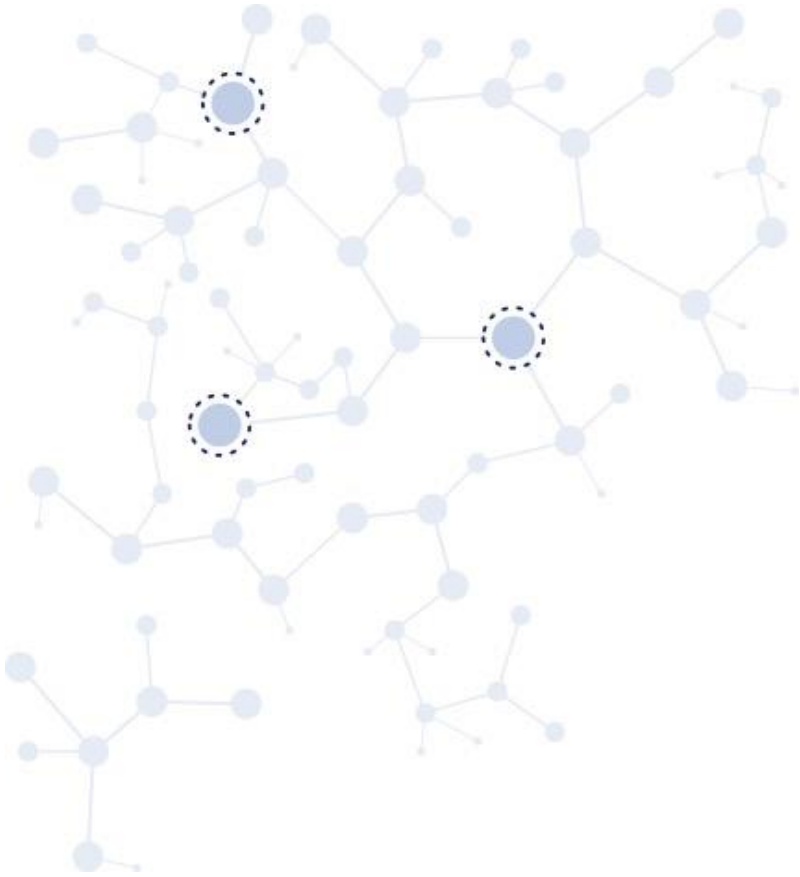


Value provider and collaboration initiator

- **BioInvent collaboration:** clinical development of BT-001
- **PersonGen collaboration:** preclinical evaluation of CAR-T cell/OV combination
- **Potential other early out-licensing** of new unique OVs or new combinations



Outlook



Company Funded to Deliver Multiple Value Generating Milestones

✓ **FINANCIAL VISIBILITY** until **early 2024**

- **€17.0 million in cash and cash equivalents** as of March 31, 2023
- In addition: **Tasly BioPharmaceuticals shares** valued at **€14.3 million** at the end of Dec. 2022 – Sale of this stake expected to be completed in mid-2023

Ownership

As of March 30, 2022



- Listed on Euronext Paris
- ISIN: FR0005175080 - Ticker: TNG

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Transgene – Frontline Player in Virus-Based Immunotherapy Against Cancer

Versatile Technology Platforms to Fit Each Patient Need

Diversified **pipeline**
(individualized and off the shelf)

2 platforms
Therapeutic vaccines
Oncolytic viruses

Multiple clinical-stage immunotherapies
in Phase I and Phase II

Dense news flow
in **2023-2024**

Unique Technology based on:

✓ Optimized viral vectors

✓ Strong clinical data

✓ Solid safety Track record

✓ Preclinical Proof of concept

✓ Robust IP portfolio

Integrated **GMP manufacturing**

Capacity for rapid delivery of pilot scale batches

Ongoing **collaborations**

MERCK **Pfizer**
MSD
Supply agreements

Orchestrating a brighter world
NEC
Technology and cost sharing agreement

Biolnvent
Co-development

Strong **Shareholder Support**
and Financial visibility

Financial visibility until early 2024
Strong shareholder support

Appendices

An Experienced Management Team



HEDI BEN BRAHIM
Chief Executive Officer

20 YEARS EXPERIENCE



ÉRIC QUÉMÉNEUR, PHD
Executive VP
Chief Scientific Officer

30+ YEARS EXPERIENCE



ALESSANDRO RIVA
Chairman
Joined in May 2022

30+ YEARS EXPERIENCE



...ichnos...



MAUD BRANDELY, MD, PHD
VP Medical Affairs
Chief Medical Officer

35+ YEARS EXPERIENCE



STEVEN BLOOM
VP, Chief Business Officer



35+ YEARS EXPERIENCE



JEAN-PHILIPPE DEL
VP, Chief Financial Officer

20 YEARS EXPERIENCE



Board of Directors - as of May 5, 2023

Hedi Ben Brahim
CEO & Director



Alain Mérieux
Honorary Chairman



Marie Landel
Independent Director



Philippe Archinard
Director



Carol Stuckley
Independent Director



Alessandro Riva
Chairman



Jean-Luc Bélingard
Director



Maya Said
Independent Director



Jean-Yves Blay
Independent Director

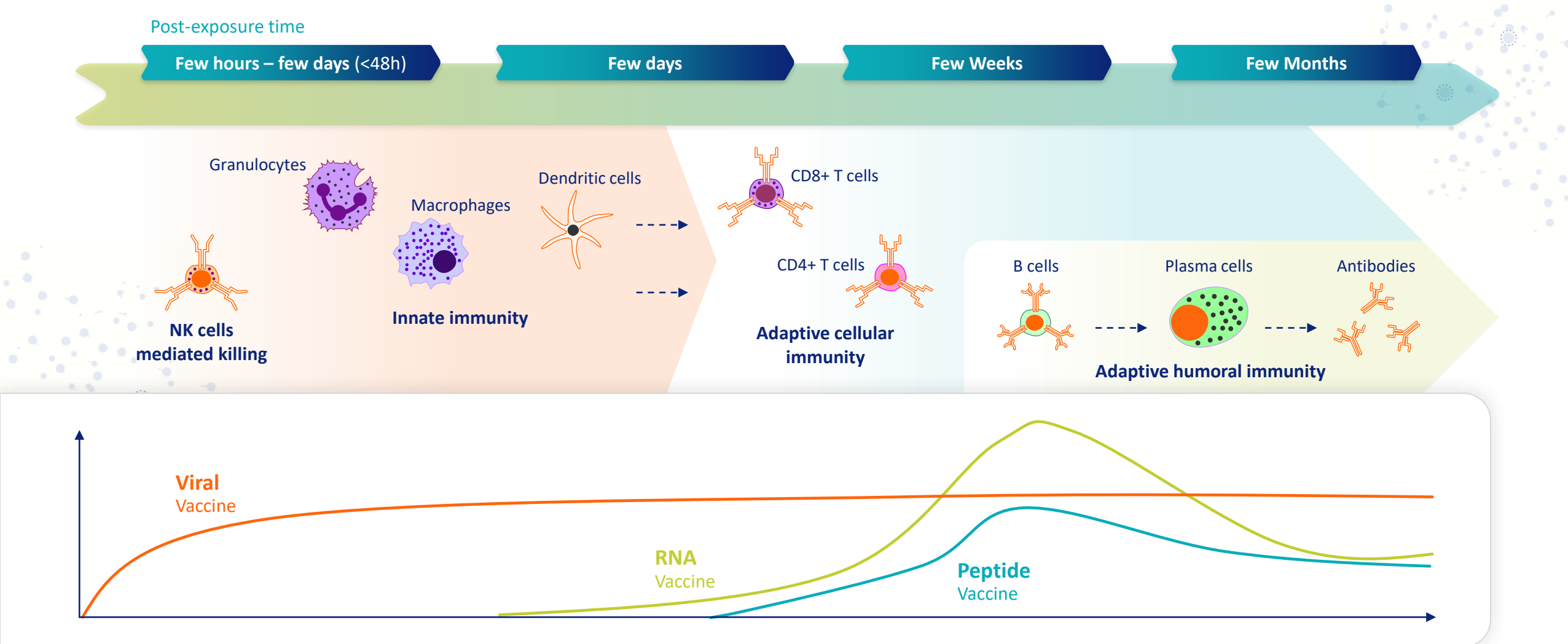


Benoît Habert
Independent Director



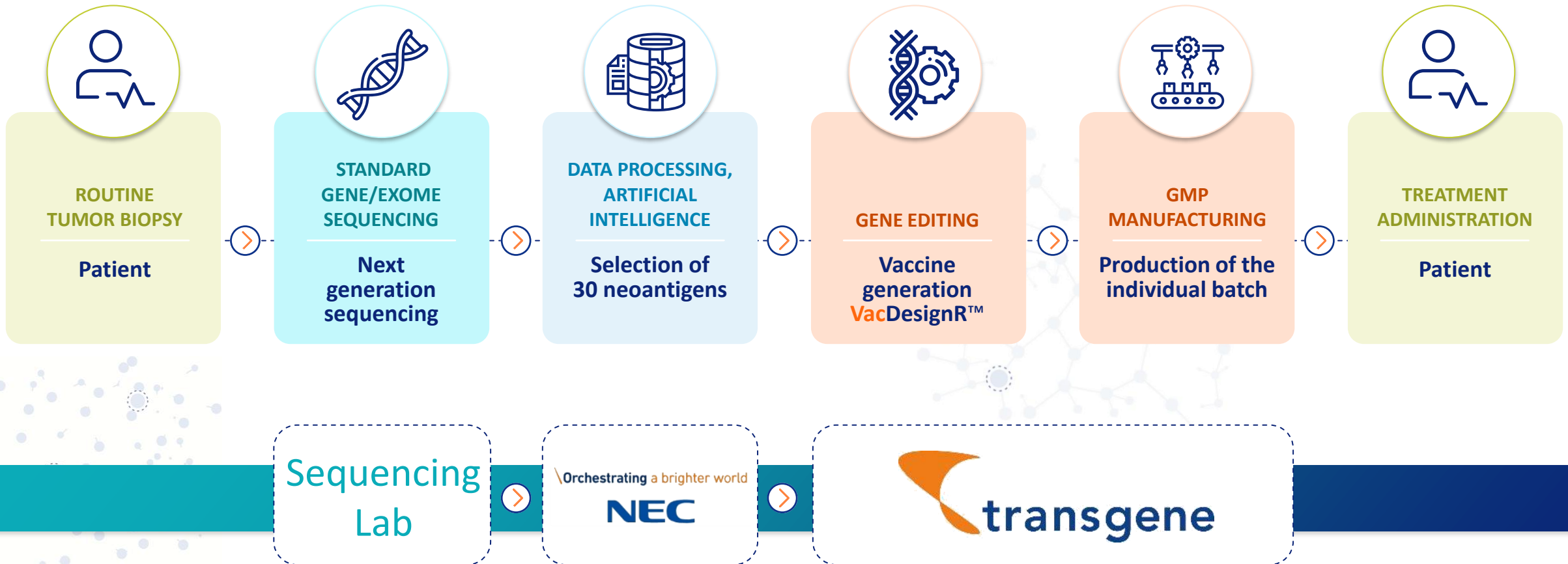
Sandrine Flory
Director*

● Viral Vaccines Prime Both Long Lasting Innate and Adaptive Immunity



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