Unlocking the Full Potential of the Immune System Against Cancer

Corporate Presentation

August 1st, 2024

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.

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Innovative Clinical-Stage Immunotherapy Portfolio Based on Viral Vectors

Cutting-edge **individualized neoantigen cancer vaccine** (TG4050)

- **Proof of principle obtained in randomized Phase I study** (H&N adjuvant)
- **Ongoing Phase II part of Phase I/II study**

Additional **immuno-oncology programs** with **clinical proof of principle**

- **Shared antigens vaccines (HPV16)**
- **Oncolytic viruses**

Significant value creation catalysts expected in **2024**

TG4050 – A Novel Individualized Cancer Immunotherapy

MVA VECTOR BENEFITS

- Induces **broad and specific immune response** – Almost all patients treated develop a polyepitopic response*
  - *Strongly differentiated from mRNAs and peptides*
- Excellent safety profile
- Proven immunogenicity in challenging immune contexture

THE RIGHT NEOANTIGENS

- Comprises **up to 30 neoantigens** selected using NEC's artificial intelligence and machine learning

Orchestrating a brighter world
NEC

INDICATION

- Targeting head and neck patients – **designed to prevent relapse**
- Only neoantigen cancer vaccine targeting this indication in adjuvant situation
- Potential to address other indications in perioperative setting

myvac

Building upon proof of principle:

Randomized Phase II part started in Q2 2024

based on promising Phase I data

*Source: A. Lalanne et al., "Personalized vaccine TG4050 induces polyepitopic immune responses against private neoantigens in resected HPV negative head and neck cancers." AACR 2024, April 10, Poster presentation

Our Pipeline – Poised to Deliver Important Data in 2024

Product	Indication	Collaboration	Discovery	Phase I	Phase II	Key upcoming catalysts
INDIVIDUALIZED NEOANTIGEN CANCER VACCINES						
TG4050 myvac	**Head and neck cancer (adjuvant)**	Orchestrating a brighter world NEC	●	●	●	**24-month median follow up on Phase I part (H2 2024)** **Completion of enrolment (Q4 2025)**
	Other indication		●	●		Additional Ph. I trial to start (2025)
SHARED ANTIGENS CANCER VACCINES						
TG4001	Anogenital HPV+ cancers		●	●	●	**Randomized Phase II trial results (H2 2024)**
Internal myvac	Shared driver mutations		●			
ONCOLYTIC VIRUSES (OVs)						
TG6050 invirio	Lung cancer (IV*)		●	●		First data (H2 2024)
BT-001 invirio	Solid tumors (IT*)	BioInvent	●	●		First data in combination with pembrolizumab to be presented at ESMO (Sept. 2024)
Internal	Synthetic OV (IV*)		●			

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** IV: intravenous administration, IT: Intratumoral administration*

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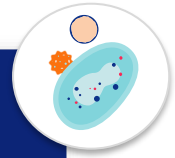
Cancer Therapeutic Vaccines

Focused on delivering the promise
of individualized cancer vaccine

myvac® - TG4050 | Combines Unique Know How and Expertise

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**

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myvac

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 clinical development costs of TG4050 in head and neck cancer**

NEC

Technology well suited to demonstrate benefit in minimal residual/molecular disease

Click here

AACR American Association for Cancer Research

*Source: Mallone et al., "Performance of neoantigen prediction for the design of TG4050, a patient-specific neoantigen cancer vaccine", AACR, June 2020, Poster presentation

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

Need to prevent or delay relapse

Clinical situation where checkpoint blockers have failed (ie. KN412, Javelin 100, NRG-HN004, Imvoke010)

Approx. 30% patients relapse within 24 months after surgery + adjuvant therapy*

Promising data obtained in randomized Phase I part

Compelling initial immunological and clinical data presented at AACR 2024
(32 patients)

- ➔ **All treated patients remaining disease-free**
- ➔ **Strong basis for Phase II extension**

Ongoing Phase I/II trial

Approx. 80 patients
with locoregionally advanced HPV-negative SCCHN** (NCT: 04183166)

Surgery +
Adjuvant chemoradiotherapy

Complete Clinical Response
RANDOMIZATION (1:1)

myvac
TG4050
(single agent)
Repeated injections

Patient monitoring
(no treatment)

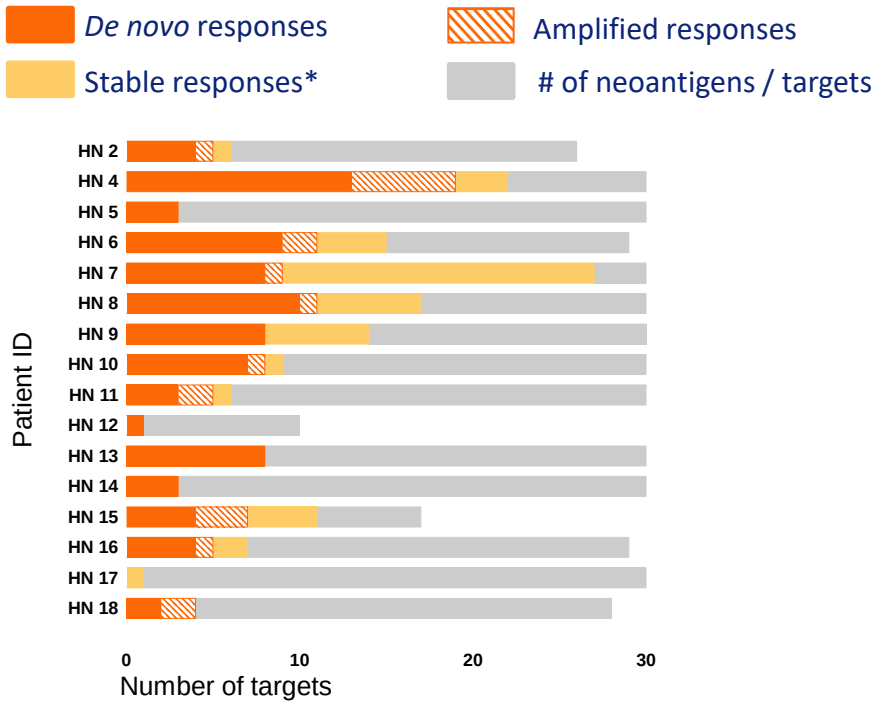
LEAD INVESTIGATOR: Pr. Christian Ottensmeier,
Clatterbridge Cancer Care Center, Liverpool

NHS The Clatterbridge Cancer Centre NHS Foundation Trust
institutCurie
INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE Oncopole
MAYO CLINIC

*Sources: Keynote 412, Javelin 100, NRG-HN004, Imvoke010 trials, company estimates
** Squamous cell carcinoma of the head and neck

TG4050 | Generates and/or Expands Tumor Specific T Cells

Number of positive responses per patients
Head and neck cancer trial



Despite low mutational burden, **immunogenic targets could be selected for all patients**

CD4+ or CD8+ responses were detected in all but one vaccinated patients

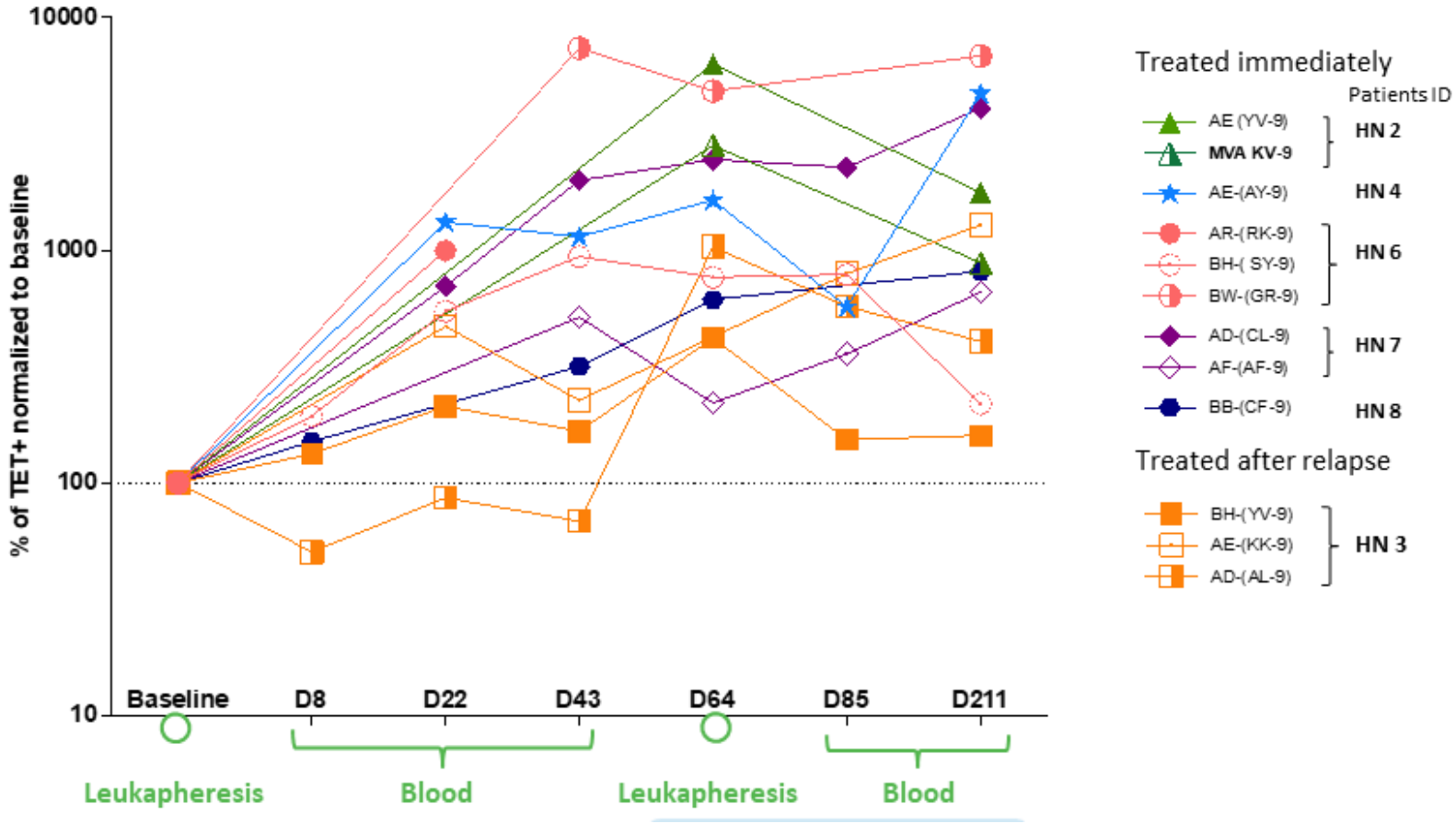
80% of immunoreactivities detected after vaccination were not detectable at baseline.

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

*Source: A. Lalanne et al., "Personalized vaccine TG4050 induces polyepitopic immune responses against private neoantigens in resected HPV negative head and neck cancers." AACR 2024, April 10, Poster presentation

TG4050 | Persistent Specific Cellular Response Following Vaccination

Patients display **persistent specific CD8+ responses** against multiple selected targets,
7 months after treatment induction

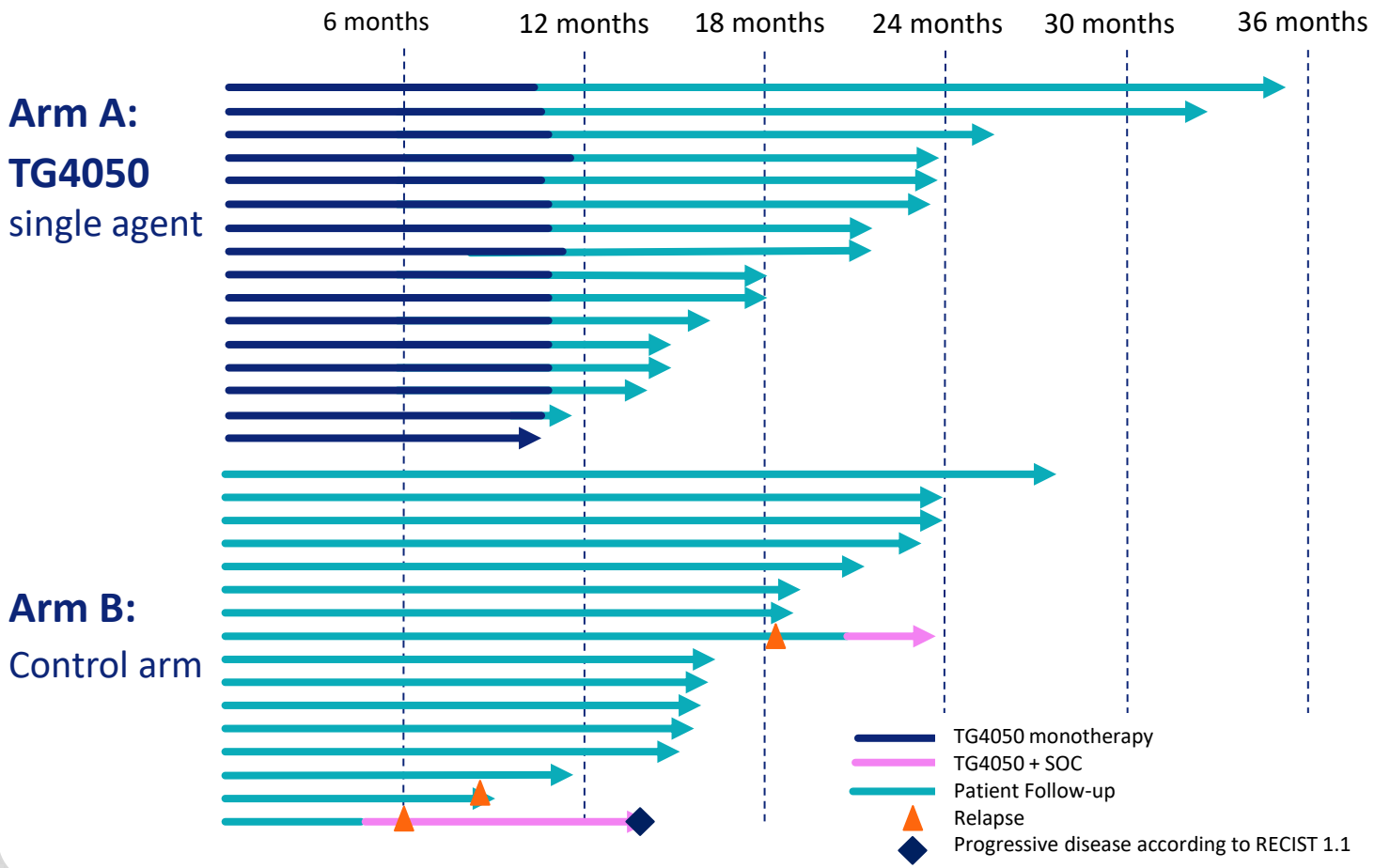


Source: A. Lalanne *et* al., "Personalized vaccine TG4050 induces polyepitopic immune responses against private neoantigens in resected HPV negative head and neck cancers." AACR 2024, April 10, Poster presentation

Promising Signals of Clinical Activity in Adjuvant Setting

Head & Neck Cancer Trial

32 patients randomized – March 2024



No related SAEs
Good safety profile
Median follow up of 18.6 months

All 16 treated patients were disease-free

Only patients in the control arm relapsed

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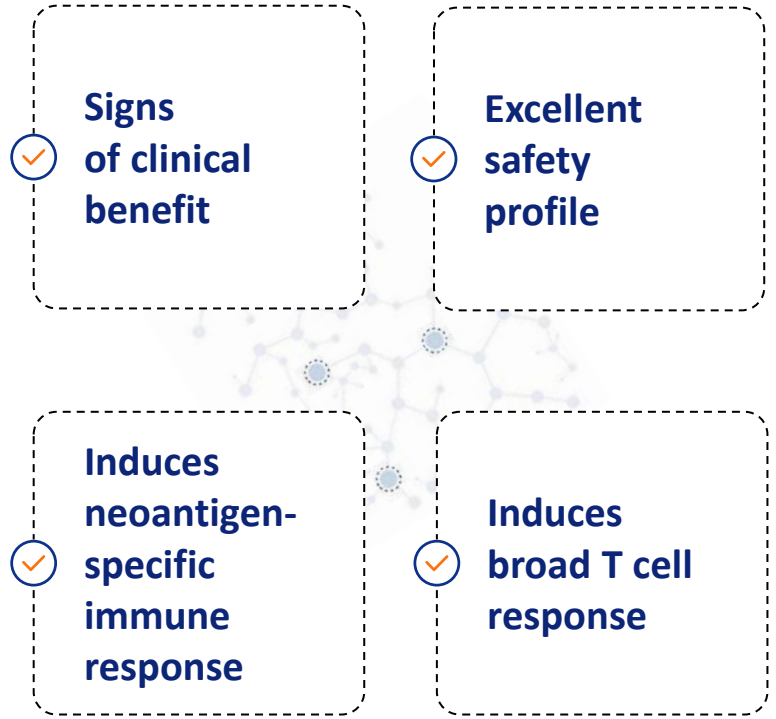
*Source: Lalanne et al., "Personalized vaccine TG4050 induces polyepitopic immune responses against private neoantigens in resected HPV-negative Head and Neck cancers", AACR, April 2024, Poster presentation

TG4050 | Additional Data in 2024

myvac
one patient • one genome • one vaccine

- **24-month median follow up expected in H2 2024 on Phase I part** (32 patients)
- **Ongoing Phase II part – Last patient to be enrolled in H2 2025**

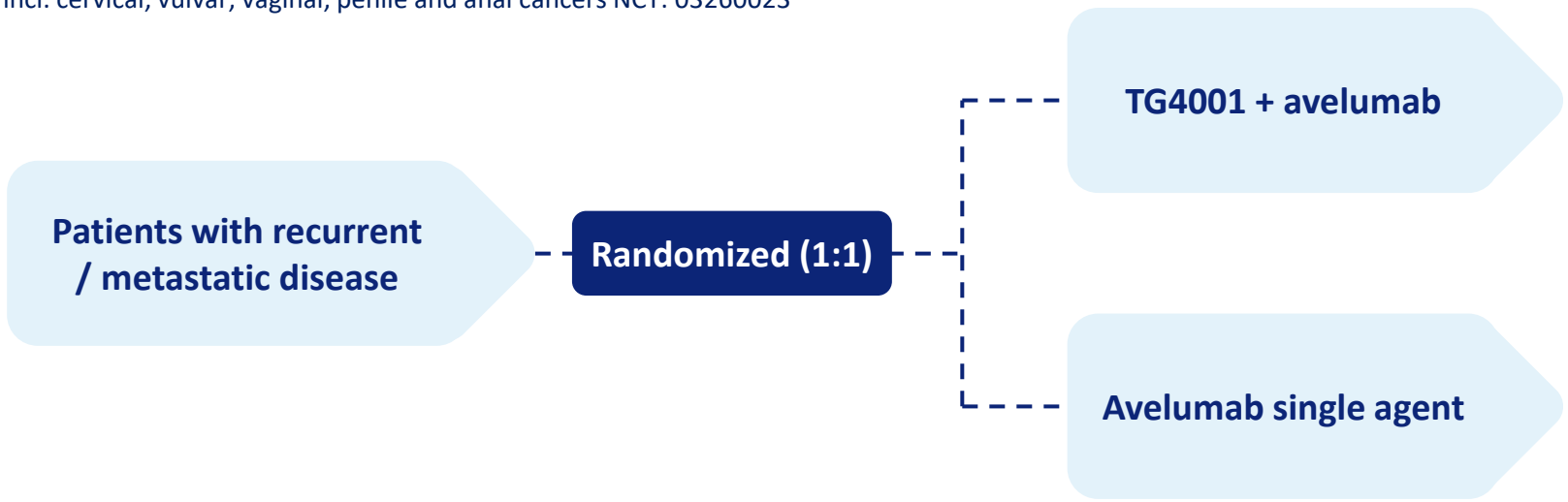
- **Potential to extend remission period and address a significant market** (head and neck cancer – adjuvant)
- **Could address other solid tumors in perioperative settings w or w/o ICIs** – Additional trial to start in 2025



TG4001 | Ongoing Proof of Concept Trial to Read out in H2 2024

Ongoing Phase II trial in patients with HPV16+ anogenital cancer

incl. cervical, vulvar, vaginal, penile and anal cancers NCT: 03260023



Treated in 1st line or in 2nd line (with a maximum of 1 prior systemic chemotherapy)

Without liver metastasis at baseline

Without previous exposure to cancer immunotherapy

Including all levels of PD-L1 expression

Clinical collaboration with

MERCK

for avelumab free supply

Topline data expected in H2 2024

- To deliver PoC data in significant patient population
- To further validate MVA platform

Clear path to approval in recently changed landscape

- Phase III in 1st line HPV+ cervix cancer in combin. with SoC (CT + ICI)
- Pivotal 2nd line after ICI

Objective

Sign partnership or licensing agreement based on Ph. II data

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Oncolytic Viruses

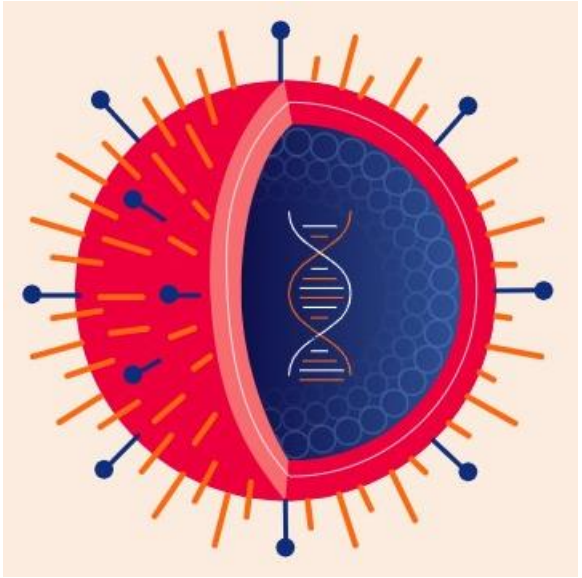
Rapidly Generating Multiple Virus-Powered
Off-the-Shelf Drug Candidates Targeting Solid Tumors

invir io

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

Compelling Clinical Data Support Intravenous (IV) Route of Administration

Cancer cell death through multiple MOAs



Virus-induced direct and specific **TUMOR ONCOLYSIS**

Antitumor activity generated by **THERAPEUTIC PAYLOADS**

Induction of **IMMUNE MECHANISMS** against tumor cells

Patented Backbone $VV_{cop}TK^{-}RR^{-}$ 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

invir io

Proof of principle obtained

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

Goal: to target multiorgan lesions and reverse tumor resistance

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

Ongoing Phase I Trial to Assess Systemic Route of Administration

Initial goal

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

Oncolytic armed with IL-12 and anti-CTLA4 Ab

- Triggers a powerful antitumor immune response
- Restores the immune defenses within the tumor
- **Outstanding preclinical data (strong antitumor activity)** presented at AACR 2023

Phase I trial - Indication: metastatic and PD1 failed tumors

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

- Initial data (single agent) in **H2 2024** – Could be combined with ICIs

Potential to address a major oncology market

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

BT-001 | 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)

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

Can be developed for multiple cancer indications

lesions with high Treg infiltration

Ongoing Phase I (NCT04725331)

monotherapy and combination w. anti-PD1

- **Ph. I part B** (combination with pembrolizumab) – Enrolment ongoing
- **First data to be presented in Sept. 2024 (ESMO 2024)**

Collaboration with MSD
which provides pembrolizumab (KEYTRUDA®)

MSD

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*IT: intratumoral administration

Outlook

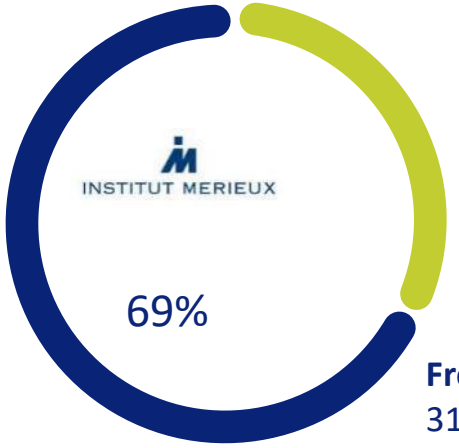
Company Funded to Deliver Multiple Value Generating Milestones

FINANCIAL VISIBILITY secured until **Q4 2025**

Enables Transgene to deliver significant milestones including key PoC data for TG4050 and data on all assets

Ownership

As of August 1st, 2024



Free float
31%

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

2024 Anticipated Value Creating News

TG4050 | Neoantigen vaccine

myvac

Proof of principle

already obtained in Head and Neck cancer (adjuvant)

➔ Strong immunogenicity, persistent cellular immune response and clinical benefit for patients

Ongoing randomized Phase I/II (head and neck cancer) – 80 patients overall

➔ Phase I part: 24-month median follow up of patients (**H2 2024**)

➔ Phase II part: inclusion of the last patient (**Q4 2025**)

Other indication

➔ Prepare new Phase I

Shared antigens cancer vaccines

TG4001: Results from ongoing randomized Phase II (**H2 2024**)

Oncolytic viruses

invir io

TG6050: Initial Phase I data (**H2 2024**)

BT-001: Initial data in combination with pembrolizumab to be presented at ESMO 2024 (**Sept. 2024**)

Investment Highlights

Unique and highly potent viral vector based immunotherapies

Lead program TG4050 to deliver data in 2024 and create significant value by 2026

Additional programs and R&I activity to deliver news flow and fuel Transgene's portfolio in the mid term

Appendices

New Leadership to Take Transgene to the Next Level

ALESSANDRO RIVA, MD
Chairman & CEO

30+ years experience

NOVARTIS ONCOLOGY GILEAD ...ichnos...

ÉRIC QUÉMÉNEUR, PharmD, PhD - Executive VP - Chief Scientific Officer

MAUD BRANDELY, MD, PhD - VP, Medical Affairs - Chief Medical Officer

LUCIE LARGUIER
VP, Chief Financial Officer

JAMES WENTWORTH
VP, Chief Business Officer

JOHN FELITTI
VP, Legal Counsel

CHRISTOPHE ANCEL, PharmD
VP, Pharmaceutical Operations

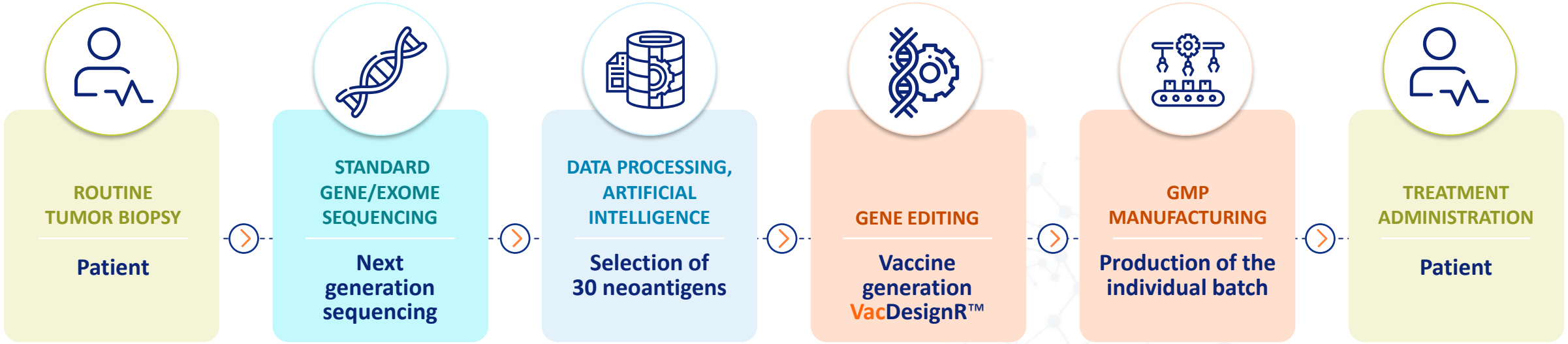
CHRISTELLE SCHWOERER
VP, Human Resources

JOHN C. BELL
Member of the Scientific Advisory Board

PEDRO ROMERO
Member of the Scientific Advisory Board

TG4050, an Individualized Neoantigen Vaccine Combining Unique Capabilities

Combines Bioengineering and Digital Transformation



Sequencing Lab

Orchestrating a brighter world NEC

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Exploration of Tumor TME

TME: tumor micro-environment, TMB: tumor mutational burden, F: fibrotic, NF: non-fibrotic

Challenging population with high prevalence of **low/negative PD-L1 expressors** and **relatively poor pro-immune infiltrates**

Arm A: TG4050 single agent

PD-L1	TMB (mt/Mb)	TME functional class	Tumor cell proliferation
Medium	3.19	Immune Desert	Medium
Not detected	1.99	Immune Desert	Low
Medium	4.34	Imm. Enriched, NF	Medium
Medium	3.28	Immune Desert	Medium
Not detected	4.2	Immune Desert	Medium
Medium	3.42	Immune Desert	Medium
Medium	3.16	Fibrotic	Medium
Medium	1.9	Imm. Enriched, NF	Low
Medium	1.99	Imm. Enriched, F	Low
Medium	1.37	Imm. Enriched, NF	Medium
Medium	4	Imm. Enriched, NF	Low
Not detected	3.05	Immune Desert	Medium
Medium	2.41	Immune Desert	High
Medium	7.7	Imm. Enriched, F	Medium
Medium	1.46	Immune Desert	Low
Medium	1.68	Imm. Enriched, NF	Medium

Arm B: Control arm

PD-L1	TMB (mt/Mb)	TME functional class	Tumor cell proliferation
Not detected	4,26	Immune Desert	Medium
Not detected	3,02	Immune Desert	Medium
Low	3,02	Immune Desert	Medium
Not detected	1,6	Immune Desert	Medium
Medium	3,64	Immune Desert	Medium
High	3,28	Imm. Enriched, NF	High
Low	3,36	Immune Desert	Medium
Medium	2,91	Imm. Enriched, NF	Low
Medium	5,24	Immune Desert	Medium
<Thresh	2,77	Immune Desert	Medium
Medium	7,95	Fibrotic	Medium
Medium	0,34	Immune Desert	Low
<Thresh	1,9	Immune Desert	Medium
<Thresh	0,03	Imm. Enriched, NF	Medium
Low	2,1	Immune Desert	Medium
Not detected	3,56	Immune Desert	Medium

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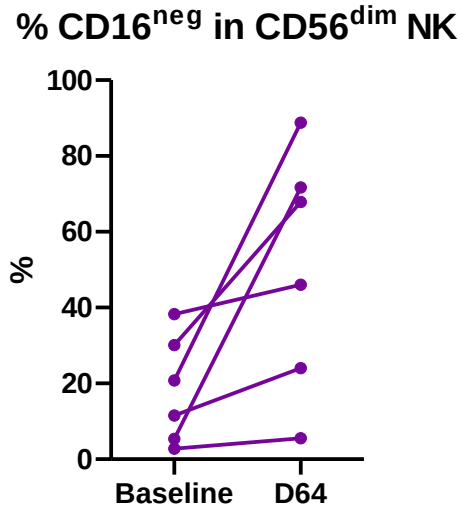
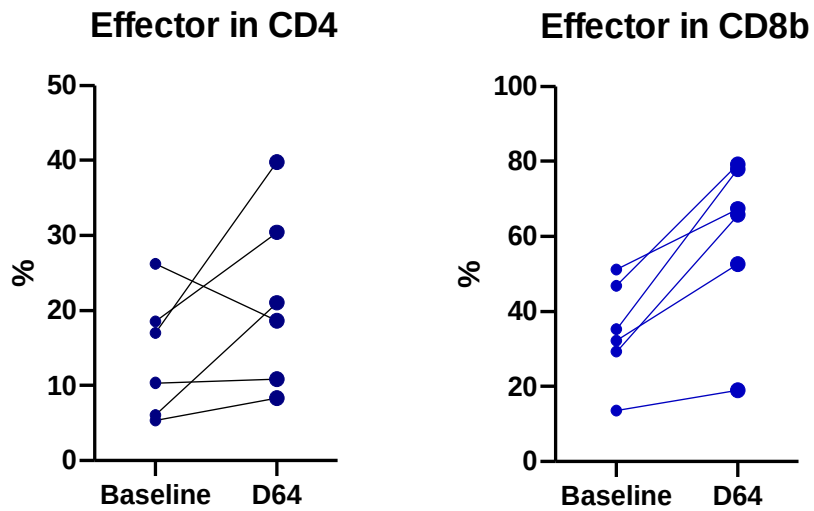
*Source: Lalanne *et al.*, "Personalized vaccine TG4050 induces polyepitopic immune responses against private neoantigens in resected HPV-negative Head and Neck cancers", AACR, April 2024, Poster presentation

Profound Remodelling of Immune Cells Consistent with Anti Tumor Response

Suggests that the Vaccine Effectively Primes the Immune System





- **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**

AACR American Association for Cancer Research ANNUAL MEETING 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

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