Unlocking the Full Potential of the Immune System Against Cancer

Investor Presentation

April 10, 2025

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Transgene in a Snapshot

Unique and highly potent viral vector-based immunotherapies

Lead program TG4050 to deliver data and create significant value in early setting solid tumors between 2025 and 2028

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

myvac® – A Novel Individualized Cancer Immunotherapy Platform

MVA VECTOR BENEFITS

- Induces **broad and specific immune response** – Almost all patients treated develop a polyepitopic response*
- 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

- Building upon **proof of principle** of TG4050, leading *myvac®*-based cancer vaccine: Randomized **Phase II part currently enrolling patients** based on **promising Phase I data**
- **Potential further acceleration** based on innovation in the adjuvant setting of operable Head & Neck cancer and other indications

*Source: G. Le Tourneau *et al.*, "Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)", SITC November 2024, Poster presentation – *Analysis based on research assay*.

Innovative Clinical-Stage Immunotherapy Portfolio Based on Viral Vectors

Product	Indication	Collaboration	Discovery	Phase I	Phase II	
LEAD ASSET: INDIVIDUALIZED NEOANTIGEN CANCER VACCINES (*myvac*® platform)						
TG4050 myvac	**Individualized neoantigen therapy**	**Head and neck cancer (adjuvant)**	●	Ⓡ	Ⓡ	**Clinical Proof of Principle** Orchestrating a brighter world NEC **24-month follow-up** (Q2 2025) **Completion of randomization** of **Ph. II part** (Q4 2025)
		Other indication	●	●		Additional Ph. I trial to start (Q4 2025)
Other viral vector-based assets						
TG4001	Shared antigens cancer vaccine	Cervical and anogenital HPV+ cancers	●	●	Ⓡ	Clinical data presented (Q2 2025)
BT-001 invirio	Oncolytic virus	Solid tumors (IT*)	●	●		Updated data expected (H2 2025) BioInvent
TG6050 invirio	Oncolytic virus	Lung cancer (IV*)	●	●		Initial data expected (Q2 2025)
Research & innovation	Internal programs		●			

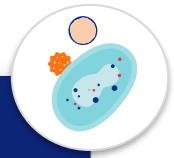
** IV: intravenous administration, IT: intratumoral administration, R: randomized*

Neoantigen Therapeutic Cancer Vaccine

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

Rapid, integrated and scalable manufacturing process – Ongoing progress

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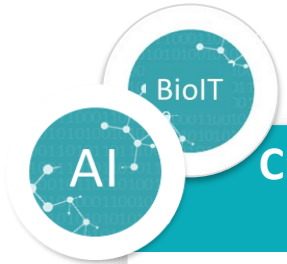
myvac

one patient • one genome • one vaccine



Clinically-validated Artificial Intelligence & Bioinformatics powered approach

Neoantigen identification

- Based on multiple parameters **to identify neoantigens** from whole tumor exome analysis*
- NEC's AI and machine learning environment

NEC

Optimal neoantigen display

- **VacDesignR**® for **optimal design of the recombinant virus**
- Improve vaccine production
- Property of Transgene

AI powered and cutting-edge software environment

- Dedicated tools for TG4050 end-to-end production

Technology well suited for early setting solid tumors to prevent relapse after/with standard treatment

Click here

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

AACR American Association for Cancer Research

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

Need to prevent or delay relapse

With currently approved treatments,
approx. 25% 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 SITC 2024 (32 patients)

➔ **All treated patients remain disease-free**

- ✓ **Primary objectives:** safety and tolerability
- ✓ **Secondary objectives:** feasibility, disease-free survival (DFS)
- ✓ **Exploratory objectives:** immunogenicity, exploratory tumor biomarkers (TMB, PD-L1)

Ongoing Phase II part

➔ **Completion of patient randomization expected in Q4 2025**
➔ **Primary objective: 24-month DFS**

Phase I/II trial design

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

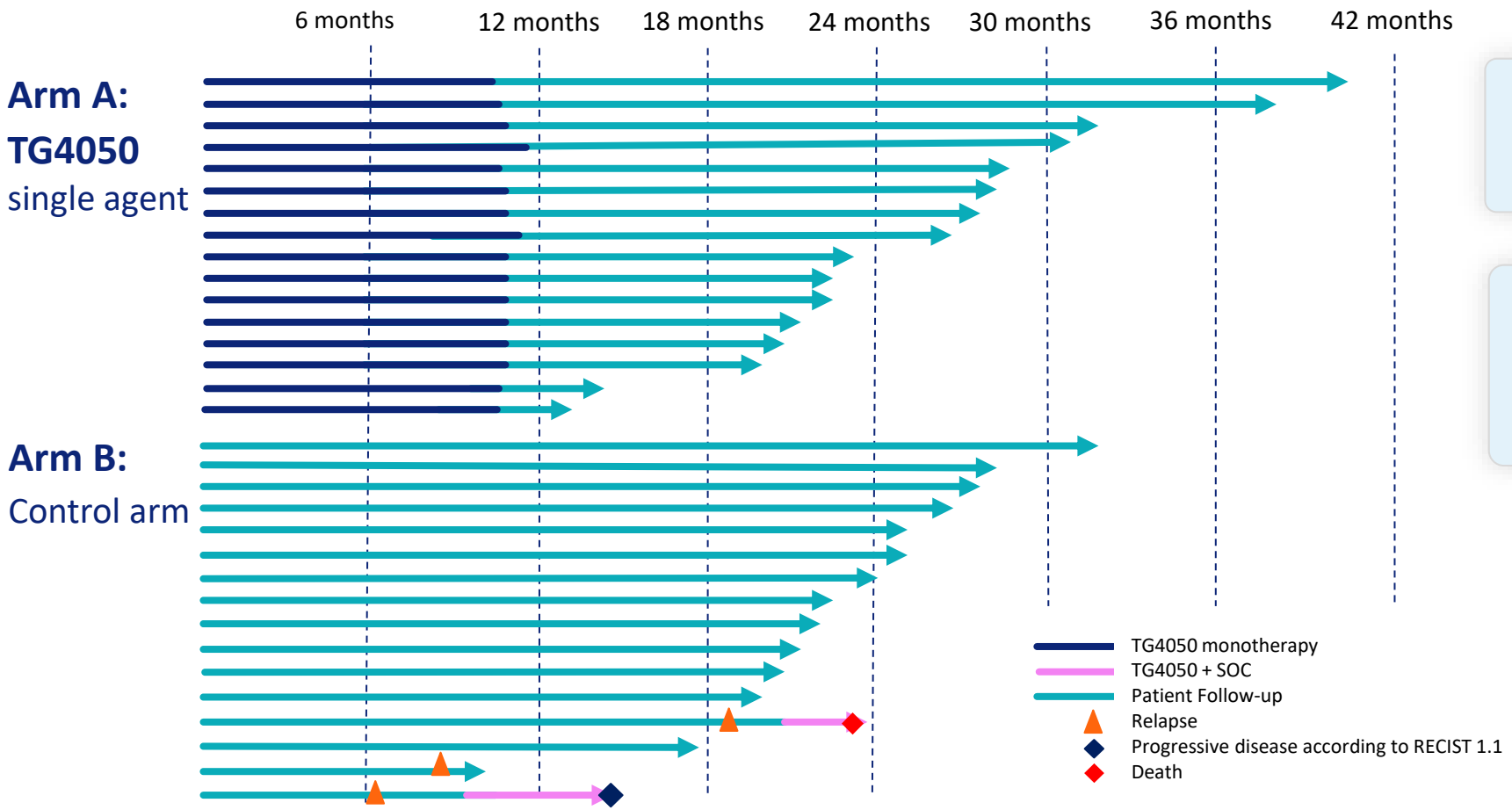
NHS The Clatterbridge Cancer Centre NHS Foundation Trust
institutCurie
INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE Oncopole
MAYO CLINIC

* Sources: Cooper JS *et al.* NEJM, 2004; DY Lee *et al.* Head Neck, 2020
** Squamous cell carcinoma of the head and neck

TG4050 | Promising Signals of Clinical Activity in Adjuvant Setting

Head & Neck Cancer Trial

32 patients randomized – September 2024



- ➔ **No related SAEs**
- ➔ **Good safety profile**
- ➔ **Median follow-up of 24.1 months**

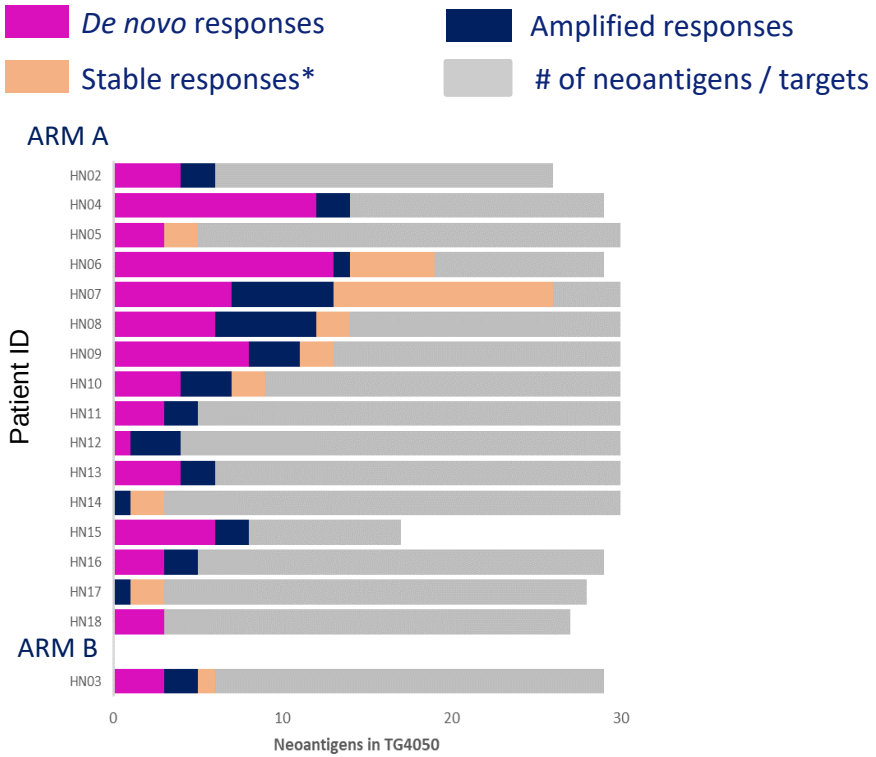
All 16 treated patients remained disease-free

Only patients in the control arm relapsed

Source: G. Le Tourneau *et al.*, "**Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)**", SITC November 2024, Poster presentation

TG4050 | Generates and/or Expands Tumor Specific T Cells

Number of positive responses per patient (Elispot assay)
Head and Neck Cancer (Phase I part)



*Immunoreactive T-cells detected at baseline but not amplified post treatment

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

Neoantigen-specific T-cell responses were detected

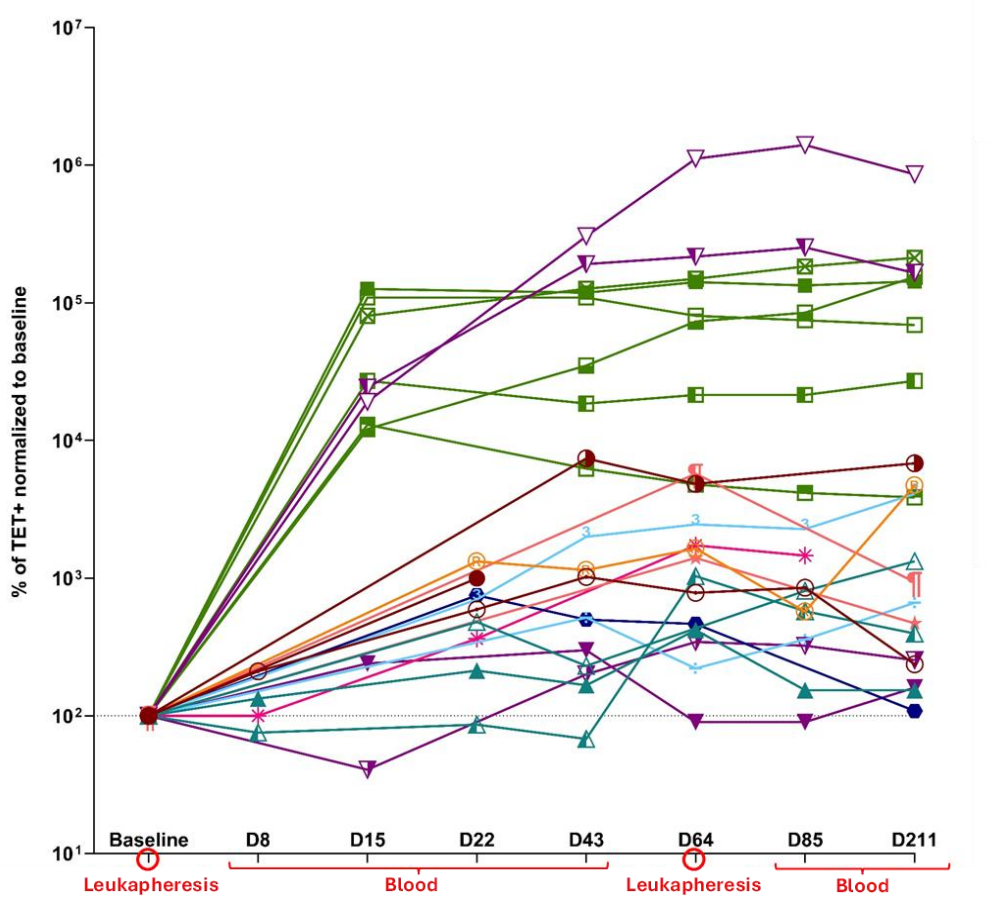
***De novo* responses were detected in a majority of patients**

Source: G. Le Tourneau *et al.*, "**Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)**", SITC November 2024, Poster presentation

NB: analysis based on research assay; independent GCLP-like analysis to be conducted

TG4050 | Persistent Specific Cellular Response Following Vaccination

Patients displayed **sustained neoantigen-specific CD8+ responses** against multiple selected targets over 7 months



Induction period

1 dose/week during 43 days

Boost period

1 dose/3 weeks during 1 year

Source: G. Le Tourneau *et al.*, "**Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)**", SITC November 2024, Poster presentation

TG4050 | Potential to Extend Remission Period and Address Significant Medical Need

Head & Neck program

- **Phase I part – 24-month follow up**
  to be presented in **Q2 2025**
- **Ongoing Phase II part – Last patient**
  to be randomized in **Q4 2025**
- **Potential acceleration** in evolving treatment landscape

myvac

one patient • one genome • one vaccine

- **Signs of clinical benefit**
- **Excellent safety profile**
- **Induces neoantigen-specific immune response**
- **Induces broad T cell response**

Expansion in other early-setting cancer indications with high risk of relapse

- **Could address other solid tumors in perioperative settings w or w/o ICIs** – Significant market opportunity
- Additional Ph. I trial to start in Q4 2025 in **new indication**

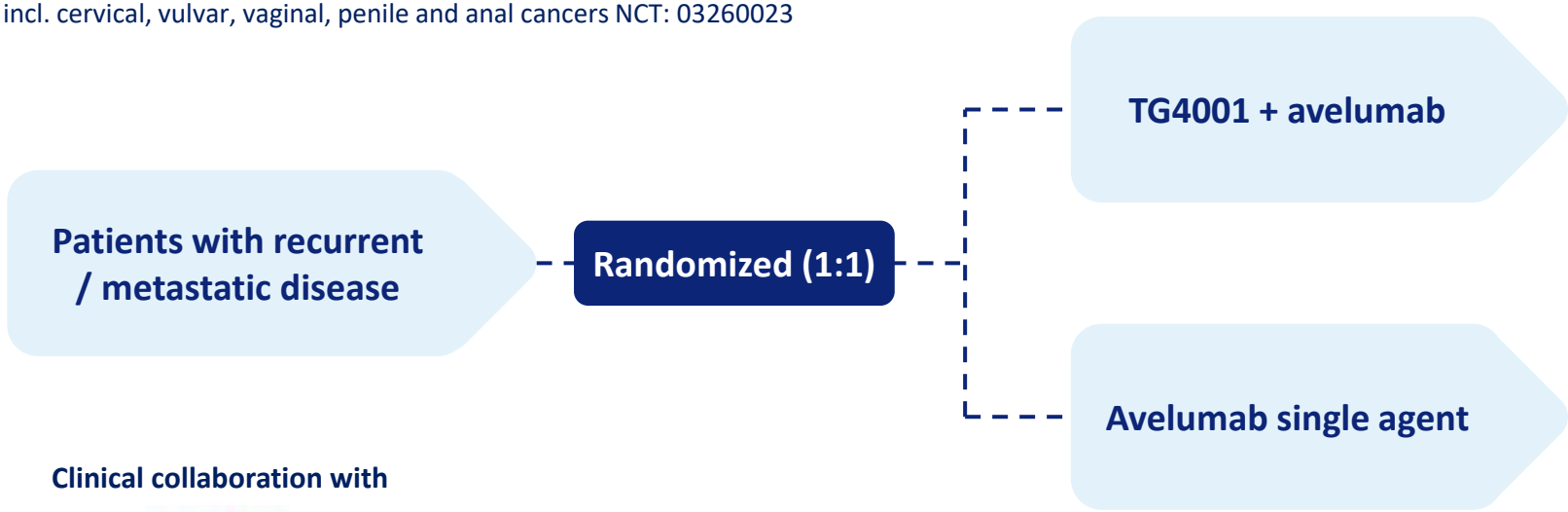
Other viral vector-based assets

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

TG4001 | Phase II Trial in Patients with HPV16+ Cervical and Anogenital cancer

Randomized Phase II trial in patients with HPV16+ cervical and anogenital cancer (n=90)

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



Clinical collaboration with

MERCK

for avelumab free supply

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

Checkpoint-blocker naïve, without liver metastasis at baseline

Including all levels of PD-L1 expression

Possible path to approval in evolving cervical cancer landscape - awaiting full data analysis

Top line data

- **Primary objective** (improvement in progression-free survival) not met in the overall patient population
- **Positive efficacy trend in cervical cancer patients** observed in pre-planned subgroup analysis

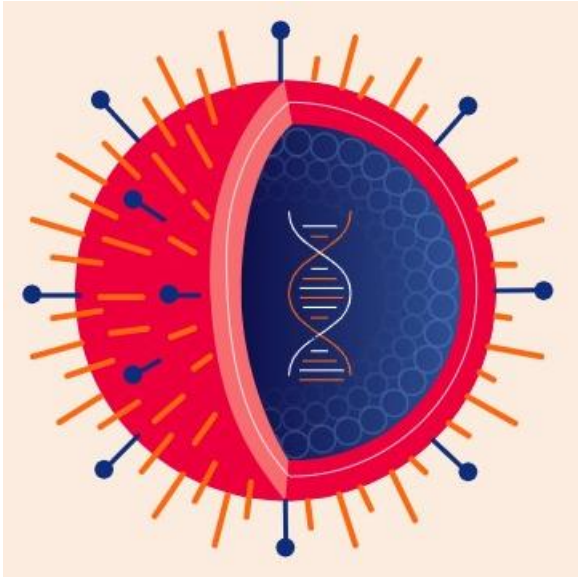
→ **Full analysis ongoing** prior to decision on the best way forward

→ **Transgene plans to communicate clinical data at a scientific conference in Q2 2025**

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

BT-001 | Promising Antitumor Activity of OV Armed with Anti-CTLA4 Ab + GM-CSF

Completed Phase I/IIa Trial Assessing IT Route of Administration

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)

Completed Phase I (NCT04725331)

monotherapy and combination w. anti-PD1

- **Ph. I part B** (pembrolizumab combination) – Enrolment completed
- **Additional data expected in H2 2025**

Promising antitumor activity*

monotherapy and combination w. anti-PD1

- **Converts the TME from "cold" to "hot"**
- **Replicates and persists in tumor tissue**
- **Anti-CTLA4 expressed in the tumor** with **no detectable systemic exposure**
- **Partial responses in 2/6 patients** (combination regimen) & **stable disease in 4/18 patients** (monotherapy)
- **Tumor shrinkage** in injected and non-injected lesions

Can be developed for multiple cancer indications

50/50 collaboration with **BioInvent**

MSD

Collaboration with MSD which provides pembrolizumab (KEYTRUDA®)

BARCELONA 2024 ESMO congress

*Champiat et al, "Initial clinical results of BT-001, an oncolytic virus expressing an anti-CTLA4 mAb, administered as single agent and in combination with pembrolizumab in patients with advanced solid tumors" ESMO 2024, September 14, 2024, Poster presentation

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IT: intratumoral administration
TME: Tumor microenvironment

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)** remodeling TME (AACR 2023 and JITC, July 2024)

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 completed (NCT: 05788926)

- Initial data (single agent) in **Q2 2025** – Could be combined with ICIs

Potential to address a major oncology market

Journal for ImmunoTherapy of Cancer

*Azar et al, TG6050, “TG6050, an oncolytic vaccinia virus encoding interleukin-12 and anti-CTLA-4 antibody, favors tumor regression via profound immune remodeling of the tumor microenvironment” JITC, July 2024.

Outlook

Company Funded to Deliver Multiple Value Generating Milestones

Business funded
until the **end of April 2026**

Enables Transgene to deliver significant milestones with *myvac®* platform and other viral vector-based immunotherapies

myvac | Neoantigen vaccine – TG4050

Proof of principle

already obtained in Head and Neck cancer (adjuvant)

➔ Clinical benefit for patients and strong immunogenicity, persistent cellular immune response

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

➔ Phase I part: 24-month follow up data to be presented in **Q2 2025**

➔ Phase II part: randomization of the last patient in **Q4 2025**

Other indication

➔ Plan to launch **new Phase I** in additional indication in **Q4 2025**

Other viral vector-based assets

TG4001: Full analysis ongoing prior to deciding on the best way forward
Transgene plans to communicate detailed results at a scientific conference in **Q2 2025**

BT-001: Phase I data presentation (H2 2025)

TG6050: Initial Phase I data (**Q2 2025**)

Appendices

New Leadership to Take Transgene to the Next Level

ALESSANDRO RIVA, MD
Chairman & CEO

30+ years experience

NOVARTIS ONCOLOGY GILEAD ...ichnos...

MAURIZIO CEPPI, PhD
VP, Chief Scientific Officer

EMMANUELLE DOCHY, MD
VP, Medical Affairs, Chief Medical Officer

LUCIE LARGUIER
VP, Chief Financial Officer

JAMES WENTWORTH
VP, Chief Business Officer

JOHN FELITTI
VP, Legal, General Counsel and Chief Compliance Officer

CHRISTOPHE ANCEL, PharmD
VP, Chief Quality Officer and Qualified Pharmacist

CHRISTELLE SCHWOERER
VP, Human Resources

SIMONE STEINER
VP, Chief Technical Officer

JOHN C. BELL
Member of the Scientific Advisory Board

PEDRO ROMERO
Member of the Scientific Advisory Board

Environmental, Social and Governance Commitments

Transgene's **ESG** strategy is based on 6 commitments

- To **patients**
- To our **partners**
- To our **employees**
- To our **shareholders** and **investors**
- To **society** and the **regions**
- To the **planet**

44/100
Vigeo Eiris (+20 pts)

85/100
Gaïa EthiFinance Award (+8 pts)

99/100
Equal Employment Index

TOP 5 French companies with the **best ESG performance** for 2023*.

ESG rating
higher than industry benchmark (Pharma/Biotech)

Our ESG policy is detailed in the chap. 4 in the URD 2024

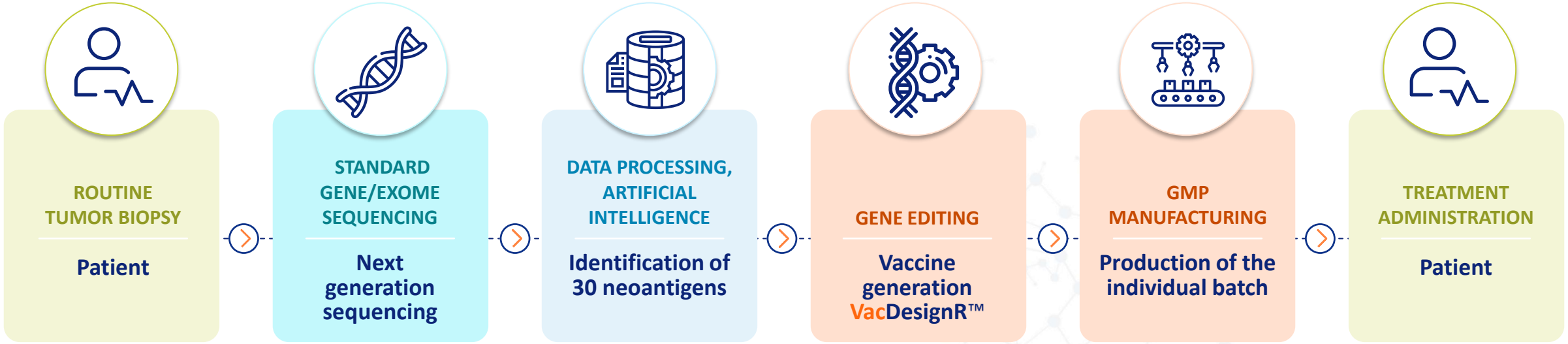
URD 2024

*with *< 250 employees*, according to the Gaia EthiFinance 2024 Award study
LinkedIn / Website

Study

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
Medium	1.99	Immune Desert	Low
Medium	4.34	Imm. Enriched, NF	Medium
Low	3.28	Immune Desert	Medium
Medium	3.42	Immune Desert	Medium
Medium	1.9	Imm. Enriched, NF	Low
Medium	3.16	Fibrotic	Medium
Low	4.2	Immune Desert	Medium
Medium	1.99	Imm. Enriched, F	Low
Medium	4	Imm. Enriched, NF	Low
High	1.37	Imm. Enriched, NF	Medium
Low	2.41	Immune Desert	High
Low	3.05	Immune Desert	Medium
Medium	7.7	Imm. Enriched, F	Medium
Medium	1.68	Imm. Enriched, NF	Medium
Medium	1.46	Immune Desert	Low

Arm B: Control arm

PD-L1	TMB (mt/Mb)	TME functional class	Tumor cell proliferation
Medium	3.02	Immune Desert	Medium
Medium	1.6	Immune Desert	Medium
Low	4.26	Immune Desert	Medium
Medium	3.02	Immune Desert	Medium
Medium	3.36	Immune Desert	Medium
High	3.28	Imm. Enriched, NF	High
Low	3.64	Immune Desert	Medium
Medium	7.95	Fibrotic	Low
Medium	1.9	Immune Desert	Medium
Medium	0.34	Immune Desert	Medium
Medium	2.77	Immune Desert	Medium
Medium	5.24	Immune Desert	Low
Medium	2.91	Imm. Enriched, NF	Medium
Medium	0.03	Imm. Enriched, NF	Medium
Low	2.1	Immune Desert	Medium
Medium	3.56	Immune Desert	Medium

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Source: G. Le Tourneau *et al.*, "**Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)**", SITC November 2024, Poster presentation

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