Unlocking the Full Potential of the Immune System Against Cancer

Corporate Presentation

November 7, 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.

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.

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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 by 2026

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

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 currently enrolling patients based on promising Phase I data

* 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

Innovative Clinical-Stage Immunotherapy Portfolio Based on Viral Vectors

Product	Indication	Collaboration	Discovery	Phase I	Phase II	
INDIVIDUALIZED NEOANTIGEN CANCER VACCINES						
TG4050	**Head and neck cancer (adjuvant)**	Orchestrating a brighter world NEC	●	R	R	**24-month median follow-up data on Phase I part** presented at SITC (Nov. 2024) **Completion of enrolment** (Q4 2025)
myvac	Other indication		●	●		Additional Ph. I trial to start (2025)
SHARED ANTIGENS CANCER VACCINES						
TG4001	Cervical and anogenital HPV+ cancers		●	●	R	**Primary objective** (improvement in PFS) not met in Phase II study **Positive efficacy trend in cervical cancer patients observed in pre-planned subgroup analysis.** Full analysis ongoing prior to decision on the best way forward
Internal myvac	Shared driver mutations		●			
ONCOLYTIC VIRUSES (OVs)						
TG6050 invirio	Lung cancer (IV*)		●	●		Initial data expected in H1 2025
BT-001 invirio	Solid tumors (IT*)	BioInvent	●	●		Finalizing the second cohort in Ph. I/IIa Part B
Internal	Synthetic OV (IV*)		●			

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

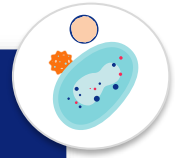
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Cancer Therapeutic Vaccines

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

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

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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 SITC 2024
(32 patients)

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

Ongoing Phase II part

➔ **Patient enrolment expected to be completed in Q4 2025**

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)



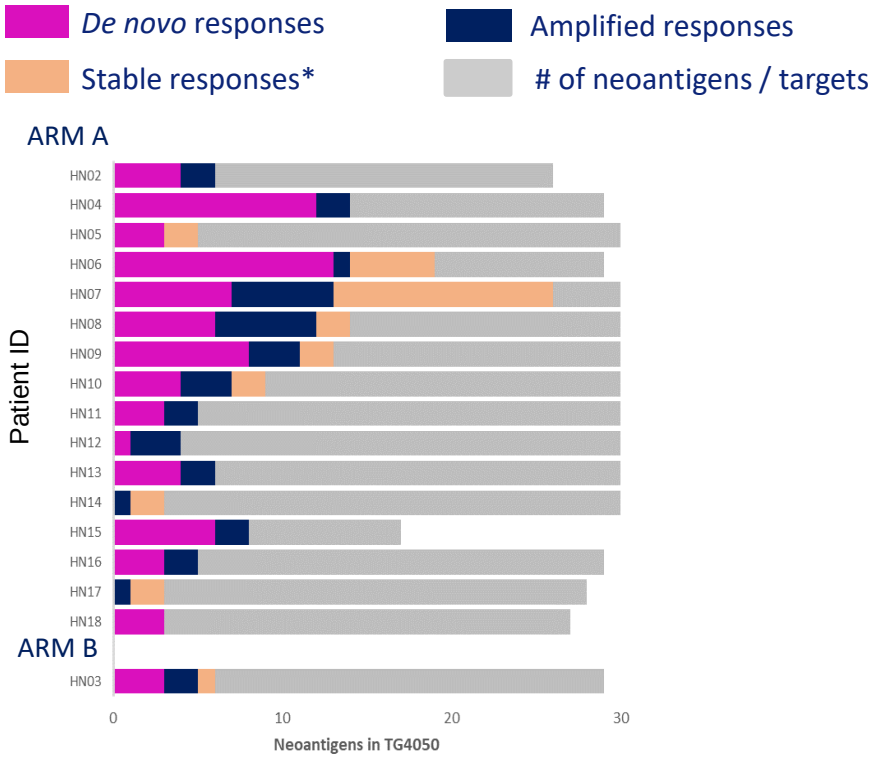
LEAD INVESTIGATOR: Pr. Christian Ottensmeier,
Clatterbridge Cancer Care Center, Liverpool

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

*Sources: 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**

Neoantigens specific T-cells responses were detected in all patients

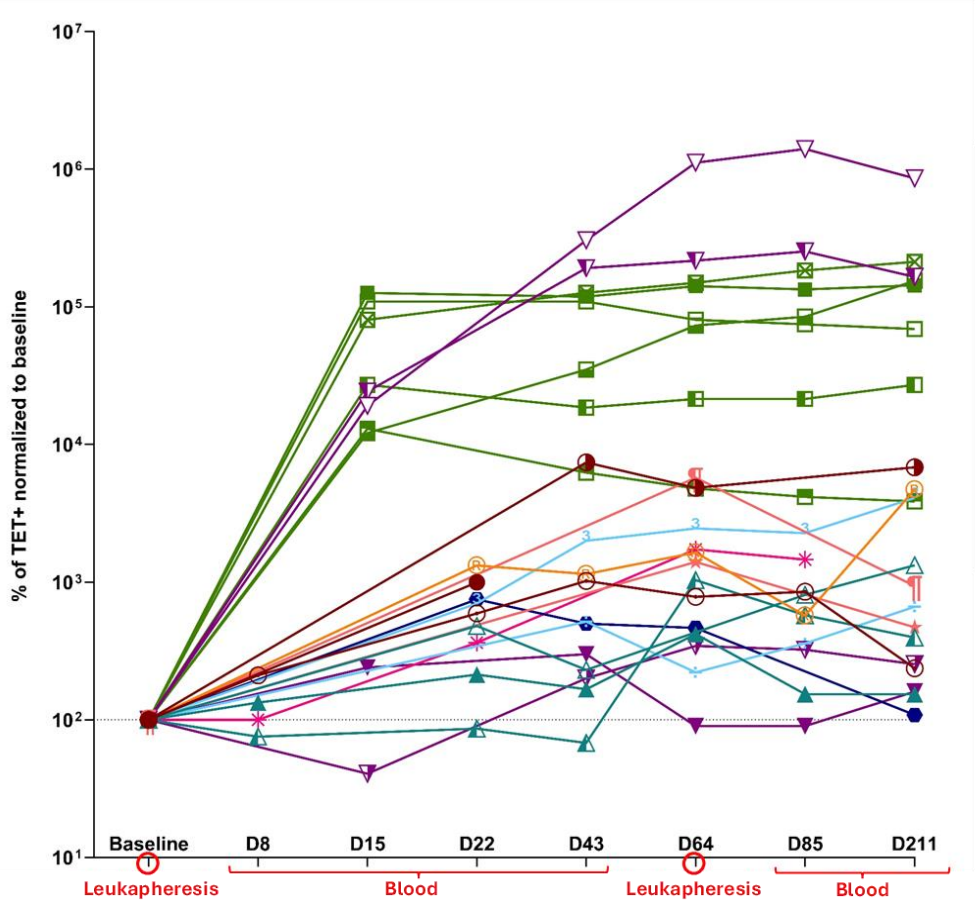
***De novo* responses were detected in 88% patients**

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

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 | Persistent Specific Cellular Response Following Vaccination

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



Introduction period

1 dose/week during 43 days

Boost period

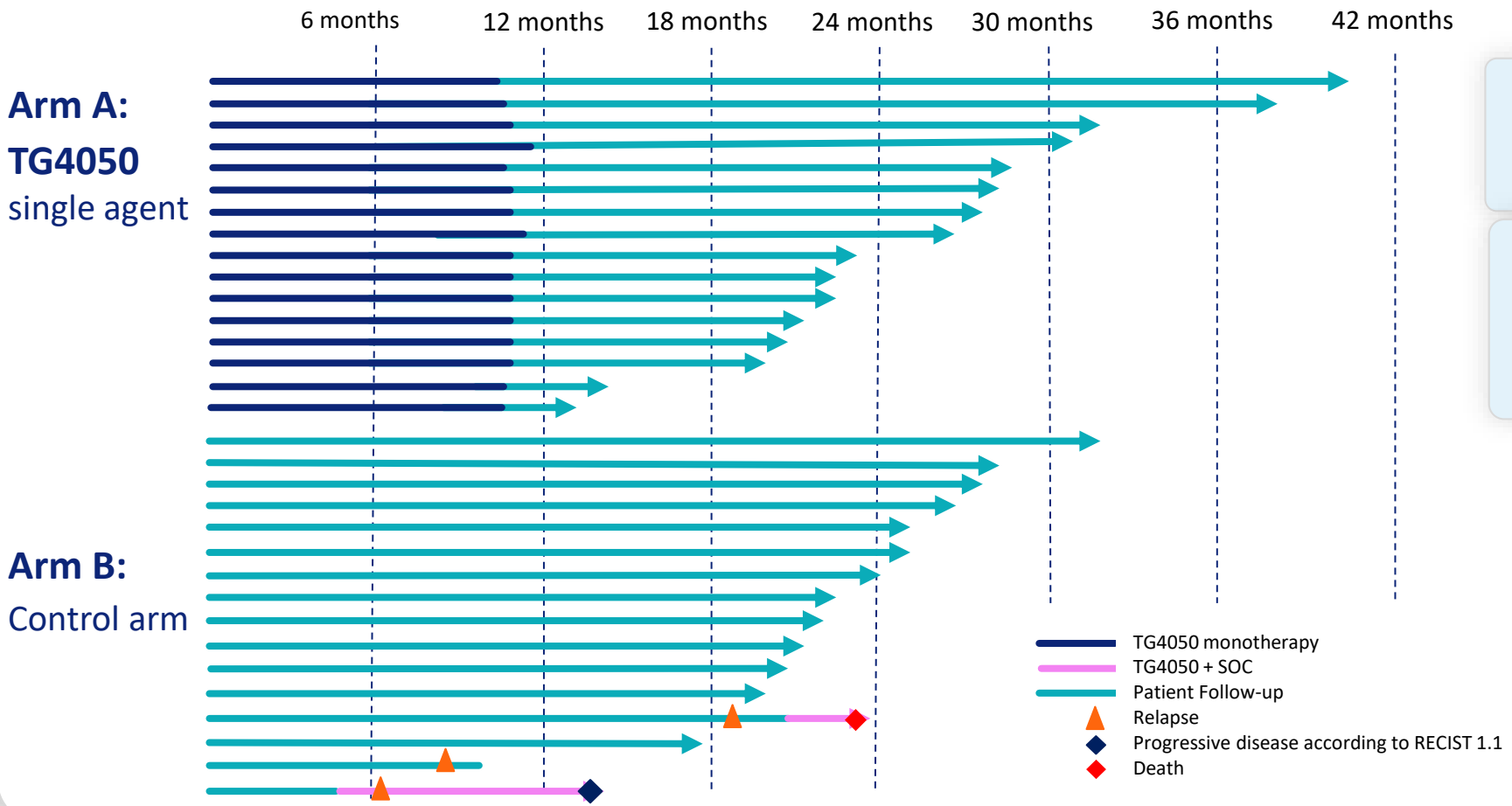
1 dose/3 weeks during 1 year

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 | 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 were disease-free

Only patients in the control arm relapsed

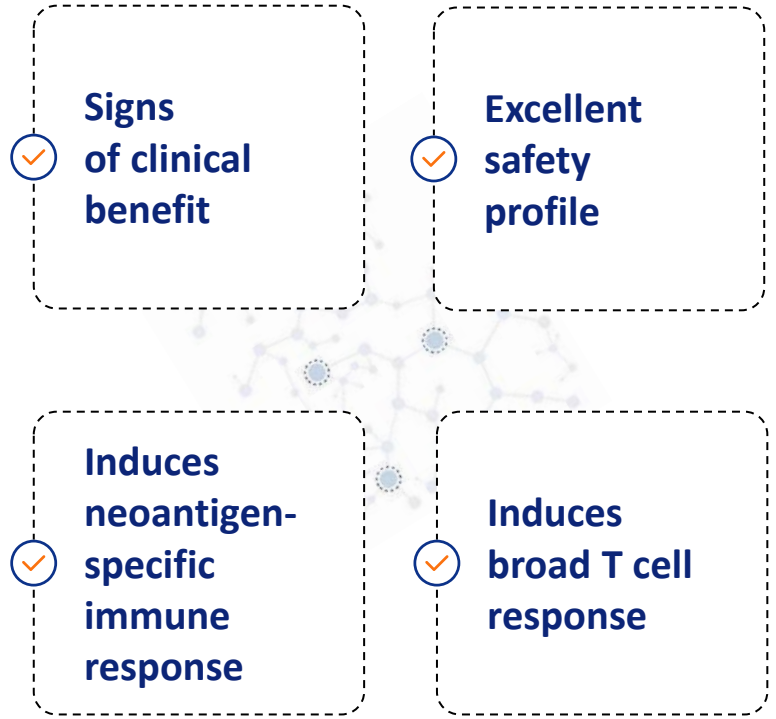
Source: G. Le Tourneau *et al.*, "**Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)**", SITC November 2024, Poster presentation

TG4050 | Additional Data to be Presented at SITC 2024

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one patient • one genome • one vaccine

- **24.1-month median follow up on Phase I part** (32 patients) presented at SITC (Nov. 2024)
- **Ongoing Phase II part – Last patient to be enrolled in Q4 2025**

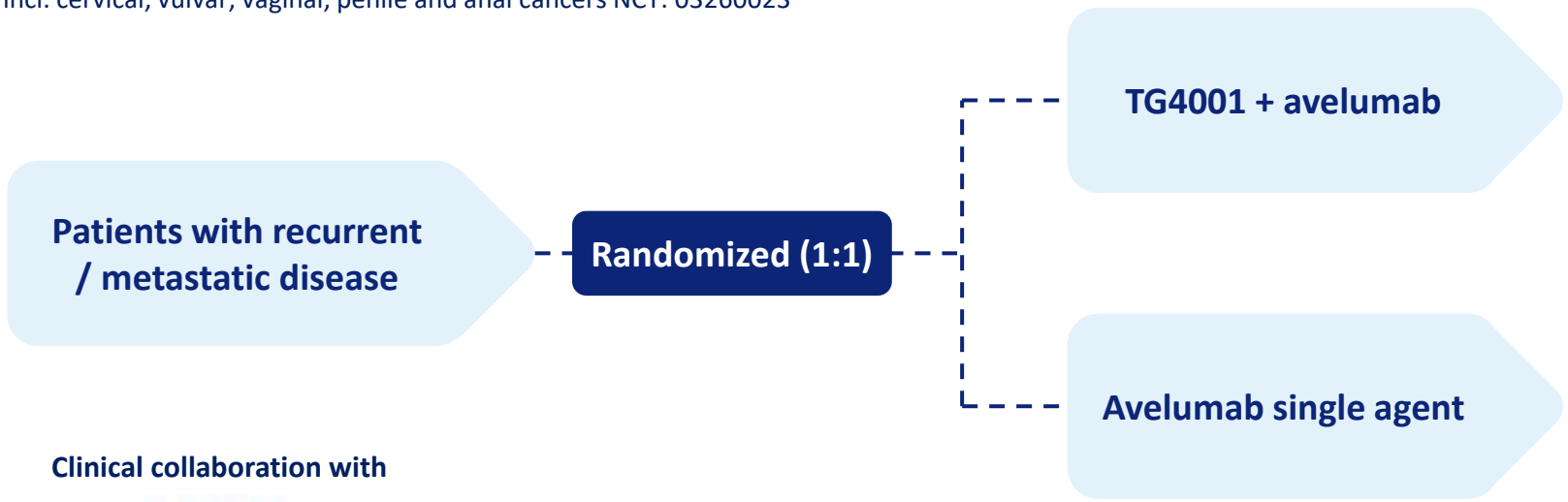
- **Potential to extend remission period and address a significant market** (head and neck cancer – adjuvant)
- **Could address other solid tumors in perioperative settings w or w/o ICIs** – Additional Ph. I trial to start in 2025



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 detailed results at a future scientific conference**

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Oncolytic Viruses

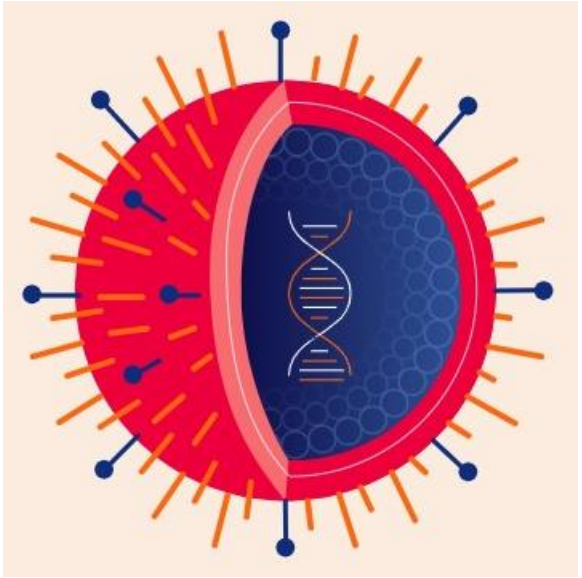
Rapidly Generating Multiple Virus-Powered
Off-the-Shelf Drug Candidates Targeting Solid Tumors

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

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

Ongoing Phase I/IIa 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)



Ongoing Phase I (NCT04725331)

monotherapy and combination w. anti-PD1

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

Promising antitumor activity

in patients (Ph. I Part A and ongoing Part B)

- **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 9/26 injected lesions and in 5/37 non-injected lesions
- **No AEs** led to BT-001 and/or pembrolizumab discontinuation

Can be developed for multiple cancer indications

lesions with high Treg infiltration

Collaboration with MSD
which provides pembrolizumab (KEYTRUDA®)

MSD

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

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 ongoing (NCT: 05788926)

Initial data (single agent) in **H1 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

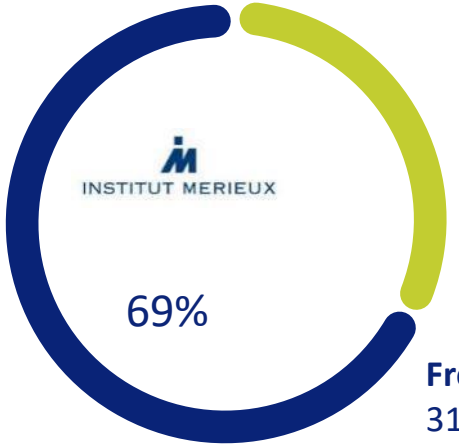
Company Funded to Deliver Multiple Value Generating Milestones

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 September 30, 2024



Free float
31%

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

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

Other indication

➔ Prepare new Phase I

Shared antigens cancer vaccines

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

Oncolytic viruses

invirio

TG6050: Initial Phase I data (**H1 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 -
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 Counsel



CHRISTOPHE ANCEL, PharmD
VP, Pharmaceutical Operations



CHRISTELLE SCHWOERER
VP, Human Resources



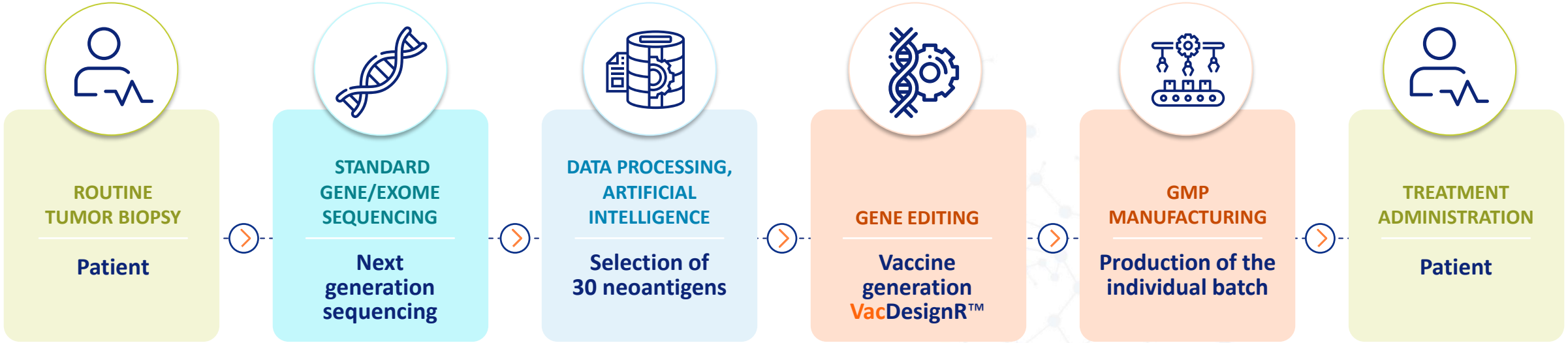
JOHN C. BELL
Member of the Scientific Advisory Board



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

transgene

Transgene, a committed company

Our CSR commitments (Corporate Social Responsibility)

Transgene's **CSR** 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)

95/100
Equal Employment Index

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

CSR notes
higher than sector averages (Pharma/Biotech)

Our CSR policy is detailled in the chap. 4 in the URD 2023

URD 2023

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

Study

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

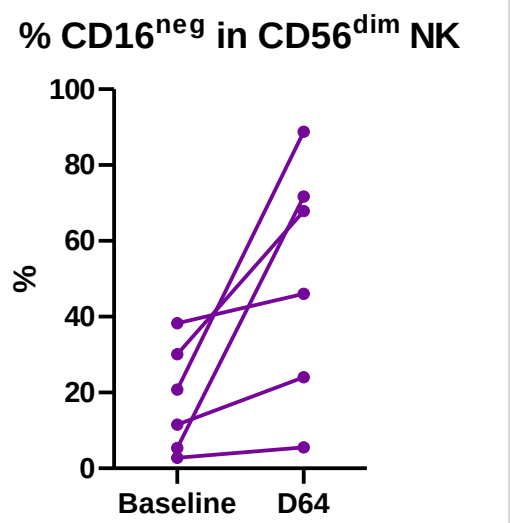
PD-L1	TMB (mt/Mb)	TME functional class	Tumor cell proliferation
Medium	3.02	Immune Desert	Medium
Medium	1.6	Immune Desert	Medium
Low	4.26	Immune Desert	Medium
Medium	3.02	Immune Desert	Medium
Medium	3.36	Immune Desert	Medium
High	3.28	Imm. Enriched, NF	High
Low	3.64	Immune Desert	Medium
Medium	7.95	Fibrotic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

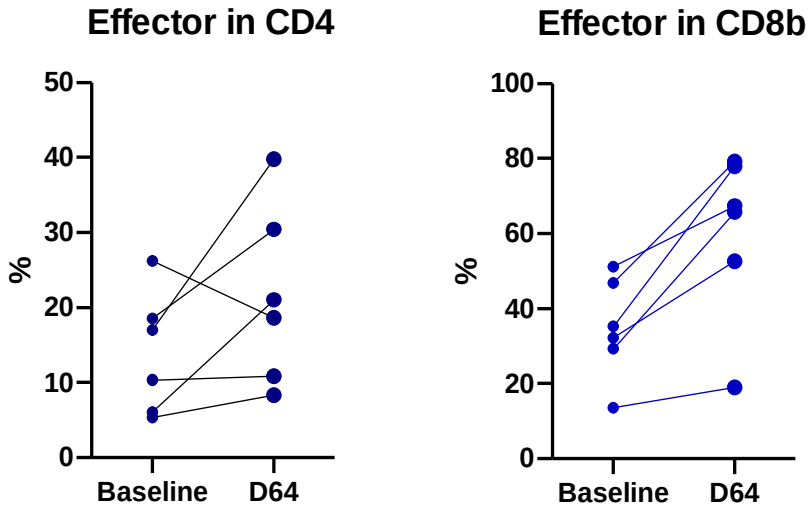
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Source: G. Le Tourneau *et al.*, "**Randomized Phase I Trial of Adjuvant Individualized TG4050 Vaccine in Patients with Locally Advanced Resected HPV-negative Head and Neck Squamous Cell Carcinoma (HNSCC)**", SITC November 2024, Poster presentation

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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