



Unlocking the Full Potential of the Immune System Against Cancer

Corporate Presentation

April 9, 2024



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Transgene

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)**
- **Randomized Phase II trial to start in Q2 2024**

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** – 100% 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



Building upon proof of principle:
Randomized Phase II trial to begin in Q2 2024
based on promising Phase I data

Our pipeline – poised to deliver important data

Product	Indication	Collaboration	Discovery	Phase I	Phase II	Key upcoming catalysts
INDIVIDUALIZED NEOANTIGEN CANCER VACCINES						
TG4050 	Head and neck cancer (adjuvant)	 NEC	●	●	●	24-month median follow up (H2 2024) Ph. II trial to start (Q2 2024)
	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 	Shared driver mutations		●			
ONCOLYTIC VIRUSES (OVs)						
TG6050 	Lung cancer (IV*)		●	●		First data (H2 2024)
BT-001 	Solid tumors (IT*)		●	●		First data in combination with pembrolizumab (H2 2024)
Internal	Synthetic OV (IV*)		●			



Cancer Therapeutic Vaccines

Focused on delivering the promise
of individualized cancer vaccine



myvac[®] - TG4050 | Combines Unique Know How and Expertise

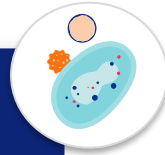
MVA viral vector: a powerful platform for vaccine development

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**



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



[Click here](#)



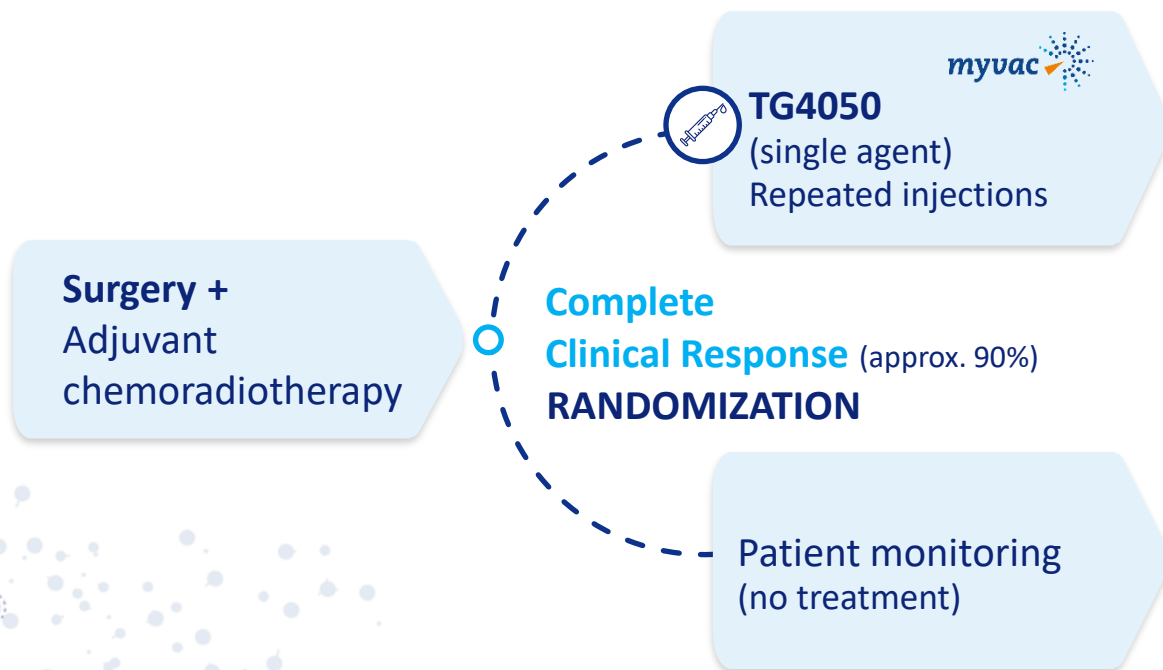
Technology well suited to demonstrate benefit in minimal residual/molecular disease



*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 | HPV-Negative 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)

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

Randomized Phase I trial – Promising initial immunological and clinical data presented at ASCO 2023

32 patients (NCT: 04183166)

- ➔ **All treated patients remaining disease-free**
- ➔ **Trial extended to Phase I/II, patient inclusions to restart in Q2 2024**



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

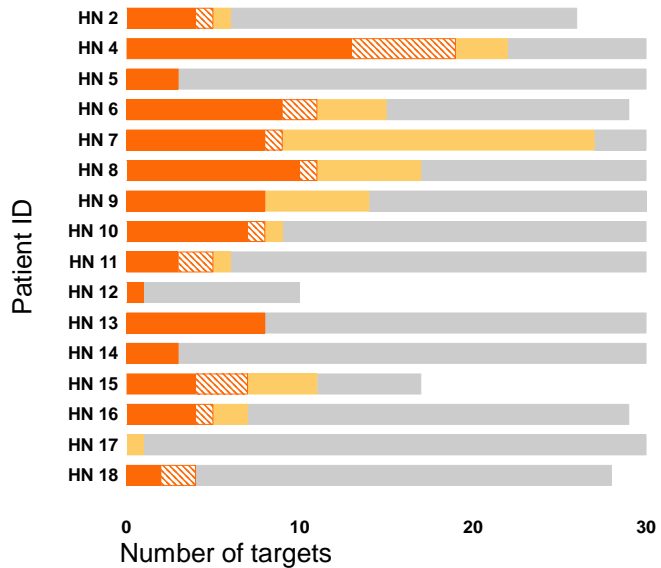


* Sources: Keynote 412, Javelin 100 trials, company estimates

TG4050 | Generates and/or Expands Tumor Specific T Cells

Number of positive responses per patients
Head and neck cancer trial

■ *De novo* responses Amplified responses
■ Stable responses* ■ # of neoantigens / targets



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

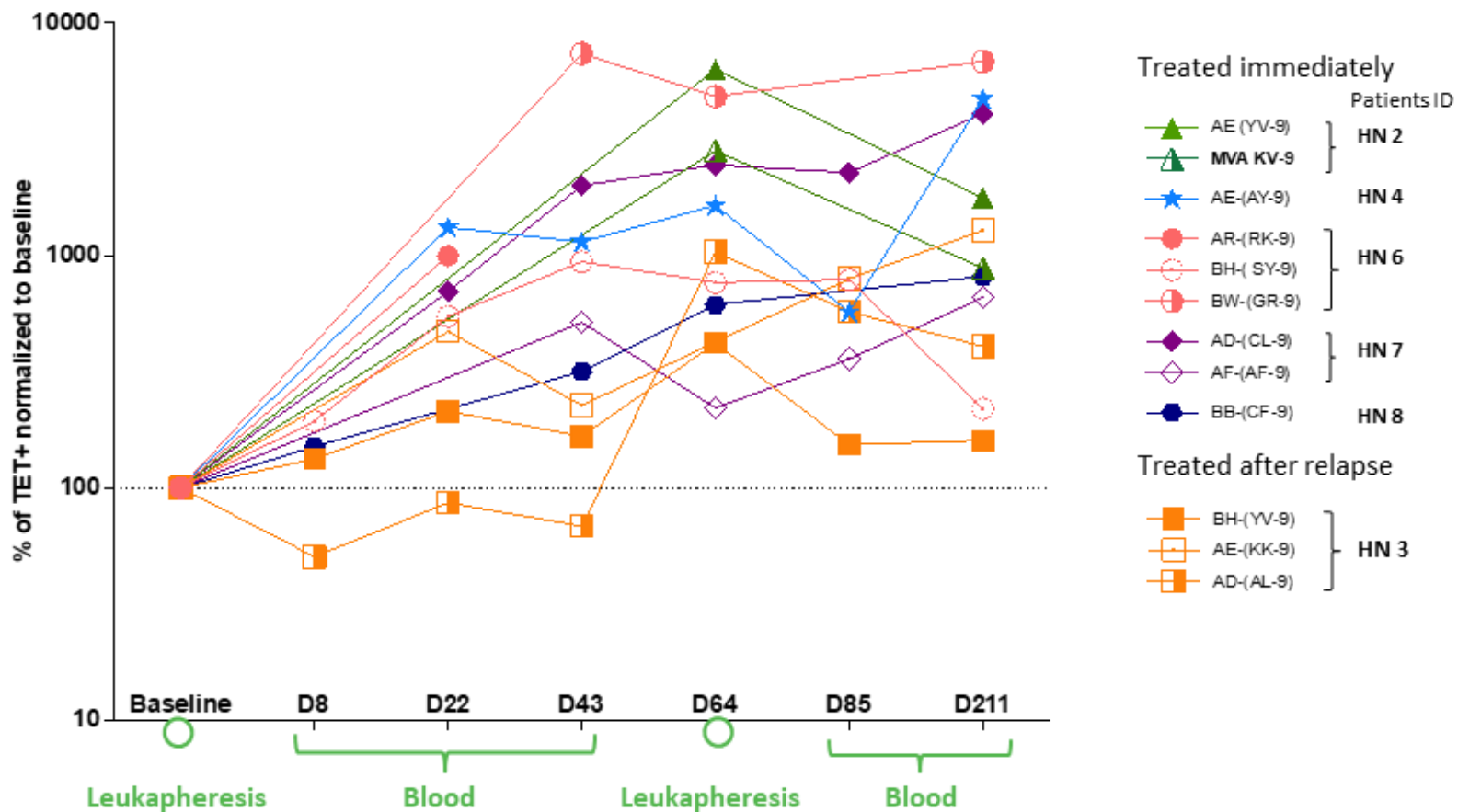
CD4+ or CD8+ responses were detected in all but one patients vaccinated patients

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

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

TG4050 | Persistent Specific Cellular Response Following Vaccination

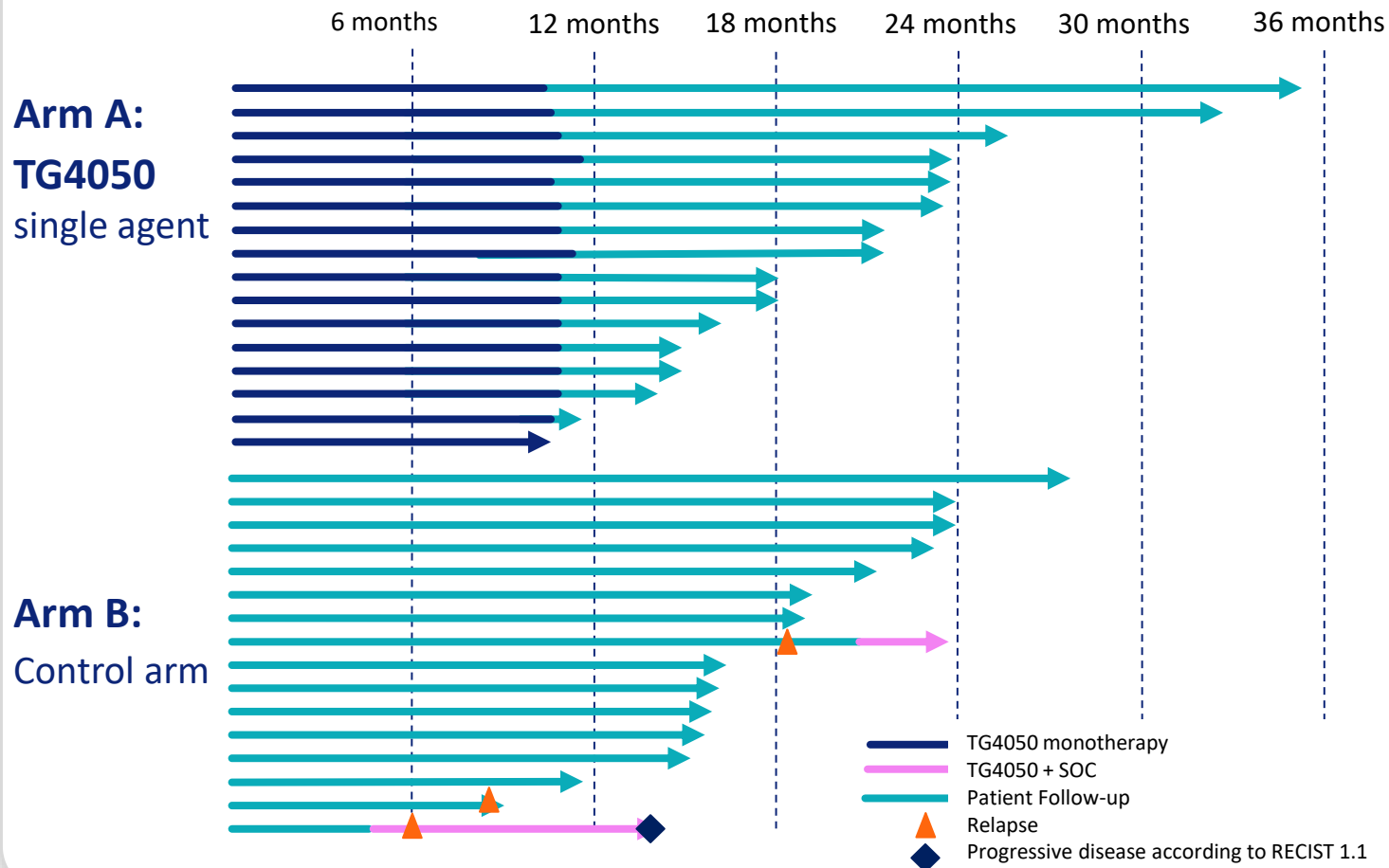
Patients display **persistent specific CD4+ and CD8+ responses** against multiple selected targets, 7 months after treatment induction



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

AACR
American Association
for Cancer Research

*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

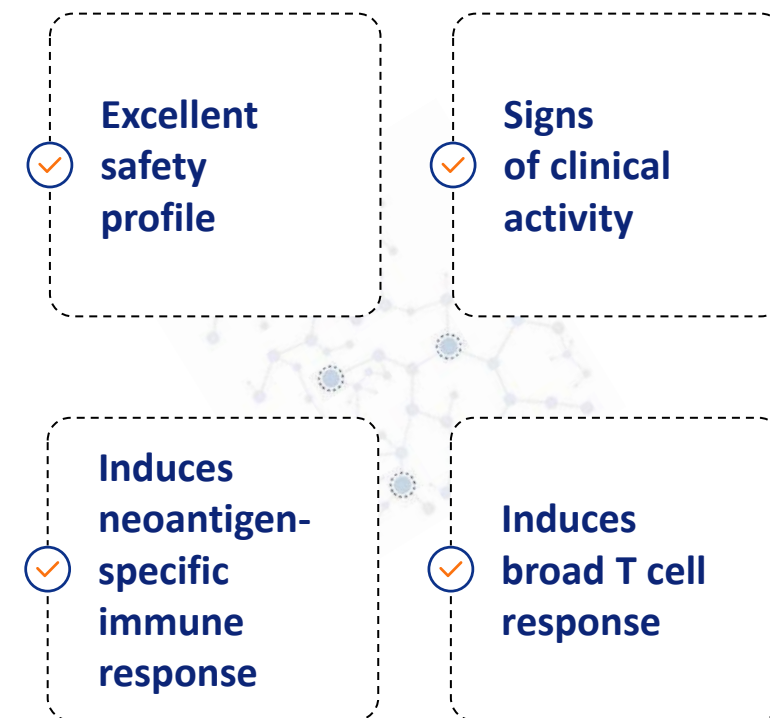
TG4050 | Additional Data Expected in 2024



one patient • one genome • one vaccine

- 24-month median follow up expected in H2 2024
- Phase II part of the trial to start in coming weeks in head and neck cancer (adjuvant setting)

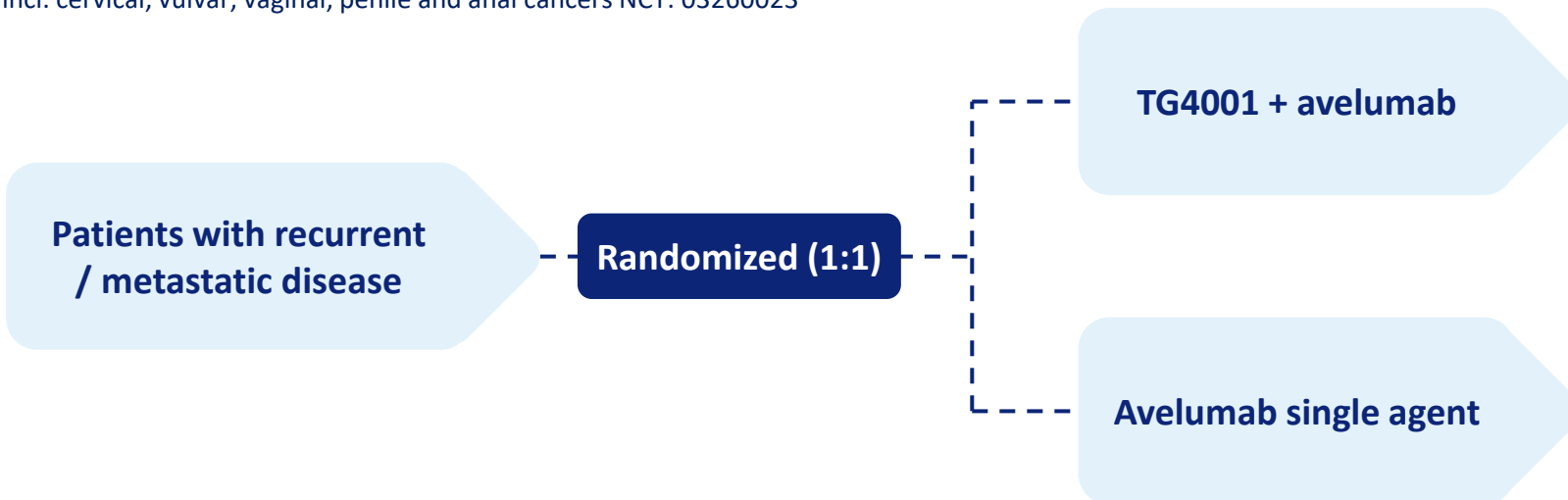
- > Potential to extend remission period and address a significant market (head and neck cancer – adjuvant)
- > Could address other solid tumors in **perioperative settings** w or w/o ICIs – Additional trial to start in 2025



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



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

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



for avelumab free supply



Oncolytic Viruses

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

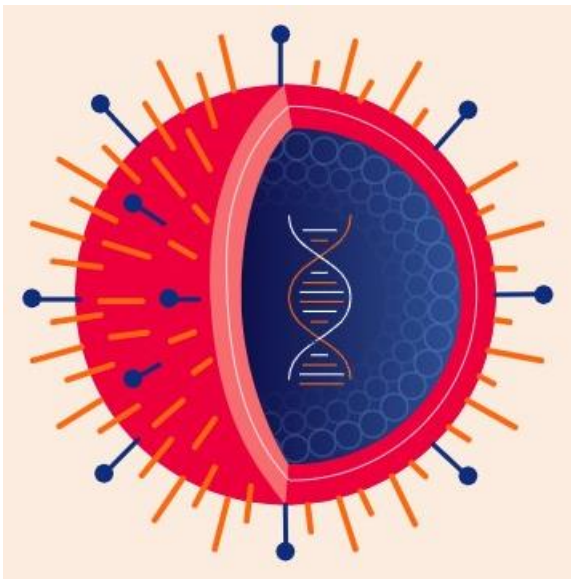
invirio



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

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 $VV_{\text{cop}}\text{TK}^{-}\text{RR}^{-}$ 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



Proof of principle obtained

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

invirio

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



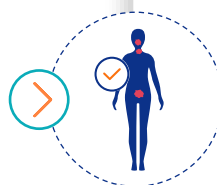
Initial goal

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)

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

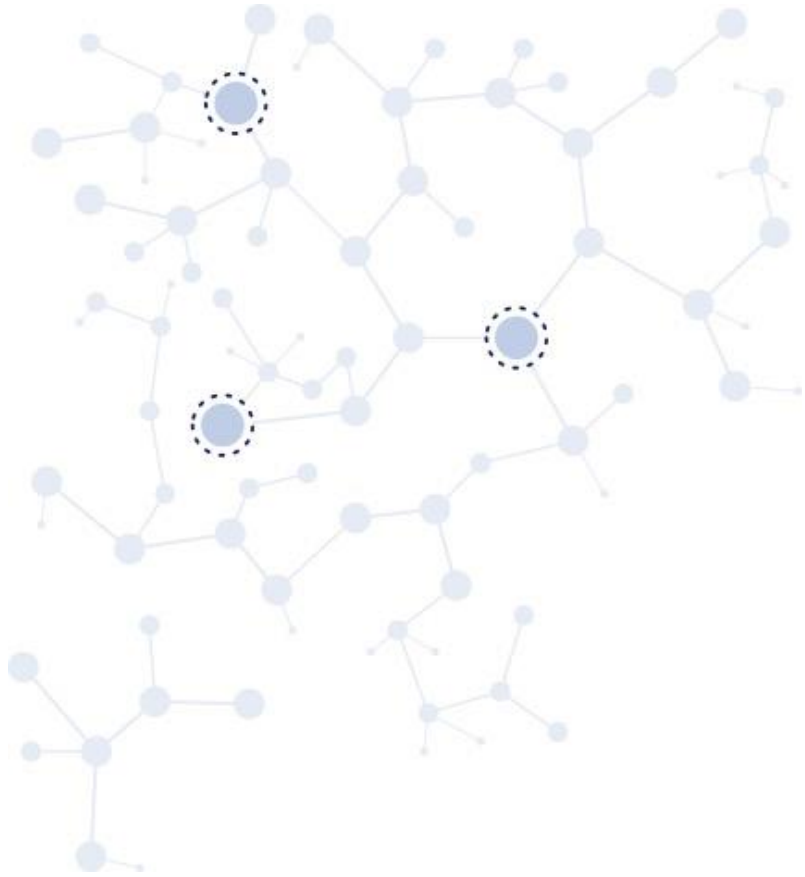
Ongoing Phase I (NCT04725331) monotherapy and combination w. anti-PD1

- **Ph. I part B** (combination with pembrolizumab) – Enrolment ongoing – **First data expected in H2 2024**

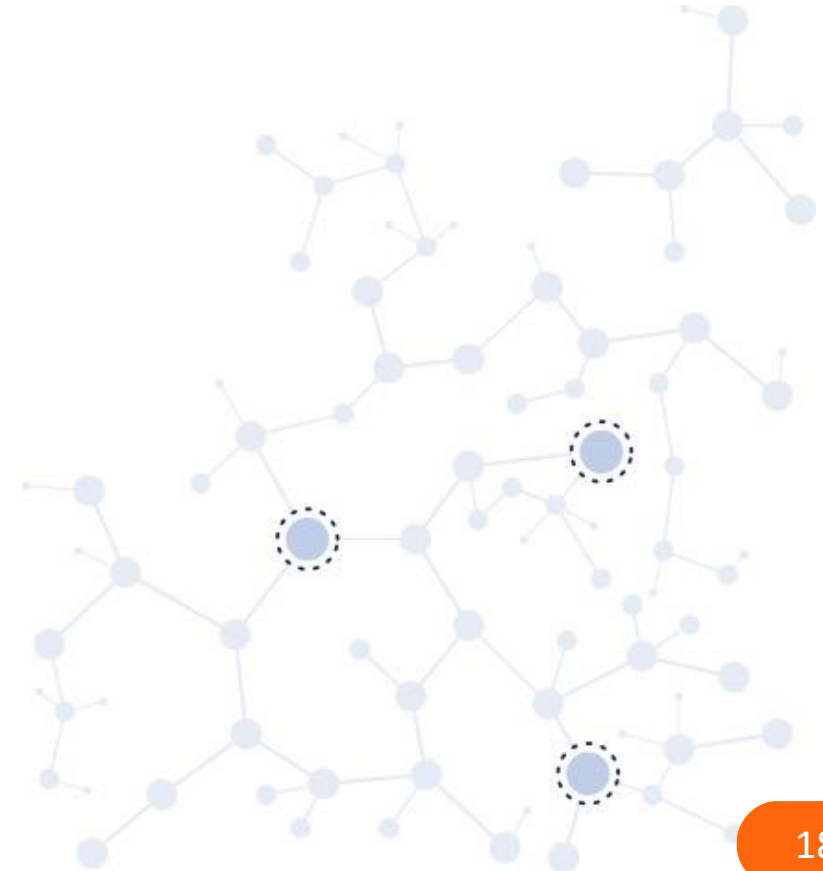
*IT: intratumoral administration

Collaboration with MSD which provides pembrolizumab (KEYTRUDA®)





Outlook



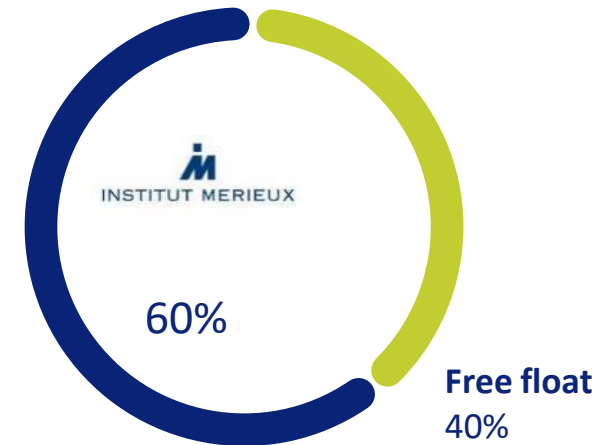
Company Funded to Deliver Multiple Value Generating Milestones

✓ **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, 2023



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

TG4050 | Neoantigen vaccine



✓ Proof of principle

already obtained in Head and Neck cancer (adjuvant)

○ Ongoing randomized Phase I (head and neck cancer)

– 24-month median follow up of patients (H2 2024)

○ Randomized Phase II (head and neck cancer)

– Initiation of the trial in collaboration with NEC (Q2 2024)

○ Other indication

– Prepare new Phase I

Shared antigens cancer vaccines

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

Oncolytic viruses



- **TG6050:** Initial Phase I data (H2 2024)
- **BT-001:** Initial data in combination with pembrolizumab (H2 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



GILEAD ...ichnos...



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



LUCIE LARGUIER
VP, Chief Financial Officer



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



JAMES WENTWORTH
VP, Chief Business Officer



JOHN FELITTI
VP, Legal Counsel



CHRISTOPHE ANCEL,
PharmD
VP, Pharmaceutical Operations



CHRISTELLE SCHWOERER
VP, Human Resources

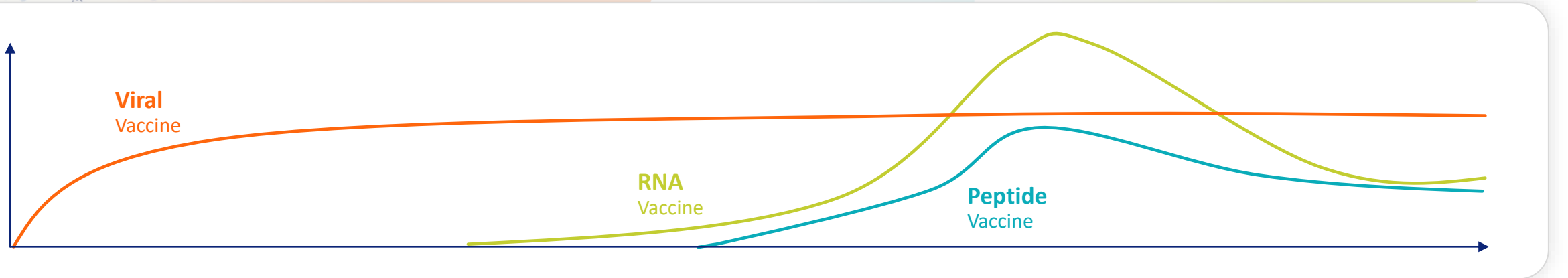
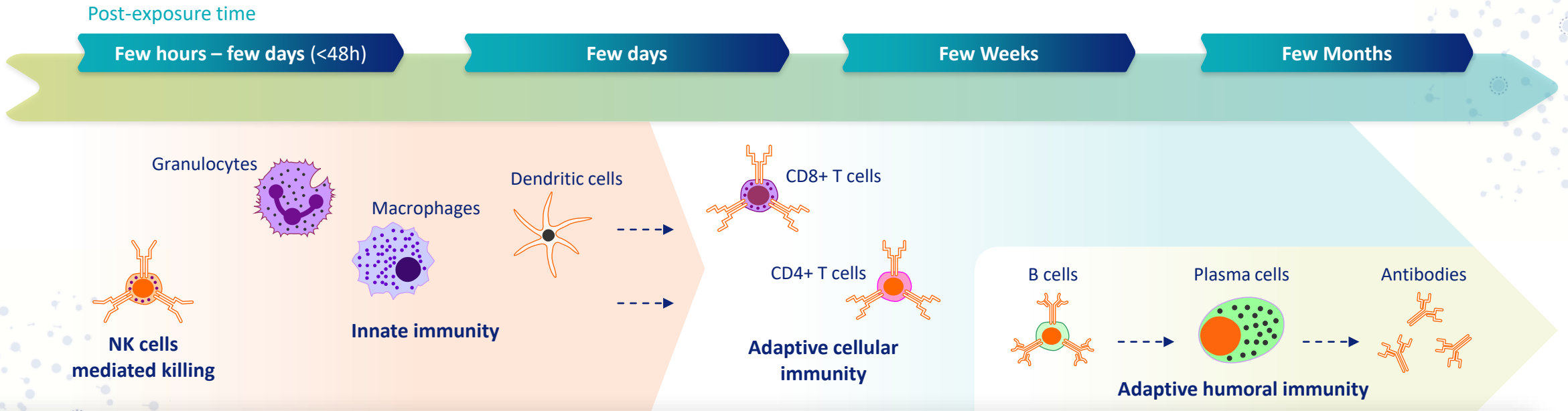


JOHN C. BELL
Member of the Scientific
Advisory Board



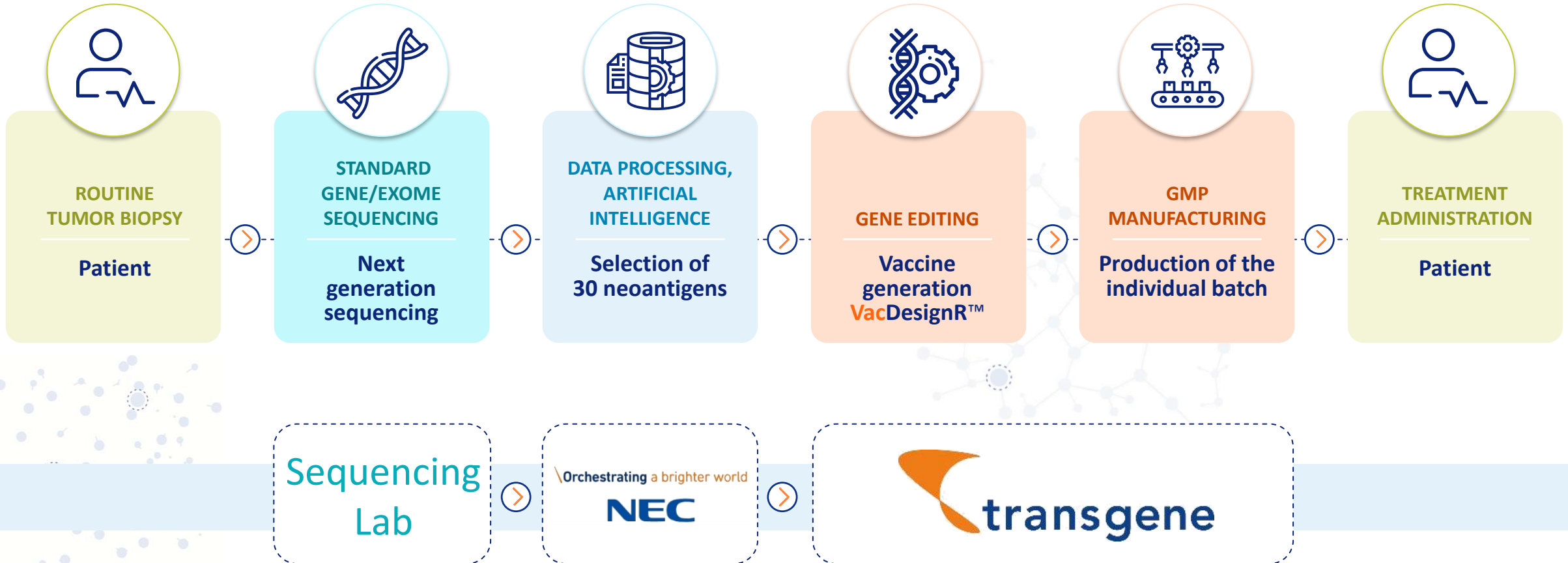
PEDRO ROMERO
Member of the Scientific
Advisory Board

Viral Vaccines Prime Both Long Lasting Innate and Adaptive Immunity

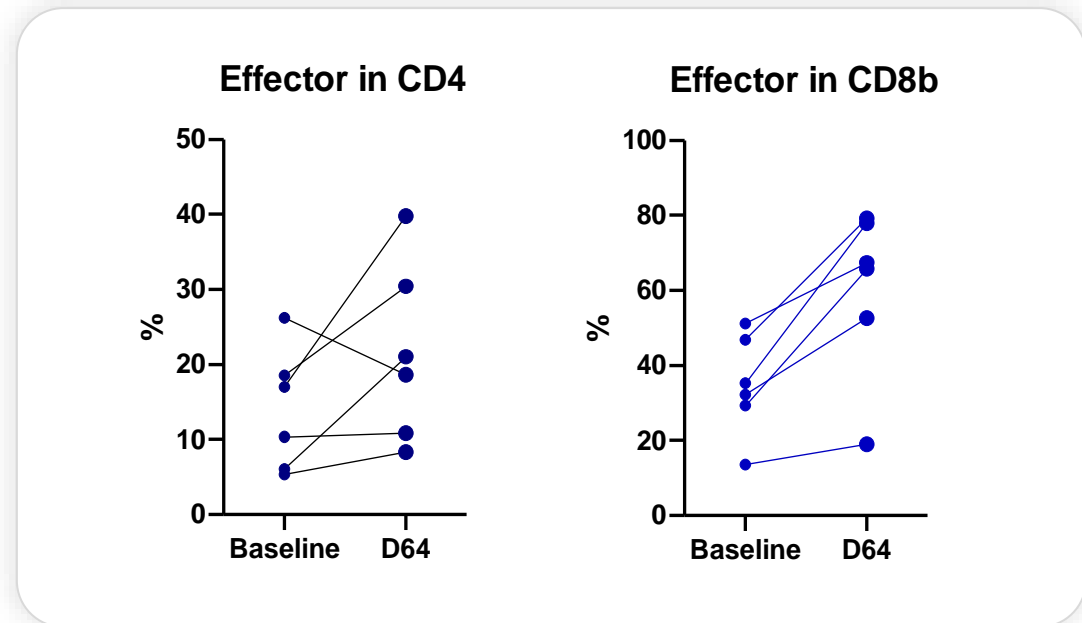
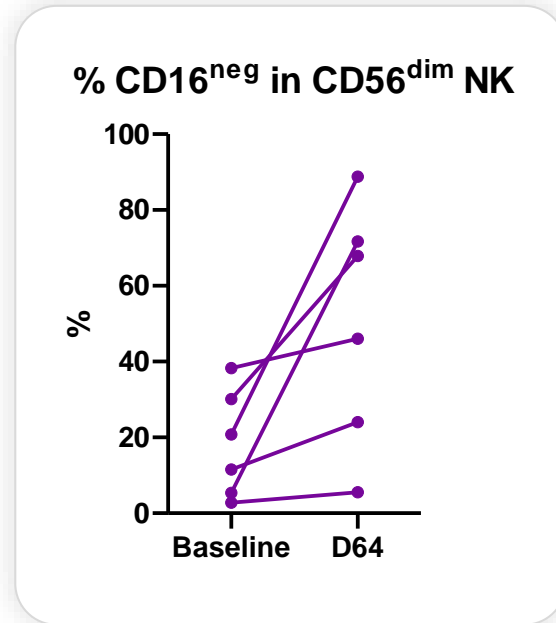


TG4050, an Individualized Neoantigen Vaccine Combining Unique Capabilities

Combines Bioengineering and Digital Transformation




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**

 **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



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