Virus Powered Immunotherapies against Solid Tumors

Corporate Presentation

June 27, 2022

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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An Experienced Management Team

HEDI BEN BRAHIM
Chief Executive Officer

20 YEARS EXPERIENCE

ÉRIC QUÉMÉNEUR, PHD
Executive VP
Chief Scientific Officer

30+ YEARS EXPERIENCE

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

35+ YEARS EXPERIENCE

STEVEN BLOOM
VP, Chief Business Officer

US-based

35+ YEARS EXPERIENCE

JEAN-PHILIPPE DEL
VP, Chief Financial Officer

20 YEARS EXPERIENCE

ALESSANDRO RIVA
Chairman
Joined in May 2022

30+ YEARS EXPERIENCE

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Transgene – Potential game changing approach to the treatment of solid tumors

Customized and Off-The-Shelf Cancer Immunotherapies

Diversified pipeline

2 platforms
Therapeutic vaccines
Oncolytic viruses

4 clinical-stage immunotherapies
in Phase I and Phase II

Significant news flow in next 18 months including:
- TG4001 Ph.2 interim analysis in Q4 22 for anogenital HPV+ cancers
- TG4050 Ph. 1 data in H2 22 for head & neck cancers and ovarian cancer
- TG6002 initial Ph.1 data in Q3 22 for colorectal cancer

Unique Technology based on:

- Optimized viral vectors
- Preclinical Proof of Concept
- Solid safety Track record
- Strong clinical data
- Robust IP portfolio

Integrated GMP manufacturing

Capacity for rapid delivery of pilot scale batches

Ongoing collaborations

- AstraZeneca — R&D and license deal
- MERCK / Pfizer — Supply agreement
- Orchestrating a brighter world NEC — Technology and cost sharing agreement
- BioInvent — Co-development

Strong Shareholder Support and Financial visibility

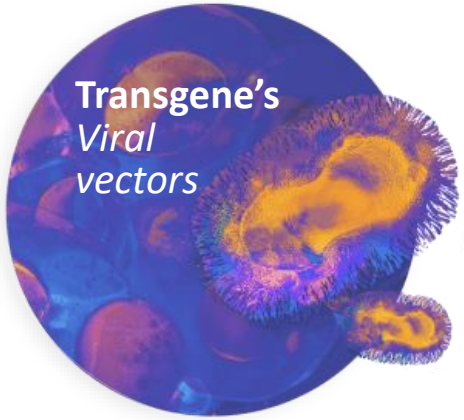
Financial visibility until the end of 2023

Strong shareholder support

INSTITUT MERIEUX

Our Expertise Translates into Two Unique Technology Platforms

Able to Target Multiple Solid Tumors



- Induces **broad immune response** (innate & adaptive) to fight cancer
- **Versatility & flexibility** - can encode wide range of payloads to target a wide range of indications
- Demonstrated **safety**

- **Easy administration**
- **Established manufacturing**
- **Not restricted to tumors sensitive to Immune Checkpoint Inhibitors**
- « **All in one** » no need for adjuvant, immunogenic by itself

1 THERAPEUTIC VACCINES

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1. **Select the right antigens: Patient specific antigens** selected to generate the optimal immune response
2. **Engineer virus:** integration of the antigen/selected sequences within the genome of the MVA virus
3. **Activate immune system: Activate T cell** through several mechanisms to kill tumour cells

2 ONCOLYTIC VIRUSES

invir io

Engineered virus ($VV_{cop}TK^{-}RR^{-}$) that **encodes therapeutic payload**

Cancer cell death through: **(1)** virus-induced **direct and specific tumor oncolysis** and **(2)** activity generated by **therapeutic payloads**

Intravenous delivery has the potential to **target multiorgan lesions**

Multiple Opportunities to Transform Solid Tumor Therapy

Product	Target/transgene	Indication	Collaboration	Preclinical	Phase I	Phase II	Next step
THERAPEUTIC VACCINE							
TG4001	HPV16 E6 – E7	Anogenital HPV+ cancers	MERCK, Pfizer				**Interim analysis Q4 2022**
myvac **TG4050**	30 neoantigens	Head and neck cancers	Orchestrating a brighter world NEC				**Additional Ph. I data to be presented in congresses in H2 2022 – Ph. II expected to start in H2 2023**
		Ovarian cancer					
ONCOLYTIC VIRUS (OV)							
TG6002	5-FU chemotherapy	Gastro-intestinal cancers (IV*)					**End of Ph. I mid-2022**
		Colorectal cancer (IHA*)					**Initial Ph. I data Q3 2022**
invir.io **BT-001**	Anti-CTLA4 + GM-CSF	Solid tumors	BioInvent				**Ph. I part B to start in H2 2022**
OVs	Undisclosed	Solid tumors					**Best candidates to enter into clinical dev.**
5 OVs	Undisclosed *(incl. 1 licensed product)*	Solid tumors	AstraZeneca				**Potential further milestones & option exercise**
OV	Undisclosed *(CAR-T combination)*	Solid tumors	博生吉 PersonGen				

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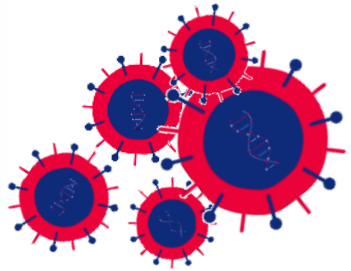
** IV: intravenous administration, IHA: intrahepatic artery administration*

Transgene & AstraZeneca to Co-Develop 5 Novel Invir.IO™ OVs

Transgene and **AstraZeneca** entered into a **collaboration** and **exclusive license option agreement** in **2019**



Up to **5 new OVs**

- For **5 innovative Invir.IO™** based **armed oncolytic immunotherapies**
- Integrating **one or more transgene(s)** chosen by AstraZeneca (not disclosed)
- **Collaboration progressing well**, AstraZeneca will oversee the clinical development

1st license option exercised by **AstraZeneca** in **Dec. 2021**

- **$8 million** option exercise payment for this 1st product
- Eligible to receive **development, regulatory and sales-based milestones payments** as well as a **royalty** based on future commercial sales

TG4001

Potential to Transform the Treatment of Anogenital HPV Positive Solid Tumors

Interim analysis expected in Q4 2022

TG4001 | Optimized Treatment for HPV-Positive Tumors

Potential to Address All HPV Positive Cancers

MVA virus
E6 and E7
HPV antigens

POTENTIAL TO ADDRESS ALL HPV POSITIVE CANCERS

Ongoing Phase II trial
Anogenital HPV16-positive cancers
without liver metastasis
25,000 new pts/year

Current SOC
1L platinum-based therapy (or other chemotherapy approved) w/ or w/o ICI (cancer-dependent)

2L platinum-based chemotherapy
(but pembro cervix cancer in the US)

Positive Phase Ib/II data
of TG4001 with avelumab
enabling launch of
randomized Phase II trial

Collaboration with

MERCK Pfizer

for Ph. Ib/II
and randomized Ph. II

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Estimated cancer cases (2025) based on: 1. ICO/IARC – HPV Information Center> Prevention at a glance // 2. HPV-positive cervical cancer: Globocan/IARC 2020 Cancer Fact Sheets: cervix uteri (C53); ICO/IARC – HPV Information Center Statistics // 3. HPV-positive vaginal cancer: Globocan/IARC 2020 Cancer Fact Sheets: vagina (C52); ICO/IARC – HPV Information Center Statistics // 4. HPV-positive vulvar cancer: Globocan/IARC 2020 Cancer Fact Sheets: vulva (C51); ICO/IARC – HPV Information Center Statistics; CDC United States Cancer Statistics: Data Visualizations; SEER Cancer stat facts: vulvar cancer // 5. HPV-positive anal cancer: Globocan/IARC 2020 Cancer Fact Sheets: anus (C21); ICO/IARC – HPV Information Center Statistics; CDC>Cancer Home>HPV and Cancer>Statistics>Rates by Race and Ethnicity>HPV-Associated Anal Cancer Rates by Race and Ethnicity; American Cancer Society: Anal Cancer // 6. HPV-positive penile cancer: Globocan/IARC 2020 Cancer Fact Sheets: penis (C60); ICO/IARC – HPV Information Center Statistics; CDC>Cancer Home>HPV and Cancer>Statistics>Rates by Race and Ethnicity>HPV-Associated Cancers Rates by Race and Ethnicity

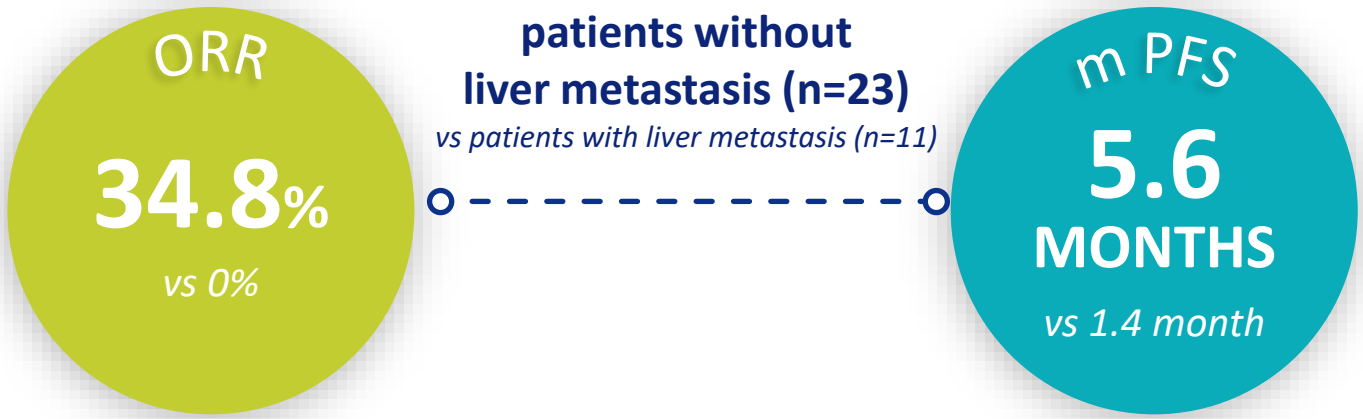
TG4001 | Phase Ib/II Data of TG4001 with Avelumab Presented at SITC 2020

Promising Results, Particularly in Patients without Liver Metastasis (NCT03260023)

34 heavily pretreated patients with metastatic HPV16+ cancer
(oropharyngeal, anogenital)

Identified target population:

patients without liver metastasis (n=23)
vs patients with liver metastasis (n=11)



1 COMPLETE RESPONSE

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

7 PARTIAL RESPONSES

Compares favorably to ICIs in monotherapy and competitive landscape

In 2L, ORR is around 10–15% , median PFS is around 2 months and median OS is less than 11 months

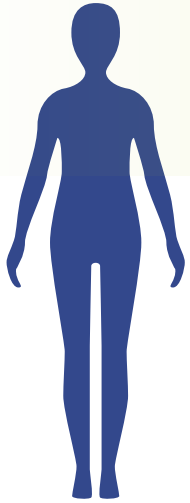
Estimations based on the following trials
- Anal 2L: NCI9673 (Nivolumab, Phase II) [ref] ; KN028 + KN158 [ref] (pooled analysis: Phase Ib KN028 and Phase II KN158); CARACAS (Phase II) [ref]
- Cervical 2L: KN158 (Phase II) [ref]
- Cervical, vaginal vulvar 2L: CM 358 (Phase II) [ref]

Source: Le Tourneau et al. "TG4001 (Tipapkinogene sovacivec) and avelumab for recurrent/metastatic (R/M) Human Papilloma Virus (HPV)-16+ cancers: clinical efficacy and immunogenicity." 2020 SITC Annual Meeting, 9-11 November 2020, Poster presentation

ORR: objective response rate (RECIST 1.1); mPFS: median progression-free survival

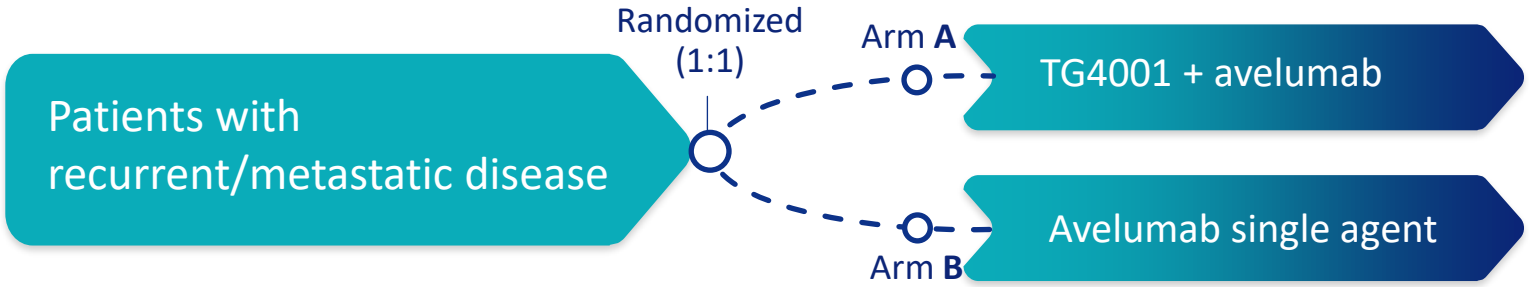
TG4001 | Randomized Controlled Phase II Trial Supported by Clinicians

Trial to Enroll up to ~ 150 Patients (NCT03260023)



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**



PRIMARY ENDPOINTS

Progression-Free Survival
(RECIST 1.1)

➔ **INTERIM ANALYSIS expected Q4 2022**

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Clinical collaboration with

Pfizer

MERCK

for avelumab free supply

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Individualized Neoantigen Vaccine

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

First positive data from the two Phase I trials

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one patient • one genome • one vaccine

TG4050 | An Individualized Neoantigen Vaccine Combining Unique Capabilities

Combines Bioengineering and Digital Transformation

50%
of development costs covered by NEC

Click to play

ROUTINE TUMOR BIOPSY
Patient

MUTANOME & EXOME SEQUENCING (NGS)
Tumor reference genome

Sequencing Lab

DATA PROCESSING, ARTIFICIAL INTELLIGENCE
Selection of 30 most immunogenic neoantigens

Orchestrating a brighter world
NEC

GENE EDITING
Vaccine generation
and optimization by virus engineering

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GMP MANUFACTURING
Production of the individual batches
up to ~2 batches/wk

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TREATMENT ADMINISTRATION
Patient

Artificial Intelligence

NEC's machine learning environment based on multiple parameters **to classify most immunogenic neoantigens** from whole tumor genome analysis

MVA Platform

Well-established safety profile
Optimal antigen display to elicit **strong, durable and specific** immune response

Viral vector Engineering

- **VacDesignR™** for **optimal design of the recombinant cassettes**
- Selection of **best promoter sequences** for optimal antigen expression, and presentation
- **Optimized pre-GMP cloning procedures** into the *myvac®* MVA backbone

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TG4050 - First Individualized Vaccine Based on the *myvac®* Technology

2 ongoing clinical trials

TG4050 monotherapy could address variety of solid tumors in patients with minimal residual disease

TG4050 demonstrated:

- Feasibility of process
- Safety
- First positive immunology data and encouraging clinical signs

DESIGNED
TO TREAT PATIENTS WITH ESTABLISHED DISEASE

TWO TRIALS DESIGNED TO PROVIDE
FIRST EFFICACY DATA AND SUPERIOR IMMUNOGENICITY

Moderately mutated tumors
Ovarian and Head & Neck cancers

Limited efficacy of checkpoint blockers (low/medium TMB*)

Patients in **clinical remission** with **undetectable residual disease**

Allows the use of TG4050 as monotherapy

Potential to extend remission period and lower relapse rate

**TMB: tumor mutational burden*

TG4050 | Ovarian Cancer Trial after Surgery and Adjuvant Chemotherapy

Phase I Trial **in up to 13 Patients** (NCT03839524)

Surgery +
Adjuvant platinum chemotherapy

Complete response
Approx. 80% of patients experience CR[1]

Patient monitoring

Clinical remission
12-month PFS of approx. 50%[1]

Asymptomatic relapse
CA-125 increase or small lesions*

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TG4050 (single agent) at first signs of asymptomatic relapse with **repeated injections** until disease progression

*low volume radiologic disease

LEAD INVESTIGATOR: Matthew S. Block,
MD, PhD, Mayo Clinic (Rochester)

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE Oncopole

MAYO CLINIC

Hôpital Pitié-Salpêtrière AP-HP

institutCurie

TG4050 is designed to **INCREASE** and **EXTEND REMISSION** period

[1] Source: Burger et al, New End J Med, 2011,365,2473
DOI: 10.1056/NEJMoa1104390

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First Patient Treated with TG4050 in Ovarian Cancer Trial

Normalization of CA-125 and ctDNA without Clinical Progression for 9 Months

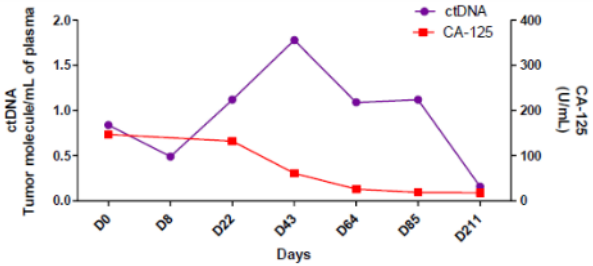
73-year-old female

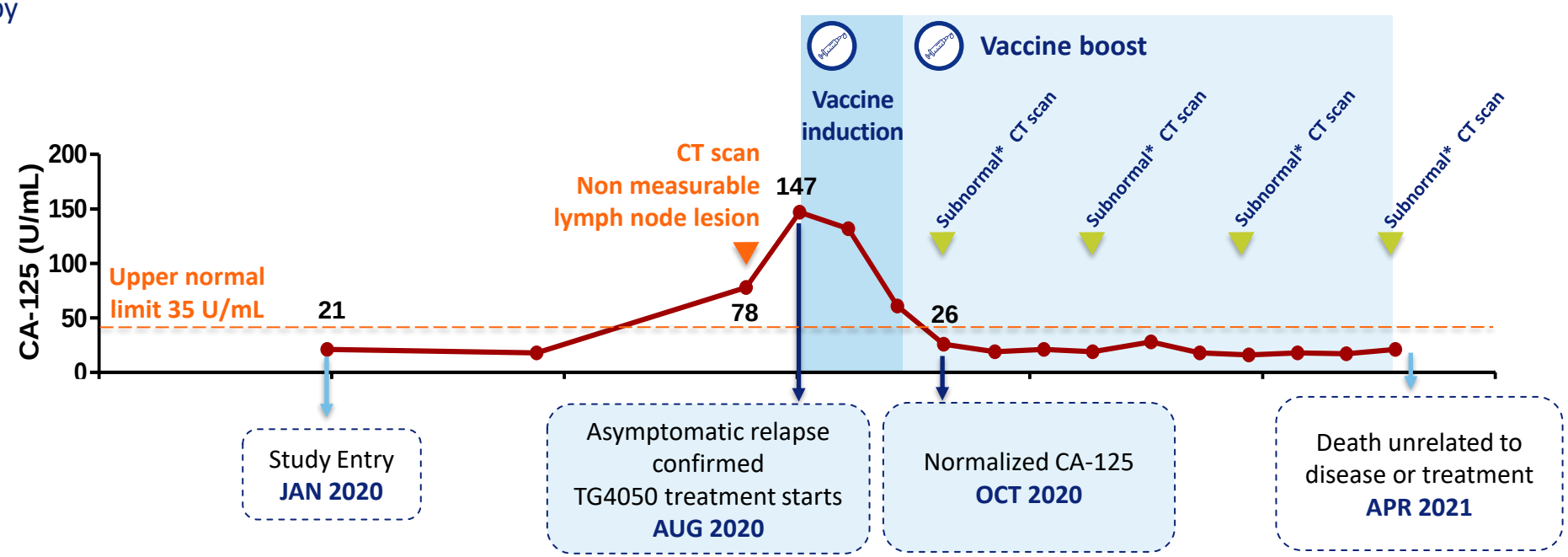
- **Grade IIIC serous carcinoma of the ovary**
- **No BRCA mutation but HRD score >45 and p53 mutation**
- **1st line/adjuvant treatment**: paclitaxel/carboplatin for 6 cycles. No maintenance therapy
- **Moderate TMB**

Relevant medical history and treatments

- Hypertension, paroxysmal atrial fibrillation, aortic valve stenosis, pulmonary embolism, obesity, dyspnea exertional
- Lisinopril, Cardia XT, Metoprolol succinate, furosemide (HTA), aspirin (atrial fibrillation)

Decline in ctDNA was concomitant with CA-125 normalization and disease control





2022 ASCO ANNUAL MEETING

Delord *et al*, "Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OvC) and head and neck squamous cell carcinoma (HNSCC)" ASCO 2022, June 5, 2022, Poster presentation

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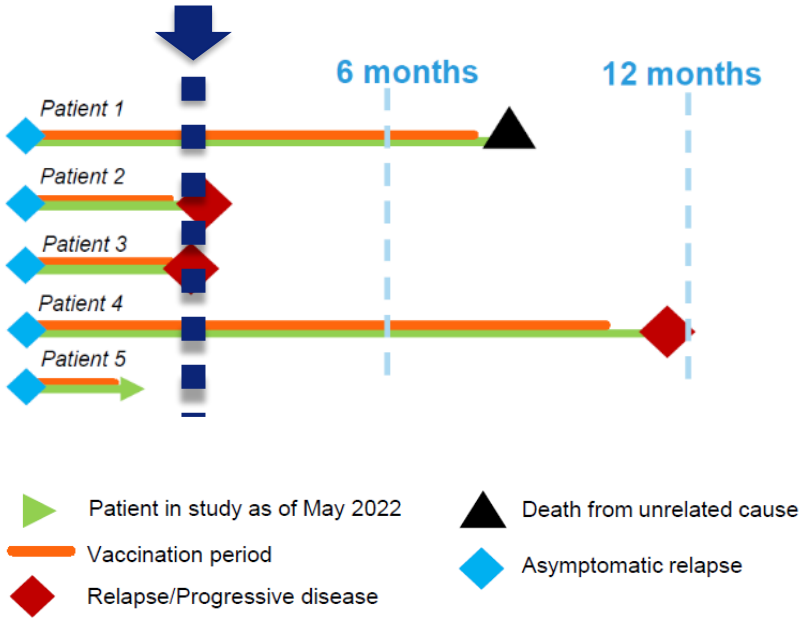
Extremely Promising First Signals of Clinical Activity

From Repeated Injections of TG4050 as Monotherapy in Patients with Minimal Residual Disease

Ovarian Cancer Trial

As of mid-May 2022

Expected time
of clinical progression[1]



Good safety profile

No related SAEs

Patient #1 treated after an elevation of CA-125 **experienced a normalization of CA-125 without clinical progression for 9 months** until death from an unrelated chronic illness.

Patient #4 with radiologic lesions was **stable** for **11.4 months** after the first injection.

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[1] Wang et al. "CA-125–indicated asymptomatic relapse confers survival benefit to ovarian cancer patients who underwent secondary cytoreduction surgery", Journal of Ovarian Research, 2013, 6:14

2022 ASCO ANNUAL MEETING

Delord *et al*, "Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OvC) and head and neck squamous cell carcinoma (HNSCC)" ASCO 2022, June 5, 2022, Poster presentation

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

TG4050 is designed to **INCREASE** and **EXTEND REMISSION** period

Randomized Phase I Trial in **30 Patients** (NCT04183166)

Surgery + Adjuvant chemoradiotherapy

Complete Clinical Response (approx. 90%)
RANDOMIZATION

Arm **A**

TG4050 (single agent) Repeated injections

Recurrence

TG4050 + SOC (incl. checkpoint blockers)

Arm **B**

Patient monitoring

Recurrence
12-month PFS is approx. 60% (w/o TG4050) [1]

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

The Clatterbridge Cancer Centre NHS Foundation Trust

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MAYO CLINIC

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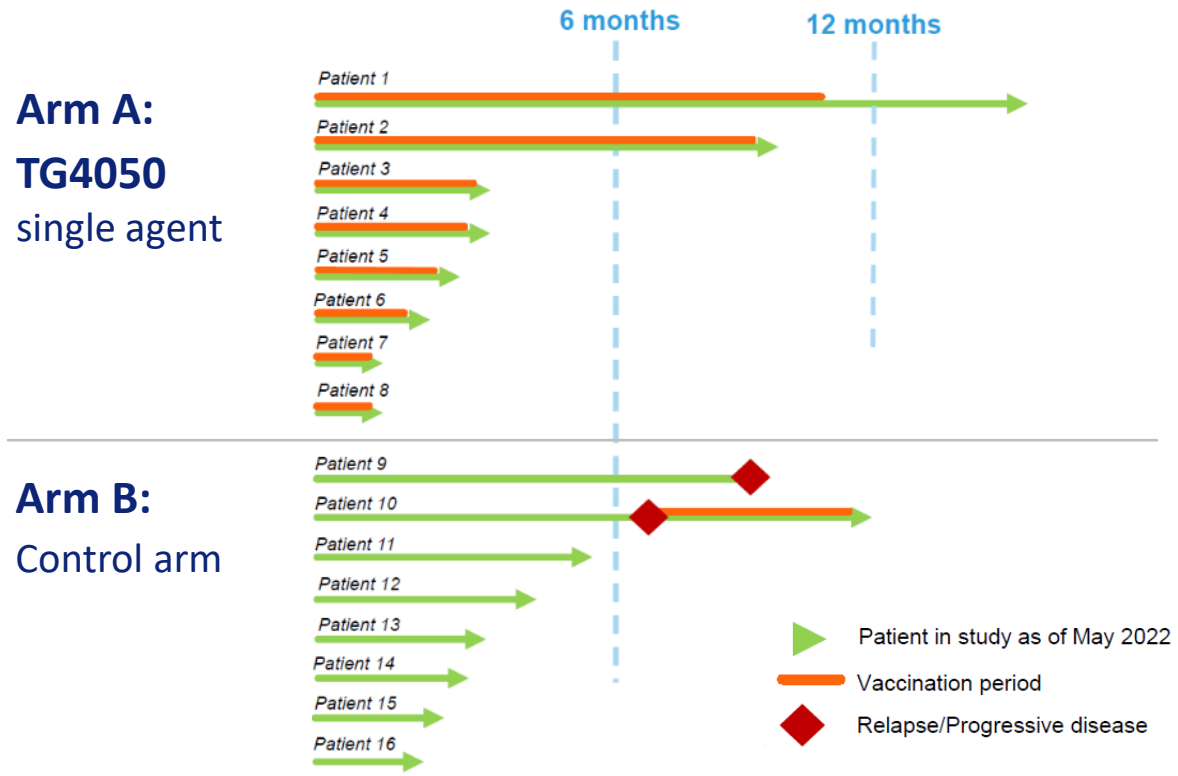
[1] Source: Bernier et al, The Oncologist,3005,10,215

Extremely Promising First Signals of Clinical Activity

From Repeated Injections of TG4050 as Monotherapy in Patients with Minimal Residual Disease

Head & Neck Cancer Trial

As of mid-May 2022



No related SAEs
Good safety profile

All 8 treated patients are stable

2 patients of the "control" arm have already progressed

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2022 ASCO ANNUAL MEETING

Delord *et al*, "Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OvC) and head and neck squamous cell carcinoma (HNSCC)" ASCO 2022, June 5, 2022, Poster presentation

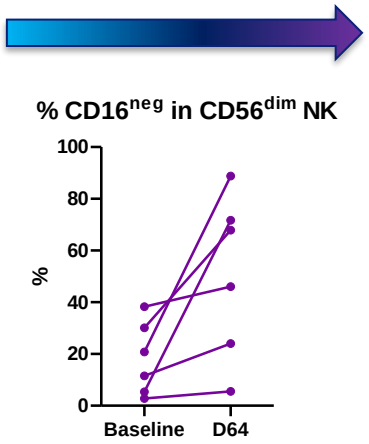
Unprecedented Rate of T Cell Response Against Tumor Specific Epitopes

Profound Remodelling of Immune Cells Consistent with Anti Tumor Response

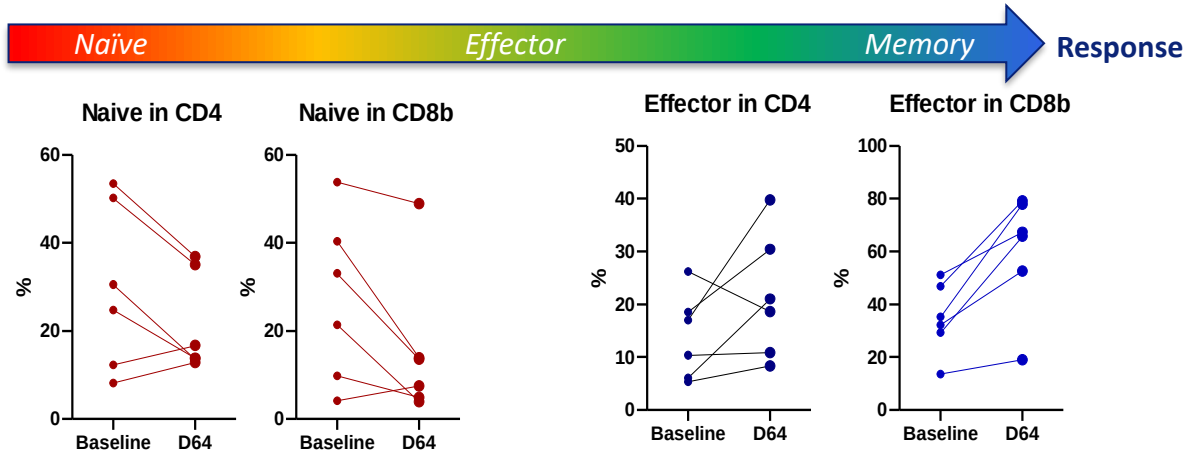
Differentiation of **CD4 and CD8 into effector cells** are consistent with the **development of an active adaptive response**

NK cells phenotype suggests **ongoing antitumor activity**

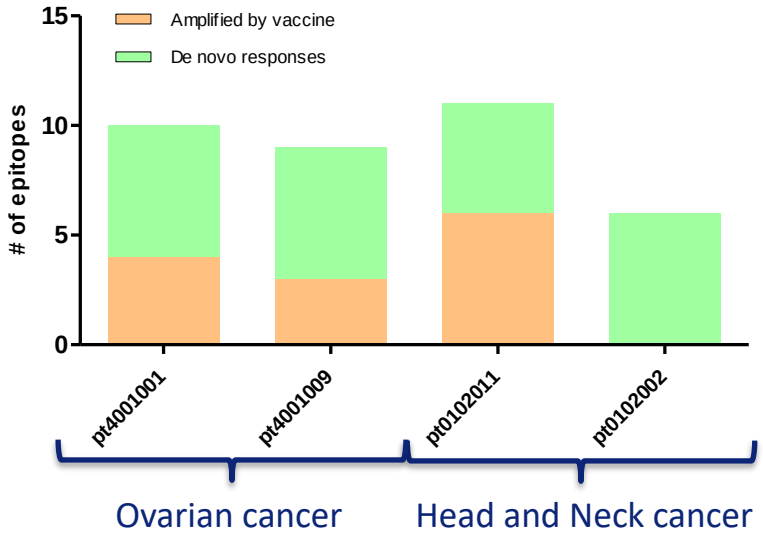
Priming of innate immunity



Immune differentiation during response to immunotherapies



Number of positive responses per patients



Responses were either **amplification of pre-existing responses or *de novo* responses** induced during vaccination

Responses were observed for all subjects with a **median of 10 positive responses** per patient, out of 30

➔ **Best-in-class**

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

Additional data to be presented at **major scientific congresses,** incl. in **H2 2022**

These **immune and clinical data** will serve to identify the most appropriate path **to take TG4050 to Phase II and forward**

myvac

one patient • one genome • one vaccine

Our Unique Invir.IO™ Platform

Rapidly Generating Multiple Virus-Powered Off-the-Shelf Drug Candidates

invir io

Administered via the Intravenous Route (IV), Oncolytic Viruses Could Be the “Next Big Thing”

Injectable lesions

Locally advanced cancers
(*e.g.* SSCC, soft tissue sarcoma, melanoma wo visceral lesions)

With IT* administration
Use restricted to superficial lesions

Non-injectable lesions

Metastatic cancers
(*e.g.* NSCLC, SCHNC, TNBC, melanoma w visceral lesions)

With IV** administration, invirio has the potential to **enlarge the number of solid tumors and expand potential addressable markets**

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*IT: intratumoral administration

**IV: intravenous administration

Invir.IO™ Oncolytic Viruses Are Designed to Address Most Cancer Indications

Competitive Advantage of the Patented Backbone $VV_{cop}TK^{-}RR^{-}$ from Invir.IO™ Platform

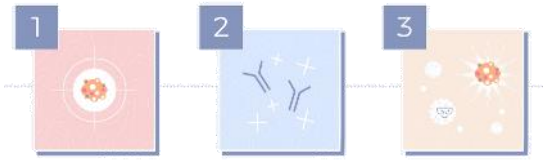
Safety and Selectivity

Patented $TK^{-}RR^{-}$ deletion for enhanced tumor selectivity

Broad spectrum infectivity
Can infect all types of tumor cells

No nucleus integration

Tumor eradication including metastases



Multiple modes of action

Highly infective capabilities and **strong lytic effect**

Good immunological balance (Th1 vs Th2, anti-tumor vs anti-viral responses, etc.)

Broad applicability

Large capacity (up to 25kb)

Several payloads can be encoded in one multi-armed OV

Immune and TME modulators (incl. full length Ab), immune booster, prodrug activators, …

Can address all solid tumors

Demonstrated PoC of IV administration

Strong back record of clinical use

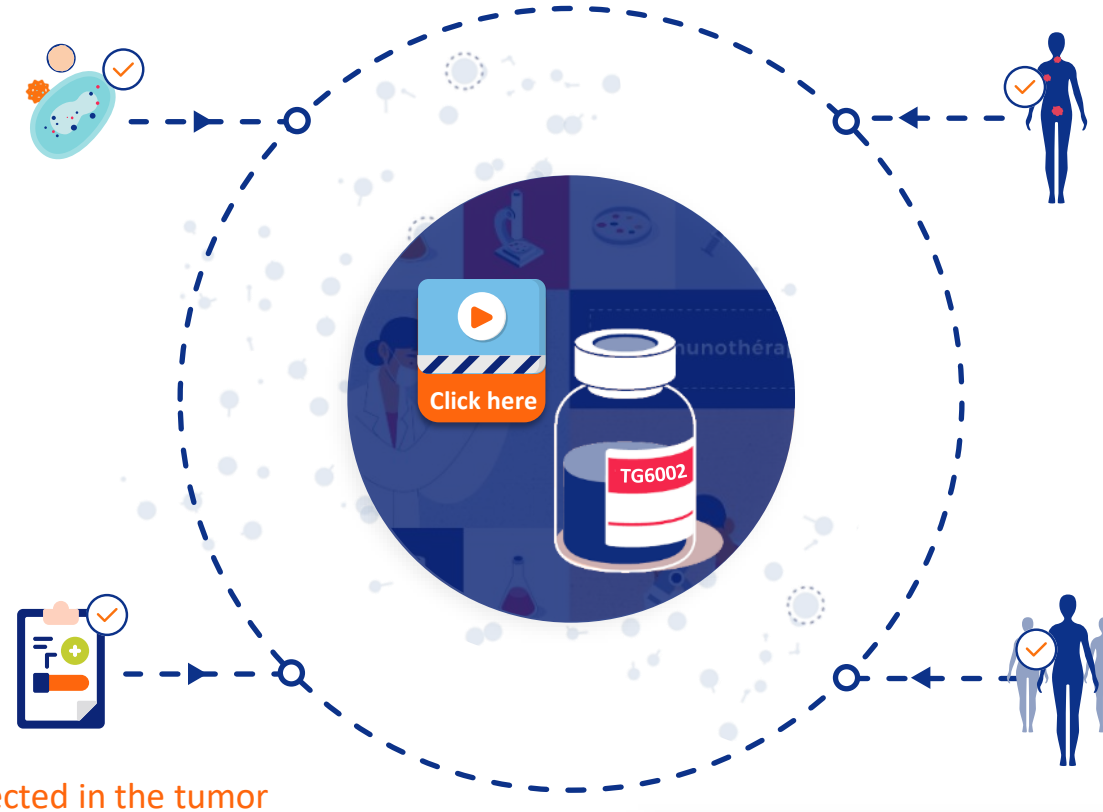
Well established process for GMP manufacturing

TG6002 | Chemotherapy Produced Directly in the Tumor

Ongoing Phase I Trials assessing systemic routes of administration

Oncolytic armed with *FCU1* gene, prodrug activator

Converts 5-FC into 5-FU, a potent chemotherapy agent



Indication: 5-FU sensitive cancers

Current SoC in 2L: bevacizumab + folfiri/folfox (3L: regorafenib, TAS-102)

OS: ~13 months

2L: 180,000 pts/year
– EU 28 & US

PoC clinical data for IV administration

After IV infusion, TG6002 was detected in the tumor and induced the production of 5-FU – no major SAE (Phase I interim results)

Two ongoing Phase I/IIa trials

evaluating IV* and IHA** administrations

Objective: determine the best regimen (route of administration, schedule and dose) to confirm TG6002 / 5-FC efficacy in Phase IIa

Initial Phase I data expected in Q3 2022

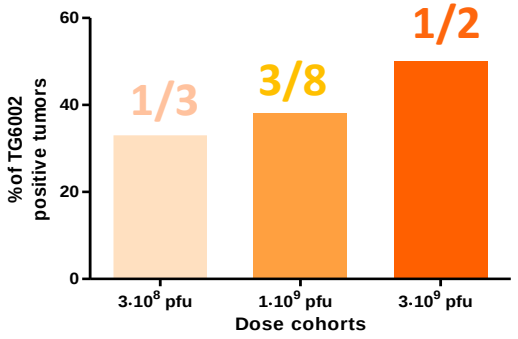
** IV: intravenous administration **IHA: intrahepatic artery administration*

TG6002 | Interim Phase I Data Presented at AACR and ESMO 2021

Clinical PoC of the Feasibility of IV Route for our Patented VV_{cop} $TK^{-}RR^{-}$ Virus

TG6002 replicates in tumor tissue without sign of widespread replication

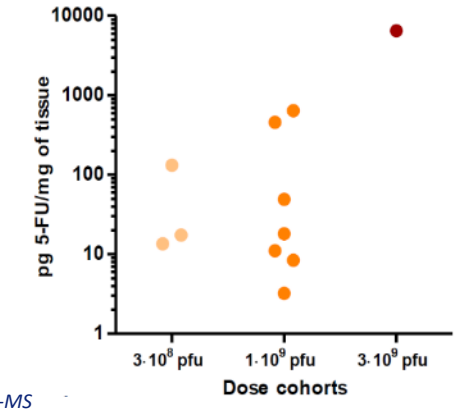
Fraction of tumor tissue positive for TG6002 by qPCR or plaque assay*



** Sensitivity of qPCR of plaque assay is impacted by scarcity of viable cells in tumor biopsies*

5-FU is expressed in tumor tissue in most of the evaluable patients (3 cohorts)

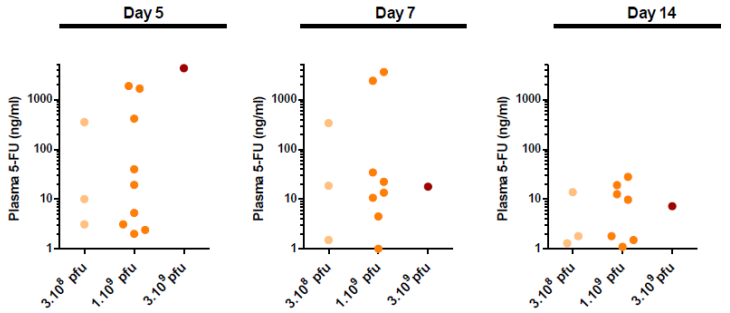
5-FU quantification in lesion biopsy on day 5*



** by HPLC-MS*

Long-lasting expression of 5-FU across the 3 dose-level cohorts

5-FU quantification in plasma



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2021 ESMO congress

Source: Cassier et al. "*Bioavailability and activity of oncolytic virus TG6002 after intravenous administration in patients with advanced gastrointestinal carcinomas*" ESMO 2021, 16–21 September 2021, Poster presentation

AACR American Association for Cancer Research

Source: Bendjama et al. "*Oncolytic virus TG6002 locates to tumors after intravenous infusion and induces tumor-specific expression of a functional pro-drug activating enzyme in patients with advanced gastrointestinal carcinomas*" 2021 AACR Annual Meeting, April 9-14, 2021, Poster presentation

BT-001 | Patented OV armed with anti-CTLA4 Ab + GM-CSF

Ongoing Phase I 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)

Exciting preclinical data

· **Outstanding and long-lasting anti-tumor activity** in several tumor models

· Strong **abscopal effect** (impact on distant lesions)

· Anti-CTLA4 Ab and GM-CSF **accumulate in tumors** with **low systemic exposure**

Can be developed for multiple cancer indications

lesions with high Treg infiltration

Ongoing Phase I

monotherapy and combination with ICI

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

50/50 collaboration with **BioInvent**

**IT: intratumoral administration*

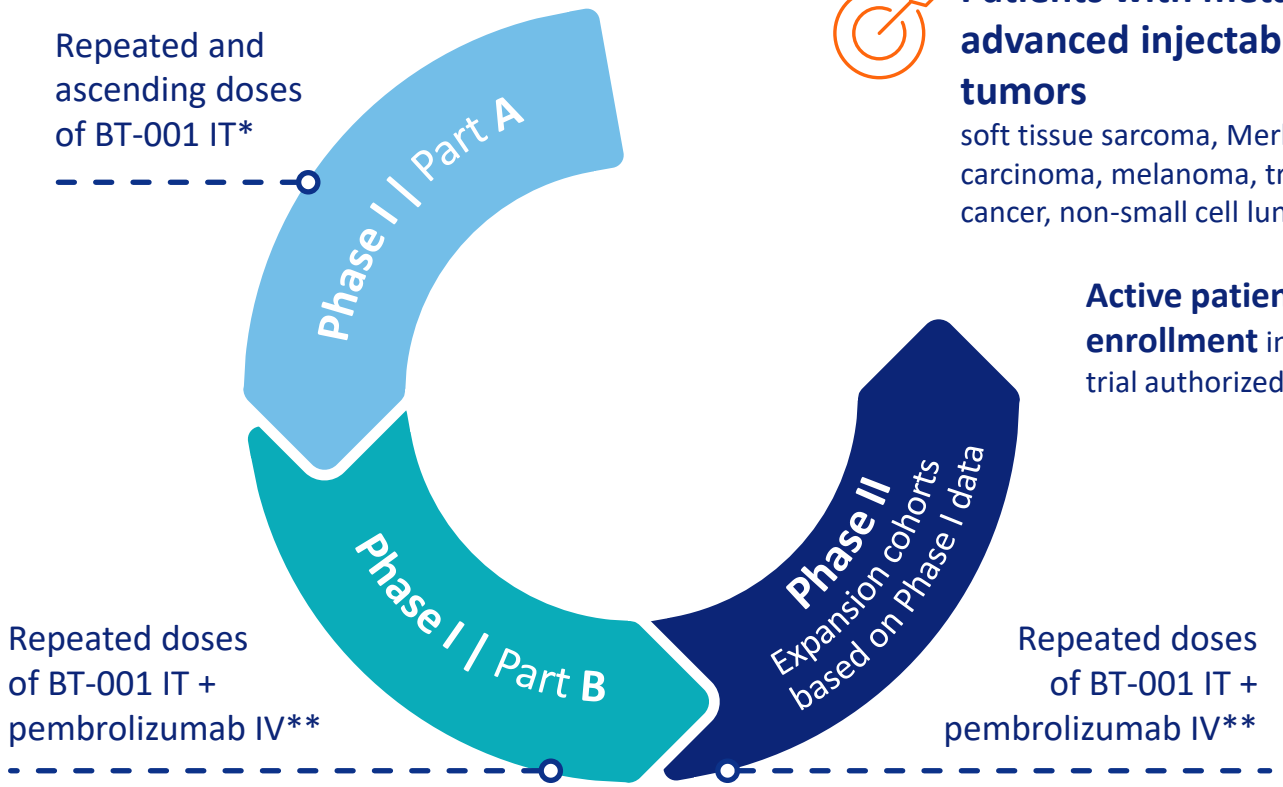
AACR ANNUAL MEETING 2022 New Orleans Marchand et al., 2022

Journal for ImmunoTherapy of Cancer Semmrich M et al., 2022

transgene

BT-001 | Phase I/II Trial Starting in Europe

Leverage the IT* Route to Accelerate Development with Anti-PD1 (NCT04725331)



Patients with metastatic or advanced injectable solid tumors

soft tissue sarcoma, Merkel cell carcinoma, melanoma, triple neg breast cancer, non-small cell lung cancer

Active patient enrollment in Europe, trial authorized in the US

Positive initial Phase I part A readout

- BT-001 is able to **replicate** and **persist in tumor tissue**
- **Anti-CTLA-4 is expressed in the tumor** with **no detectable systemic exposure**
- **No spreading** in blood or biological fluids have been detected, suggesting **high tumor specificity**
- **Tumor shrinkage** observed in one patient **at the lowest dose level**

Ph. I part B to start in H2 2022

**IT: intratumoral administration ;*
***IV: intravenous administration*

Invir.IO™ Pipeline Will Allow us to Generate Significant Value

Next Candidates are Already in Preclinical Development

invirio

Backbone with unique properties and potential

- Ability to safely be **administered IV**
- **Express selectively its payload in the tumor**, including with IV administration

Highly productive platform

- Potential to generate **multiple novel oncolytics until POC**
- **New OV(s) in clinical development** in near term

Value provider and collaboration initiator

- **AstraZeneca collaboration:** development of new OVs
- **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

AstraZeneca

BioInvent

博生吉 PersonGen

Outlook

Company Funded to Deliver Multiple Value Generating Milestones

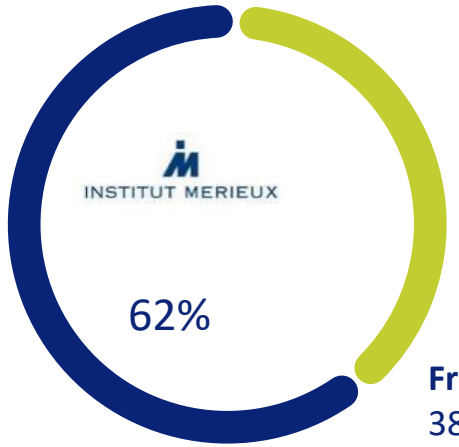
€46.8 million in **cash and cash equivalents** as of March 31, 2022

In addition: **Tasly BioPharmaceuticals shares** valued at **€18.9 million** at the end of December 2021

FINANCIAL VISIBILITY until **end** of **2023**

Ownership

As of March 31, 2022



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

2022 Upcoming Milestones

A World Leader in Virus-Powered Immunotherapies against Solid Tumors

TG4001

HPV-positive cancers therapeutic vaccine

- **TG4001**
  Phase II interim analysis
  Q4 2022

myvac

MVA individualized **neo-antigen therapeutic cancer vaccine**

- **TG4050**
  Additional Phase I data to be presented at upcoming oncology congresses **in H2 2022**

  Phase II expected to start in H2 2023

invir.io

$VV_{cop}TK^{-}RR^{-}$ **multi-armed oncolytic viruses**

- **BT-001**
  Ph. I part B (combination with pembrolizumab) to start| **H2 2022**
- **TG6002**
  End Ph. I | **mid-2022**
  Initial Phase I data | **Q3 2022**
- **AstraZeneca** Ongoing collaboration

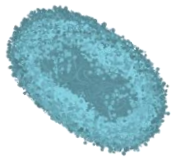
Appendices

Engineering viral vectors as immunotherapeutics

Turning foes into friends

Viral-vector vaccine

myvac

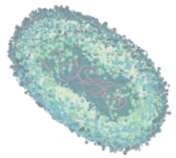


Local induction of immuno-stimulatory pathways

Expression of cancer antigens

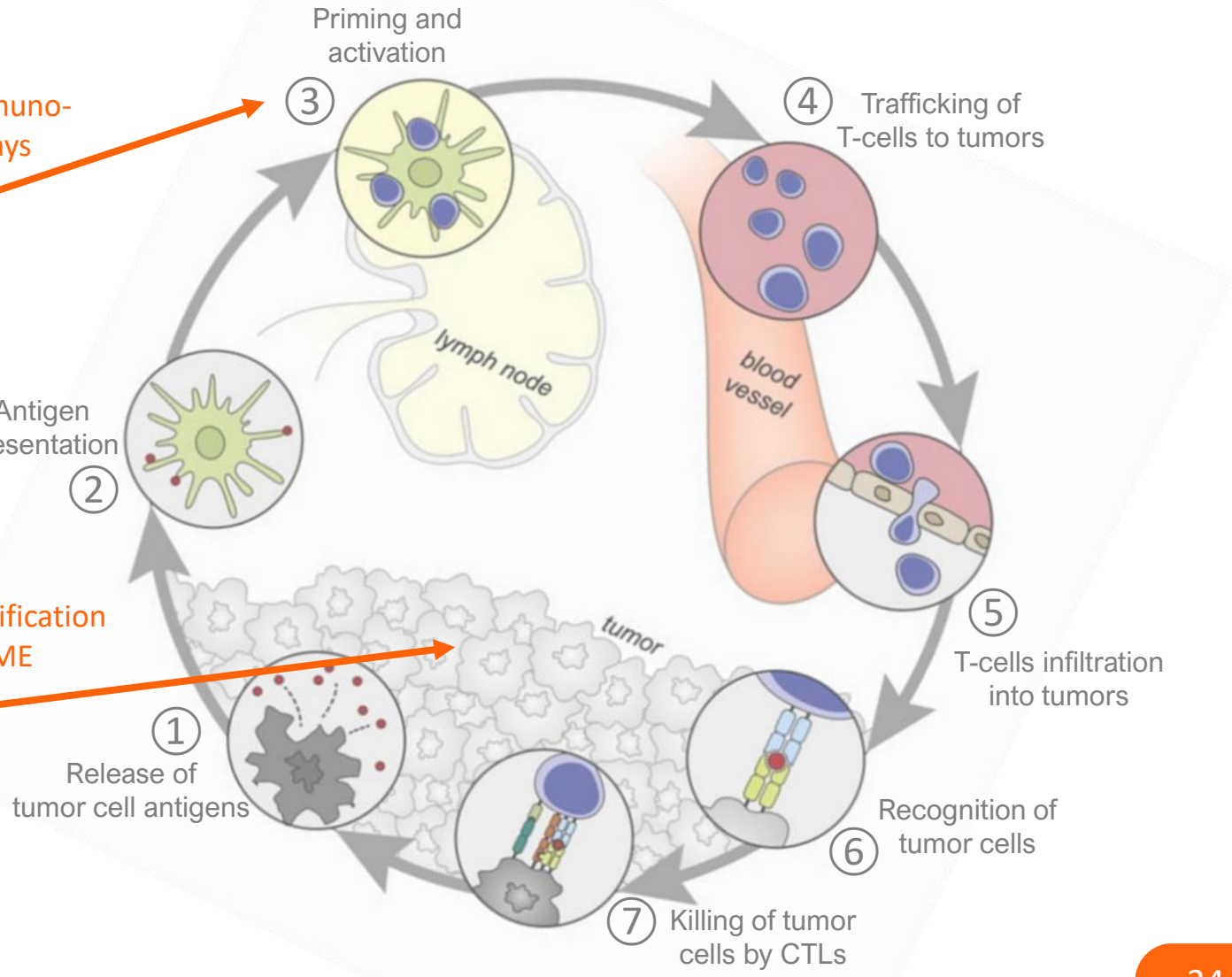
Oncolytic vector

invir io



Targeted modification of the TME

Immunogenic cell death

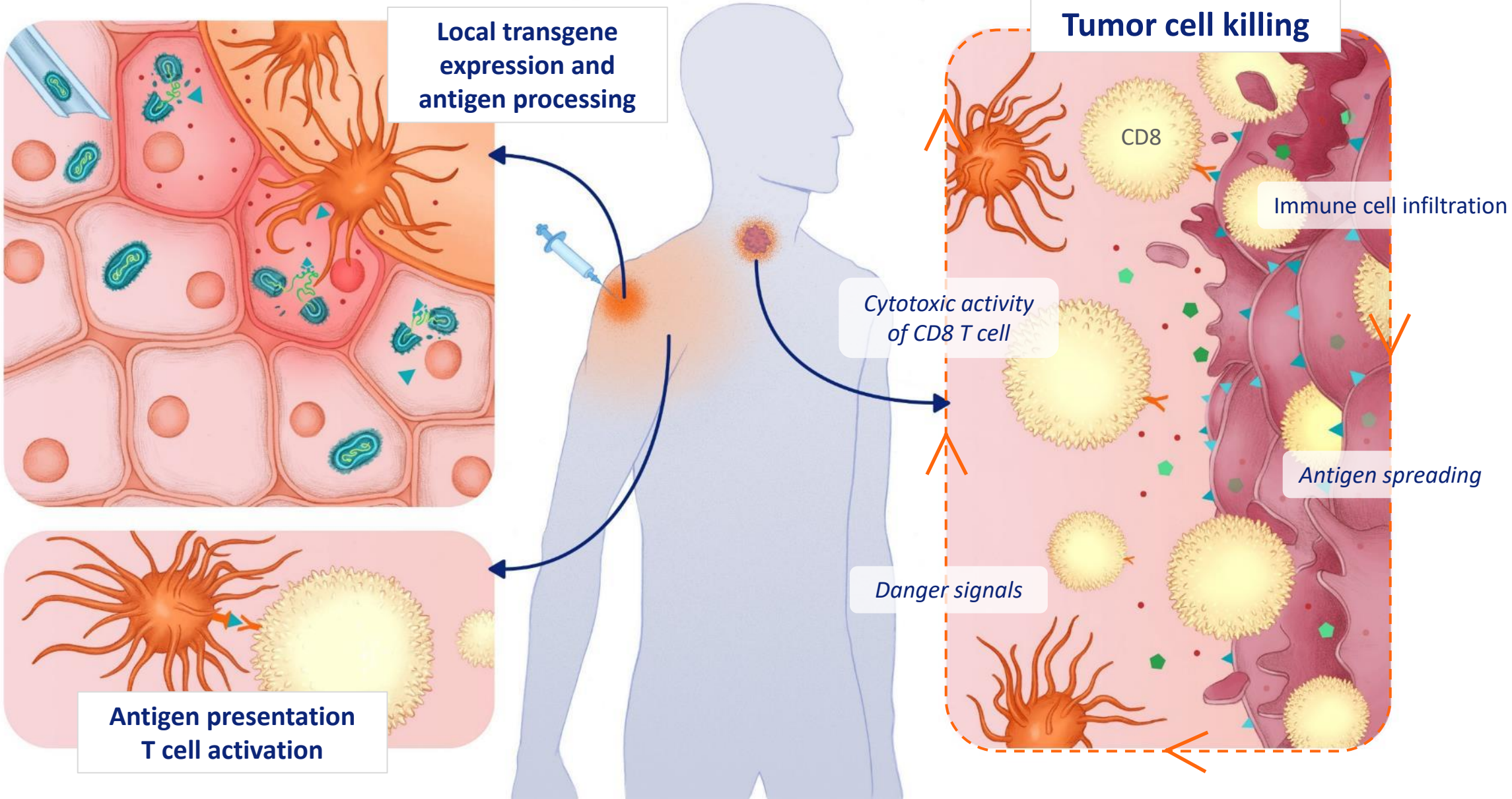


Inspired from Chen and Mellman (2013) *The tumor immunity cycle*

transgene

How Virus Powered Vaccines Treat Solid Tumors

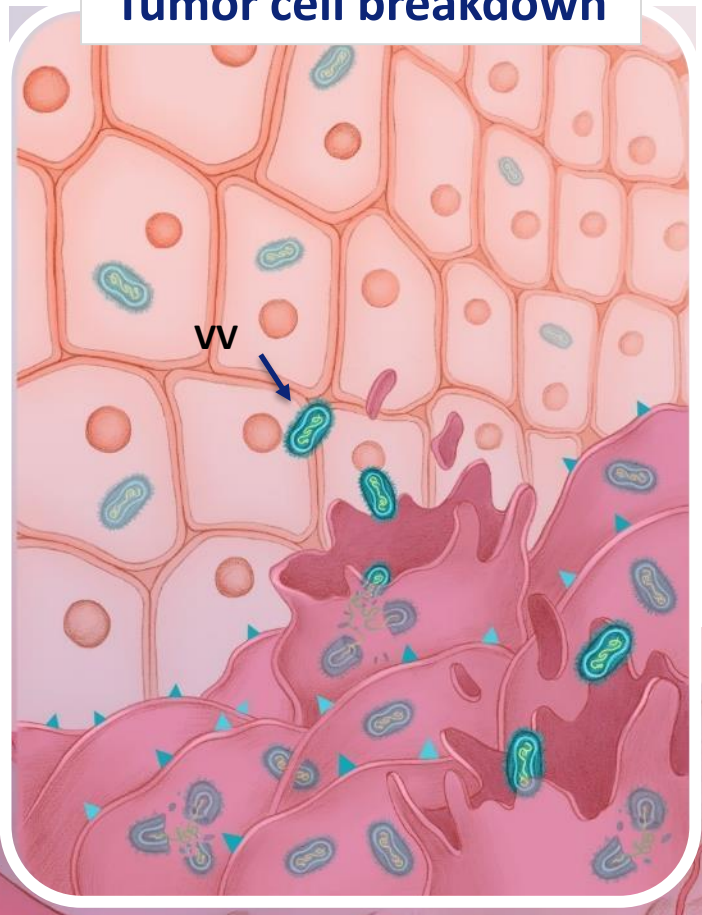
Our vaccines induce specific and strong immune response



Invir.IO™ Products Display Multiple Modes of Action in the Tumor Micro-Environment

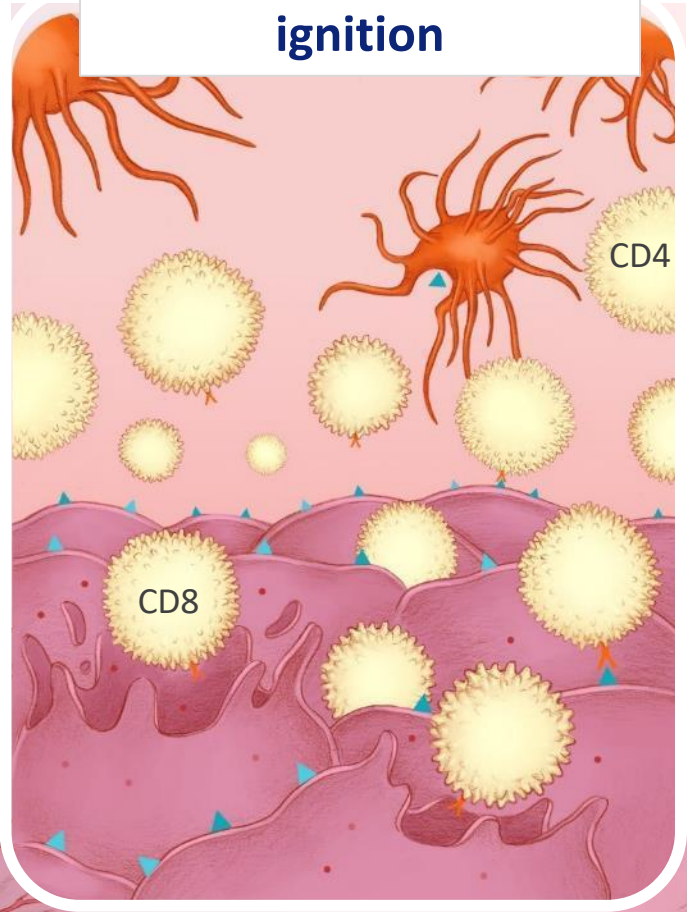
Armed oncolytics designed to improve the treatment of primary and secondary tumors

Tumor cell breakdown



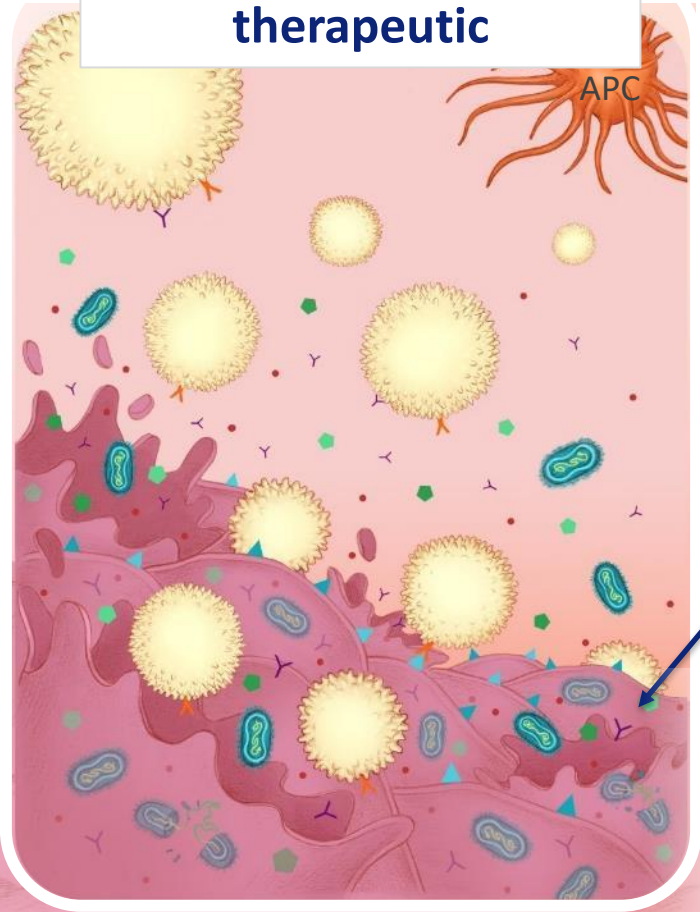
VV_{cop} $TK^{-}RR^{-}$ selectively replicate in tumor cells and triggers apoptotic cell death

Immune system ignition



OV-induced cell death is immunogenic with released of DAMPS, thus promoting immune cell infiltration and activation

Local delivery of therapeutic



Secretion of modulators of the TME from infected tumor cells

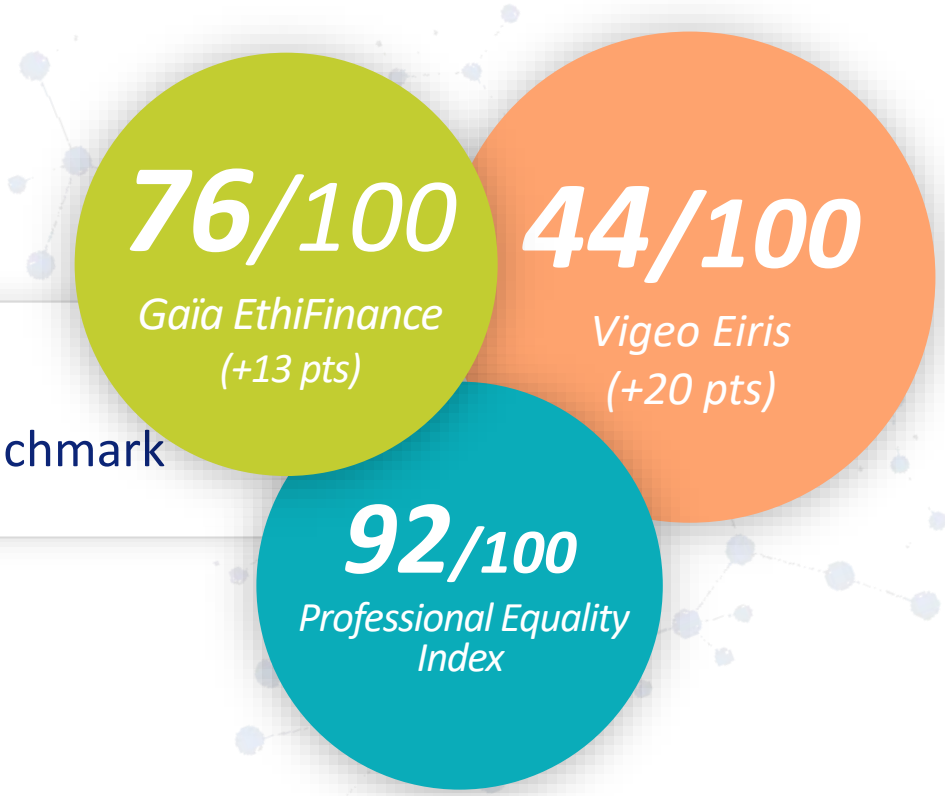
Our Vision and Environmental, Social and Governance Policy

Maintain Company's Sustainability by Creating Value, Strengthening Social Contribution and Minimizing Environmental Impact

Transgene's ESG strategy is based on six commitments

- to **patients**
- to **our partners**
- to **our employees**
- to **our shareholders and investors**
- to **society and territories**
- to **the planet**

ESG rating
above industry benchmark



Our ESG policy is detailed in the Universal Registration Document 2021, chapter 4.

URD 2021

Transgene Teams

Board of Directors

Hedi Ben Brahim
CEO & Director

Alain Mérieux
Honorary Chairman

Marie Landel
Director

Philippe Archinard
Director

Laurence Espinasse
Director

Alessandro Riva
Chairman

Jean-Luc Bélingard
Director

Maya Said
Director

Jean-Yves Blay
Director

Benoît Habert
Director

Sandrine Flory
Director*

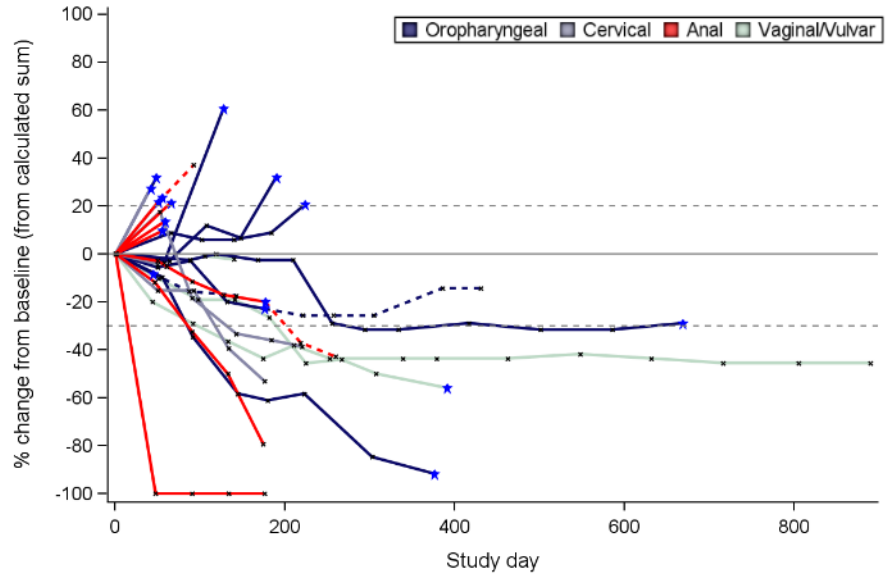
*TSGH representative

Appendices

TG4001

TG4001 | Treatment Induced Long-Lasting Responses and Changes in the Tumor Micro-Environment

Evolution of tumor size
in patients without liver metastases



TG4001 elicits strong, long-lasting and specific T-cell response against HPV16 E6 and E7

Treatment shifts « cold » tumor into « hot » tumor

- Increased CD3+ and CD8+ infiltrate
- Higher PD-L1 expression
- Expression of several genes associated with activation of the immune system

Source: Le Tourneau et al. "TG4001 (Tipapkinogene sovacivec) and avelumab for recurrent/metastatic (R/M) Human Papilloma Virus (HPV)-16+ cancers: clinical efficacy and immunogenicity." 2020 SITC Annual Meeting, 9-11 November 2020, Poster presentation

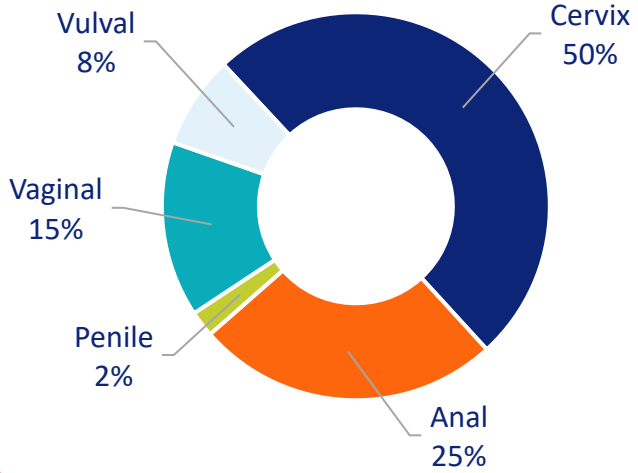
Significant Opportunity for TG4001 in Anogenital HPV16-Positive Cancers

HPV16 etiology creates a significant market opportunity

Incidence of anogenital HPV16 positive cancers w/o liver metastases

Newly diagnosed patients with metastatic disease and patients with recurrent disease

~ 25,000
new patients
per year



65%
EU27 + UK

35%
USA

Clinical outcome needs to be improved

- Current treatments, mostly radio/chemotherapy, do not address the etiology (viral origin) of the disease
- No IO drugs (ICIs) approved yet in 1L of treatment
- Pembrolizumab approved in 2L cervix cancer (USA)

Estimated cancer cases (2025) based on: 1. ICO/IARC – HPV Information Center> Prevention at a glance // 2. HPV-positive cervical cancer: Globocan/IARC 2020 Cancer Fact Sheets: cervix uteri (C53); ICO/IARC – HPV Information Center Statistics // 3. HPV-positive vaginal cancer: Globocan/IARC 2020 Cancer Fact Sheets: vagina (C52); ICO/IARC – HPV Information Center Statistics // 4. HPV-positive vulvar cancer: Globocan/IARC 2020 Cancer Fact Sheets: vulva (C51); ICO/IARC – HPV Information Center Statistics; CDC United States Cancer Statistics: Data Visualizations; SEER Cancer stat facts: vulvar cancer // 5. HPV-positive anal cancer: Globocan/IARC 2020 Cancer Fact Sheets: anus (C21); ICO/IARC – HPV Information Center Statistics; CDC>Cancer Home>HPV and Cancer>Statistics>Rates by Race and Ethnicity>HPV-Associated Anal Cancer Rates by Race and Ethnicity; American Cancer Society: Anal Cancer // 6. HPV-positive penile cancer: Globocan/IARC 2020 Cancer Fact Sheets: penis (C60); ICO/IARC – HPV Information Center Statistics; CDC>Cancer Home>HPV and Cancer>Statistics>Rates by Race and Ethnicity>HPV-Associated Cancers Rates by Race and Ethnicity

TG4001 - Anogenital cancer patients undergoing 2nd line treatment still have poor prognosis

Overview of phase 1 and 2 clinical trials in anogenital cancers – 2nd line of care

	H&N+ Anogenital	Anal Cancer			Cervical, Vaginal and Vulval Cancers	
Therapy	TG4001	Nivolumab	Pembrolizumab	Avelumab	Pembrolizumab	Nivolumab
Study	Phase Ib/II	Phase 2[ref]	Phase 1b and Phase 2[ref]*	Phase 2[ref]	Phase 2[ref]	Phase 2[ref]
Number of patients	N = 34	N = 37	N = 137	N = 30	N = 98	N = 19 cervical N = 5 vaginal/ vulvar
Indication	Head and Neck + anogenital Cancers	Anal Cancer	Anal Cancer	Anal Cancer	Cervical Cancer	Cervical, vaginal and vulval Cancer
Line of Care	2nd Line	2nd Line	2nd Line	2nd Line	2nd Line	2nd Line
Overall Response Rate	35%	24%	10.9%	10%	12.2%	26.3% 20.0%
Median Progression Free Survival (months)	5.6	4.1	2.1	2.1	2.1	5.1
Median Overall Survival (months)	N/A	11.5	11.7	10.8	9.4	21.9

TG4001 Phase 2 clinical trial ongoing – expecting interim analysis in Q4 2022

* Pooled analysis

TG4001 Competitive Landscape - Off the Shelf HPV16 Cancer Treatment

Overview of modalities approved and in development to treat HPV+ Cancers

	In Development						Approved	
	Cancer Vaccines						Checkpoint Inhibitor	Checkpoint Inhibitor
	Viral vectors			mRNA	Peptide		Antibody	Antibody
Company	transgene	HOOKIPA PHARMA		BIONTECH	ISA Pharmaceuticals		Pembrolizumab (Merck)	Nivolumab (BMS)
Technology	MVA virus	Arenavirus		mRNA	Long peptide		mAb	mAb
Clinical stage	Phase II Randomized	Ph. I/II Phase I	Ph. I/II Part II	Phase II Randomized	Phase II	Phase II	Approved	Approved
Indication	Anogenital cancer without liver metastasis	HNSCC	HNSCC	SCCHN	Incurable solid tumors	Cervical cancer	SCCHN	SCCHN
Line of Care	2L locally advanced or 1L metastatic	1L + post-standard of care (2L)	1L advanced or metastatic	1L recurrent or metastatic PDL1>0		2L recurrent or metastatic	1 Line Metastatic	2 Line Recurrent or metastatic
Next milestone	Interim Analysis in Q4 22	Data in H2 2022	Data in H2 2022	Primary completion date 2025	Completed	Completion date 2024	n.a.	n.a

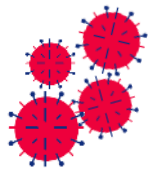
Appendices

TG4050

myvac® | An Integrative Approach Capitalizing on Multiple Cutting-Edge Technologies

Taking the Treatment of Each Patient to a New Level

MVA Viral Vector: a Powerful Platform for Vaccine Development



Well-established safety profile

- Strong track record from both prophylactic campaigns, and from clinical trials in oncology
- Safe in a large variety of routes of administration

Optimal antigen display

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

Click here

Multiple Proprietary Innovative Technologies

Artificial Intelligence

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

Viral vector Engineering

- **VacDesignR™** for **optimal design of the recombinant cassettes**
- Selection of **best promoter sequences** for optimal antigen expression, and presentation
- **Optimized pre-GMP cloning procedures** into the *myvac*® MVA backbone

GMP Manufacturing Capabilities

Production process in place

- Scaled up to **~2 batches/wk**
- Optimization in progress

*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 has a unique positioning among personalized cancer vaccines

Company	transgene		BIONTECH			vaccibody / nykode therapeutics		gritstone ONCOLOGY	
Technology	Modified Vaccinia Ankara (MVA) virus		mRNA			DNA		self replicating RNA (+adenoviral vectors)	
# targets	Up to 30		20			20		20	
Administration	SC injection (like prophylactic-vaccine)		Intravenous			Intramuscular needle-free injection		Intramuscular injection	
Clinical stage	Phase I Randomized	Phase I	Phase II Randomized	Phase II Randomized	Phase I	Phase I/IIa	Phase Ib	Phase I/II	Phase II/III Randomized
Indication	HPV- SCCHN	Ovarian cancer	Advanced melanoma	Rectal and colon cancers	PDAC*	Adv/met solid tumors	Adv/met solid tumors	Advanced solid tumors	MSS-CRC*
Setting	Monotherapy	Monotherapy	Combination	Monotherapy	Combination	Combination	Combination	Combination	Combination
Endpoints	Reduction of CA-125 Rate of patients with immune response Tumor response rate	Event-free survival duration Tumor response rate	Progression-free survival Overall response rate	Recurrence-free survival	Safety, RP2D Immunogenicity Tumor size assessment	Safety Immunogenicity ORR	Safety Immunogenicity ORR	Safety, RP2D ORR Immunogenicity	Decrease of ctDNA PFS
Next milestone	• Additional data in H2 2022 • Start Phase 2 trial in H2 2023		Data expected H2 22	Primary completion date Sept. 2023	Completed	Primary completion date March 2024	Primary completion date Dec. 2024	Completed	Primary completion date Feb. 2027

TG4050
Areas of Differentiation

Simple drug delivery method: Subcutaneous injection of a single product

Deliver single-agent activity data

Aims to extend remission period of patients with residual disease

Additional Phase 1 data in H2 2022
Start Phase 2 trial in H2 2023

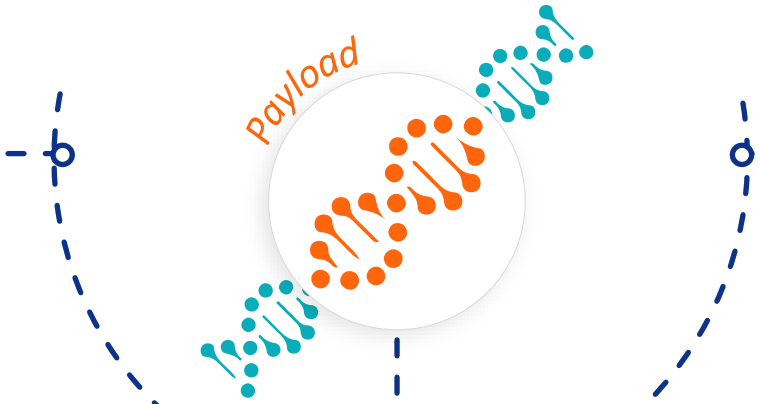
*MSS-CRC: microsatellite stable colorectal – PDAC: Pancreatic ductal adenocarcinoma

Appendices

Multiple Payloads | Deliver Significant Patient Benefits

Local payload delivery helps better neutralize the tumor in an effective and safe manner by limiting systemic exposure

Targeted insertion of recombinant payload at selected loci in the Vaccinia genome



IMMUNE MODULATORS

- **ICIs** (e.g. PD-1/PD-L1, CTLA4, TIM-3, …)
- **Monoclonal antibodies or fragments** (full length antibody, scFV, Fab, …)
- **Enzymes** controlling immunosuppressive metabolites (e.g. ADA)

PRODRUG ACTIVATORS

- ***e.g.* Fcu1 (TG6002), an enzyme that locally converts 5-FC into 5-FU, a chemotherapeutic agent**

IMMUNE BOOSTERS

- **Cytokine** (e.g. GM-CSF, interleukins, …)
- **Agonistic ligands** (e.g. CD40L, Flt3L, …)
- **Growth Factors** (e.g. VEGF)

Several payloads can be encoded in one multi-armed OV

(several loci, up to 20-25 kb capacity)

Multiple payload sourcing approaches

TG6002 | Phase I/IIa Trial to Evaluate Intravenous Administration of $VV_{cop}TK^{-}RR^{-}$ (NCTNCT03724071)

Phase I (dose escalation completed)

Patients with **advanced gastro-intestinal carcinomas**

Patients having failed and/or intolerant to standard therapeutic options

Administration schedule optimization

Arm **A**: $1x10^6$ to $3x10^9$ pfu - 3 infusions in 3 weeks (days 1, 8 and 15)

6 cohorts - Completed

Arm **B**: $1x10^9$ pfu and $3x10^9$ pfu - 3 infusions in 1 week (days 1, 3 and 5)

2 cohorts - Ongoing

Multicenter trial ongoing in Spain, France and Belgium

End of Phase I expected in mid-2022

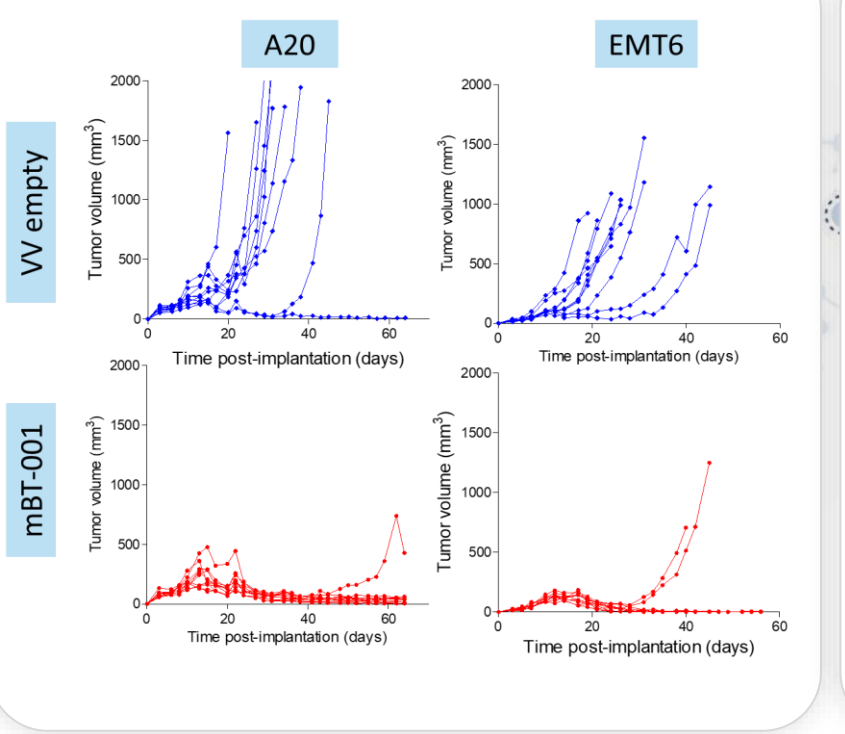
Phase IIa

Patients with **5-FU sensitive tumors**

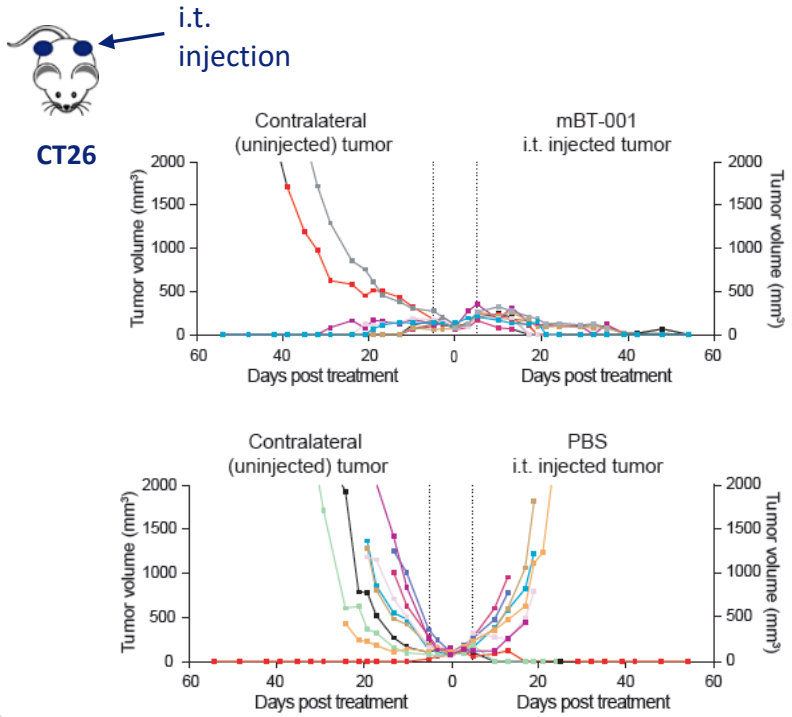
Study design based on best regimen (recommanded Phase II dose and administration schedule)

BT-001 | Exciting Preclinical Data

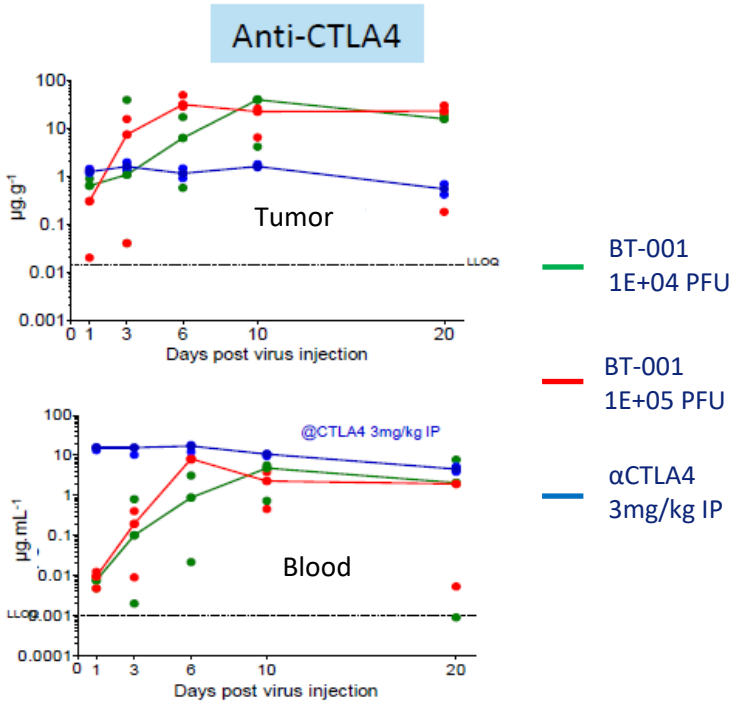
Outstanding and long-lasting anti-tumor activity in several tumor models



Strong abscopal effect (impact on distant lesions)



Anti-CTLA4 Ab and GM-CSF accumulate in tumors with low systemic exposure



Semmrich et al., BT-001, an oncolytic vaccinia virus armed with a Treg-depleting human recombinant anti-CTLA4 antibody and GM-CSF to target the tumor microenvironment, SITC, Nov. 2020

Marchand et al., "BT-001, an oncolytic Vaccinia virus armed with a Treg-depletion-optimized recombinant human anti-CTLA4 antibody and GM-CSF to target the tumor microenvironment", AACR, June 2020

CONTACT

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and Corporate Communication

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