Virus Powered Immunotherapies against Solid Tumors

Corporate Presentation

January 10, 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.

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Transgene | A World-Leader in Virus Powered Immunotherapies

Ability to select and engineer various products, thanks to our experience in viral vectors, protein engineering, and tumor antigens

Customised and **off-the-shelf** products

Solid safety track record

Demonstrated induction of immune response, including tumor-specific T cell response, associated with anti-tumor activity

Integrated GMP manufacturing capacity for rapid delivery of pilot scale batches

Ability to **conduct clinical studies until POC**

Attractive technologies

Collaborations with NEC, Merck/Pfizer, AstraZeneca,

Mayo Clinic, Institut Curie

Transgene's technologies could deliver a game changing approach to the treatment of solid tumors

Right **virus**

Right **payload**

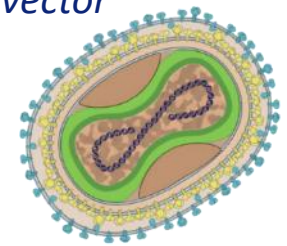
Right **indication**

Right **patient population**

Our Expertise Translates into Two Unique Technology Platforms

Able to target multiple solid tumors

Viral vector



- Priming of innate and adaptive immunity
- Demonstrated safety

THERAPEUTIC VACCINE (MVA)

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Patient specific antigens selected to generate the optimal immune response

Immune T cell activation through multi-mechanisms

ONCOLYTIC VIRUS ($VV_{cop}TK^{-}RR^{-}$)

invir io

Direct and specific tumor oncolysis

Additional activity generated by **therapeutic payloads**

Immune cells activation through multi-mechanisms

TUMOR CELL **DEATH**

Enlarged immune response & repertoire

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2021 - All programs progressing in line with forecast

Significant milestones expected in next 18 months

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

- **TG4050**
  First positive data from the first patients treated in two Phase I trials

  Additional data to be presented at an oncology congress | **1H 2022**

TG4001

HPV-positive cancers therapeutic vaccine

- **TG4001**
  First patients enrolled in randomized Phase II trial

  Interim analysis data | **end of 2022**

invir io

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

- **BT-001**
  First patients enrolled – US IND approval
  Initial Phase I data | **1H 2022**
- **TG6002**
  Clinical PoC of IV admin. presented @AACR & ESMO 2021
  Next readout | **1H 2022**
- **AstraZeneca** 1st licence option exercised

Multiple Opportunities to Transform Solid Tumor Therapy

Product	Indication	Target/Transgene	Design	Preclinical	Phase I	Phase II	Next step
THERAPEUTIC VACCINES							
TG4050 myvac Orchestrating a brighter world NEC	Ovarian cancer Head and neck cancers	30 neoantigens					**Additional Phase I data to be presented in 1H 2022**
TG4001	Anogenital HPV+ cancers	HPV16 E6 – E7					**Interim analysis end of 2022**
ONCOLYTIC VIRUSES (OV)							
TG6002	Gastro-intestinal cancers (IV*) Colorectal cancer (IHA*)	5-FU chemotherapy					**End of Ph. I 1H 2022** **1st Ph. I data mid-2022**
BT-001 invirio BioInvent	Solid tumors	Anti-CTLA4 + GM-CSF					**1st Ph. I data 1H 2022**
OVs invirio	Solid tumors	Undisclosed					**Best candidates selection to enter into clinical dev.**
5 OVs invirio AstraZeneca		Undisclosed					**Potential further option exercise**

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

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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

ROUTINE TUMOR BIOPSY

Patient

STANDARD GENE/EXOME SEQUENCING

Next generation sequencing

DATA PROCESSING, ARTIFICIAL INTELLIGENCE

Selection of 30 neoantigens

GENE EDITING

Vaccine generation

GMP MANUFACTURING

Production of the individual batch

TREATMENT ADMINISTRATION

Patient

Sequencing Lab

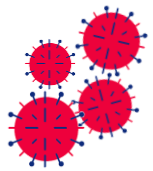
Orchestrating a brighter world NEC

transgene

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

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GMP manufacturing capabilities

Production process in place, scaled up to ~2/3 batch/wk
Optimization in progress

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*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 | Ovarian Cancer Trial after Surgery and Adjuvant Chemotherapy

Phase I trial in up to **13 patients** (NCT03839524)

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

First patient treated in **August 2020**

Surgery + Adjuvant Platinum chemotherapy

Complete response

Approx. 80% of patients experience CR

Clinical remission

Asymptomatic relapse
(CA-125 increase or small lesions*)

12-month PFS is approx. 50% (w/o TG4050) [1]

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

Data generated from **4 patients** with advanced high grade ovarian cancer who received TG4050

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

MAYO CLINIC

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE Oncopole

Hôpital Pitié-Salpêtrière AP-HP

institutCurie

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*low volume radiologic disease

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

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

Randomized Phase I trial in **30 patients (NCT04183166)**

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

First patient treated in **January 2021**

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]

6 patients with HPV-negative, advanced-stage head and neck cancer were randomized (Arm A + Arm B),
o/w **2** patients received TG4050 (Arm A) – which generated data
o/w 4 patients randomized in Arm B

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

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

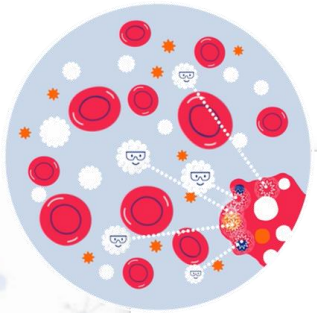
Positive Initial Data Generated in the First 6 Patients Treated With TG4050

Demonstrate the Strong Potential of this Individualized Immunotherapy

Antitumor responses observed suggest that the vaccine is able **to effectively prime the immune system**

- **Priming of innate immunity**
- **Development of adaptive responses** concomitant with maturation and activation of the patients' circulating immune cells
- Results confirmed the **capability of the AI** to **accurately select immunogenic neoantigens**

Good safety profile
No related SAEs



In addition, **first signals of clinical activity** are extremely promising for TG4050

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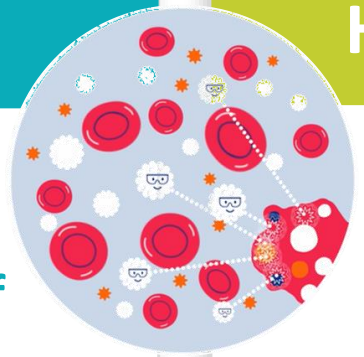
Extremely Promising First Signals of Clinical Activity

From repeated injections of TG4050 as monotherapy in patients with minimal residual disease

Ovarian Cancer Trial (n=4)



One patient treated after an elevation of CA-125 **experienced a normalization of CA-125 without clinical progression during 9 months** until death from an unrelated chronic illness.

Another patient with radiologic lesions is **stable and is still under treatment 9 months** after the first injection.

Head & Neck Cancer Trial (n=2)

One patient is **stable and is still under treatment 10 months** after the first injection.

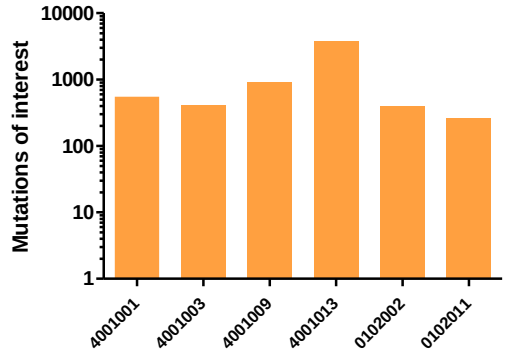
Another patient is **stable and still under treatment 5 months** after the first injection.

Their treatments are ongoing

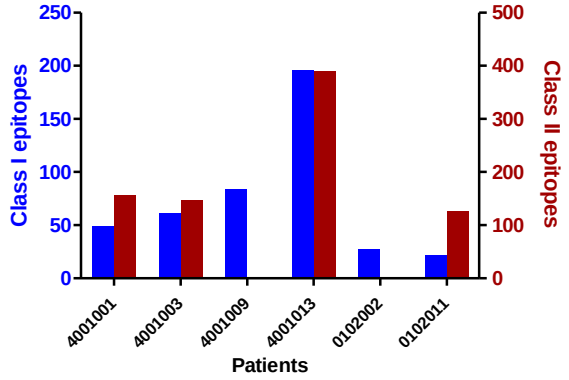
Unprecedented Rate of T Cell Response Against Tumor Specific Epitopes

A median of **10 responses** were observed across the 4 evaluated patients

Number of mutations identified in treated patients

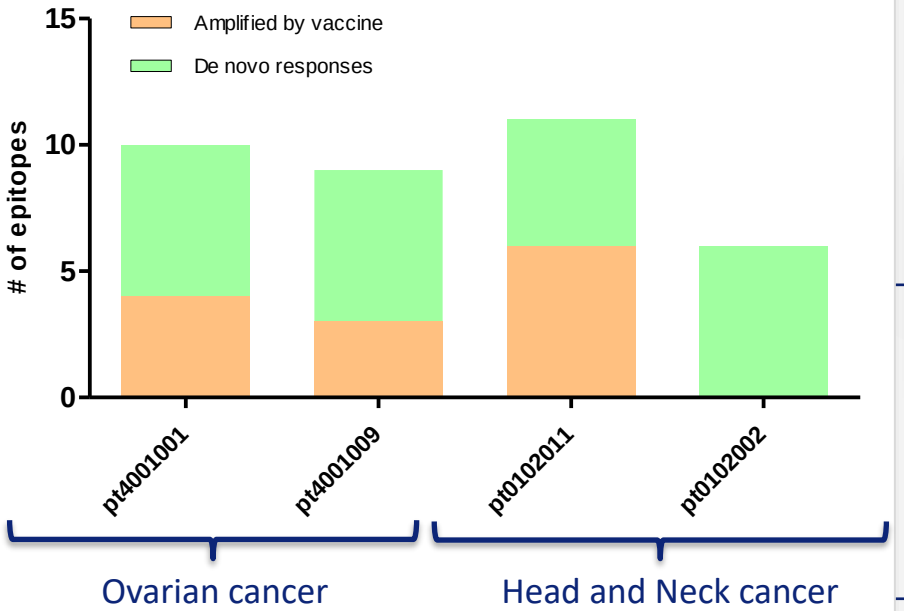


Number of class I and class II epitopes



30 targets

Number of positive responses per patients



6 to 11 responses to the vaccines were detected at **Day 64 following initiation of TG4050 treatment**

Responses were observed for **all subjects** in **both indications with a median of 10 positive response per patient**

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

Starting from a sample obtained **through routine medical procedures** we could identify **mutations, discover *bona fide* epitopes** of class I and II, **and design a vaccine** able to **induce multiple T cell responses** in treated patient

Profound Remodelling of Immune Cells consistent with Anti Tumor Response

Suggesting that the Vaccine is Able to Effectively Prime the Immune System

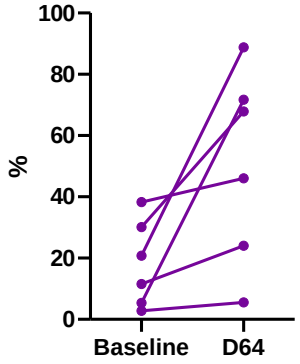
Priming of innate immunity

Immune differentiation during response to immunotherapies

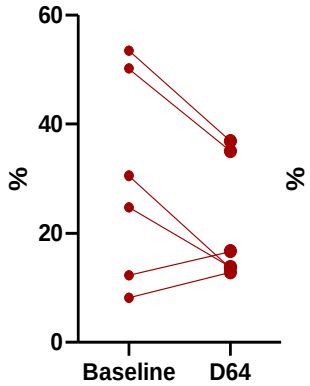
Response

Naïve ***Memory*** ***Effector***

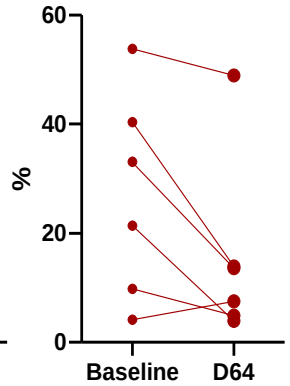
% CD16^{neg} in CD56^{dim} NK



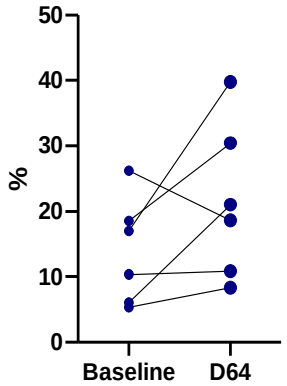
Naive in CD4



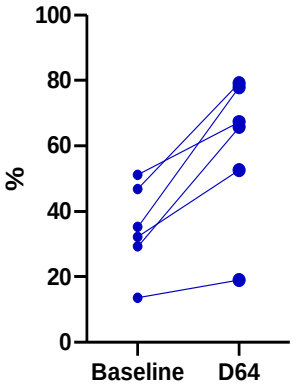
Naive in CD8b



Effector in CD4



Effector in CD8b



- CD27 and CD45 staining shows a **decrease in naive and memory CD4 and CD8 T-cell** over treatment
- **Effector subgroups of CD4 and CD8 T-cells are increased** at D64
- Maturation and differentiation of CD4 and CD8 into effector cells are consistent with the **development of an active adaptive response**
- Loss of CD16 on CD56^{dim} NK cells suggests **ongoing anti-tumor activity**

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First Patient Treated With TG4050

Enrolled in ovarian cancer trial in January 2020

73-year-old female

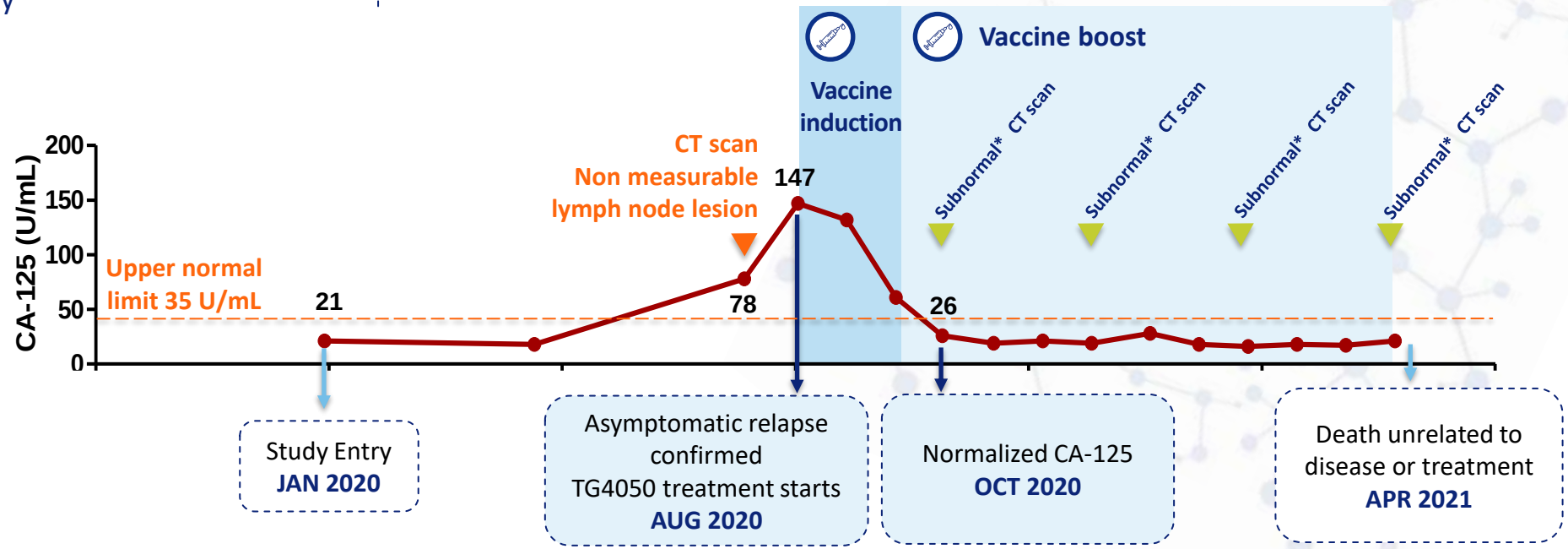
- **Grade IIIC serous carcinoma of the ovary**
- **No BRCA mutation but HRD score >45 and p53 mutation**
- **1st line/adjuvant treatment**: paclitaxel/carboplatin for 6 cycles. No maintenance therapy
- **Moderate TMB**

Relevant medical history

- Hypertension (May 2018, ongoing)
- Paroxysmal atrial fibrillation (2009, ongoing)
- Aortic valve stenosis(May 2020, ongoing)
- Pulmonary embolism (2018)
- Obesity (2016, ongoing)
- Dyspnea exertional (2018, ongoing)

Relevant treatment ongoing

- Lisinopril, Cardia XT, Metoprolol succinate, furosemide (HTA)
- Aspirin (atrial fibrillation)



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Additional data to be presented at a **major scientific congress in** H1 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

TG4001

Potential to Transform the Treatment of Anogenital HPV Positive Solid Tumors

Interim analysis expected around the end of 2022

TG4001 | Virus Powered Candidate Vaccine

The right virus
MVA

The right HPV antigens
E6 and E7

OPTIMIZED **TREATMENT FOR HPV-POSITIVE TUMORS**

The right indication
anogenital HPV16-positive cancers

The right
patient population
Patients without liver metastasis

TG4001 has potential to address all HPV positive cancers

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

Promising results, particularly in patients without liver metastasis (NCT03260023)

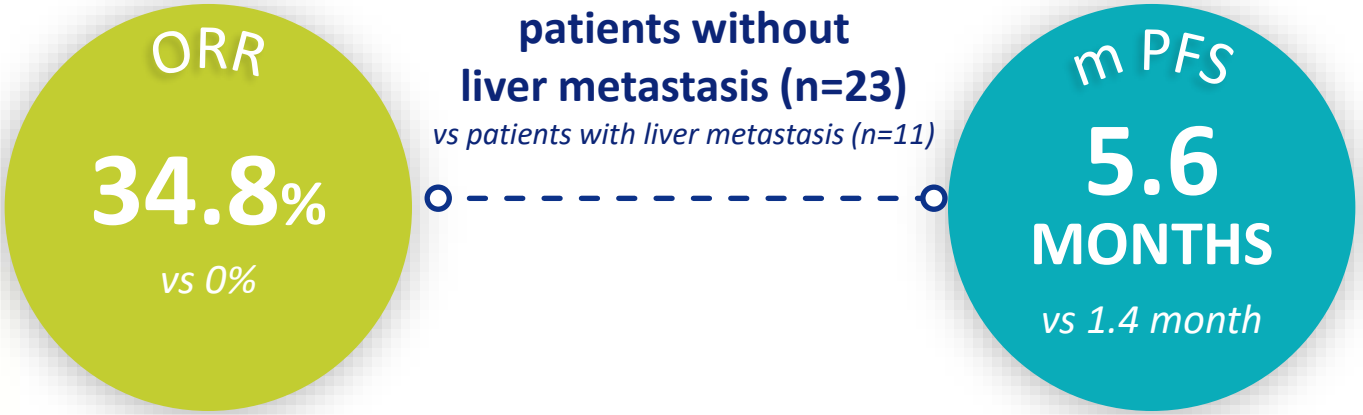
34 heavily pretreated patients with metastatic HPV16+ cancer
(oropharyngeal, anogenital)

Collaboration with

MERCK Pfizer

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

SITC 2020

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

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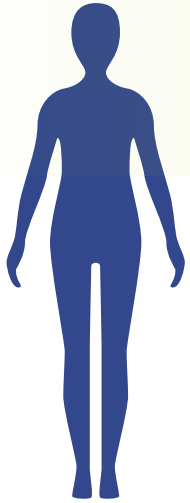
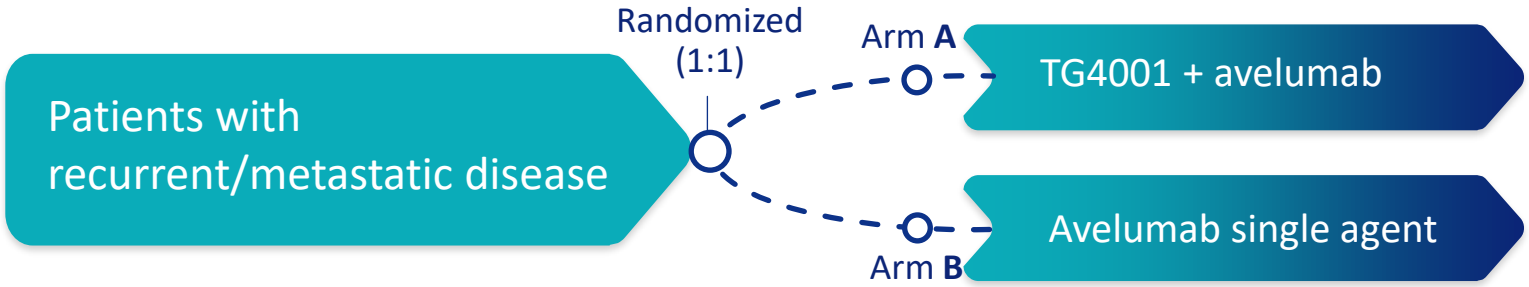
TG4001 | Randomized Controlled Phase II Trial Supported by Clinicians

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)

SECONDARY ENDPOINTS

- **Overall Response Rate**
- **Disease Control Rate**
- **Overall Survival**
- **Other Immunological Parameters**

Extended clinical collaboration with Pfizer, MERCK

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A Methodologically Sound Phase II Trial to Further Validate the Potential of TG4001

First patient enrolled in June 2021

- Trial received regulatory clearance in the US, France and Spain

Interim analysis data expected around the end of 2022

Positive interim analysis data to be leveraged:

- to discuss best way forward to registration with health authorities
- for partnering opportunities

TG4001 has potential to address all HPV positive cancers

Our Unique Invir.IO™ Platform

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

invir io

Oncolytic virus | Features of an Ideal Oncolytic Virus

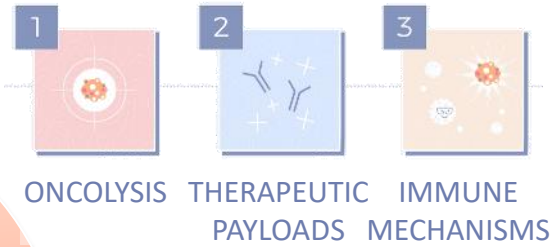
Competitive advantage of the patented backbone $VV_{cop}TK^{-}RR^{-}$ from Invir.IO™ platform

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, …

Tumor eradication including metastases



Highly infective capabilities and **strong lytic effect**

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

Multiple modes of action

Tumor-specific replication

Accentuated with TK-RR- double deletion

Broad spectrum infectivity
Can infect all types of tumor cells

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

Safe in a large variety of routes

Strong back record of clinical use

Clinical PoC of the functionality of **IV administration**

No nucleus integration

Pure cytoplasmic replication
Should not integrate into host DNA, and/or be mutagenic

Enveloped virus

Less prone to vector neutralization

Well established process for GPM manufacturing

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TG6002 | Chemotherapy Produced Directly in the Tumor

Interim Phase I data (IV*) presented at AACR and ESMO 2021

The right virus + payload

Oncolytic armed with FCU1 gene, prodrug activator

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

The right 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)

The right design

Two ongoing Phase I/IIa trials evaluating IV* and IHA** administrations

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

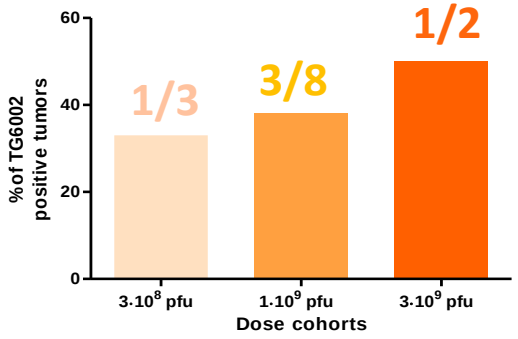
** IV: intravenous administration **IHA: intrahepatic artery administration*

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

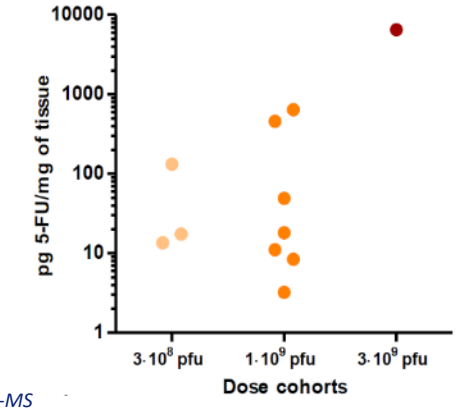
Fraction of tumor tissue positive for TG6002 by qPCR or plaque assay*



** 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)

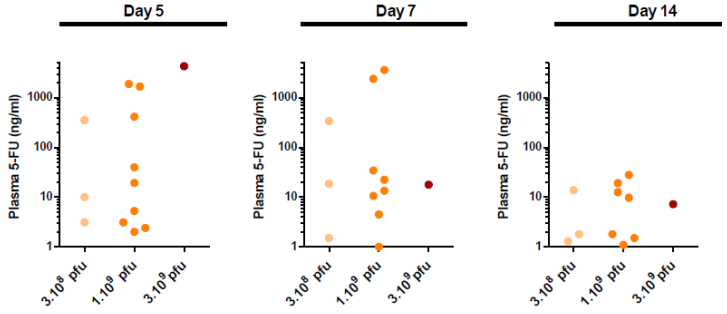
5-FU quantification in lesion biopsy on day 5*



** 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

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

Phase I part (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 1H 2022

Phase IIa part

Patients with **5-FU sensitive tumors**

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

BT-001 | Oncolytic Virus Encoding for an Anti-CTLA4 Antibody (Ab)

Transgene's patented
Invir.IO™ backbone

· Oncolysis
· Anti-tumor immune induction
· Safe delivery of payload

BioInvent's potent
anti-CTLA4 Ab

· Activates and increases T-effector cells
· Treg depleting activity

BT-001
is designed to achieve:

- Strong and sustained **anti-tumor activity**
- **Better safety** vs anti-CTLA4 IV
- **Immune change** in tumor microenvironment

Can be developed for
multiple cancer indications

GM-CSF
cytokine

Stimulates immune cells (incl. APC)

Selected publications:

Kleinpeter et al., 2016
OncoImmunology

Vargas F. et al., 2018
Cancer Cell

Marchand et al., 2018
sitc
Society for Immunotherapy of Cancer

Semmrich et al., 2020
2020 SITC

transgene

50/50 collaboration with **BioInvent**

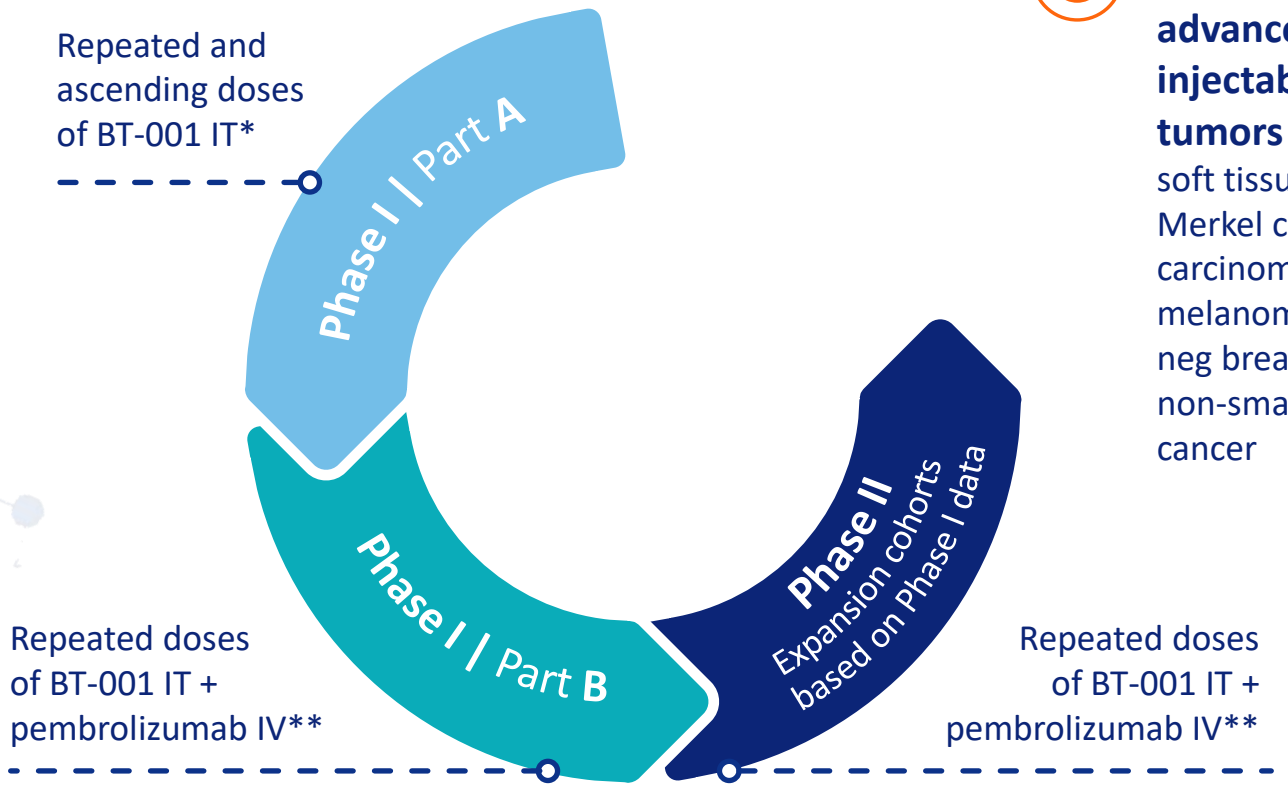
BT-001 | Phase I/II Trial Starting in Europe

Leverage the IT* route to accelerate development with anti-PD1 (NCT04725331)

Trial authorized
in Europe and in the US

First patient enrolled in Feb. 2021

First Phase I data to be presented in 1H 2022
(safety and translational data)



Patients with metastatic or advanced injectable solid tumors such as:
soft tissue sarcoma, Merkel cell carcinoma, melanoma, triple neg breast cancer, non-small cell lung cancer

*IT: intratumoral administration **IV: intravenous administration

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

Next candidates are already in preclinical development

Patented backbone demonstrated:

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

Potential to generate multiple novel immunotherapies with multiple modes of action against established or novel targets

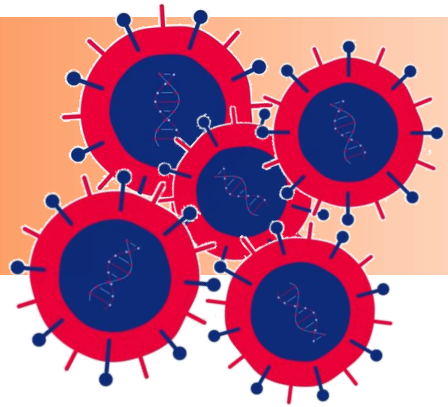
Highly productive platform
Several candidates in preclinical development

Optimize Invir.IO™ value creation
via a combination of early out-licensing and in-house clinical development until POC

Transgene & AstraZeneca to co-develop novel Invir.IO™ OVs

First License Option Exercised

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



- For **innovative Invir.IO™** based **armed oncolytic immunotherapies**
- Based on **$VV_{cop}TK^{-}RR^{-}$** integrating **one or more trangene(s)** chosen by AstraZeneca

Up to **5** targets

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

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

Outlook

Company Funded to Deliver Multiple Value Generating Milestones

€40.9 million in **cash and cash equivalents** at September 30, 2021

- further strengthened by the **€17.4 million** received in October 2021 from the partial sale of Tasly BioPharmaceuticals shares

FINANCIAL VISIBILITY until **end 2023**

Ownership

As of September 30, 2021

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

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**

1,883 h *dedicated to occupational training*

85% *permanent work contract*

16 interns
4 PhD students
11 apprentices

91/100 *Professional Equality Index*

100% *of employee evaluations include ESG criterion*

Gaïa EthiFinance: **76/100** (+13 pts)
Vigeo Eiris: **44/100** (+20 pts)

➔ **Above industry benchmark**

Our ESG policy is detailed in the Universal Registration Document 2020, chapter 4.

URD 2020

2022 **Milestones**

A World Leader in Virus-Powered Immunotherapies against Solid Tumors

myvac

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

- **TG4050**
  First data from two on-going clinical trials presented at a major oncology congress | **1H 2022**

TG4001

HPV-positive cancers therapeutic vaccine

- **TG4001**
  Interim analysis data | **end of 2022**

invirio

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

- **BT-001** Initial Phase I data | **1H 2022**
- **TG6002** End of Phase I (IV) | **1H 2022**
  Phase I data (IHA) | **mid 2022**
- **AstraZeneca** Ongoing collaboration

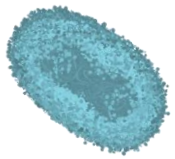
Appendices

Engineering viral vectors as immunotherapeutics

Turning foes into friends

Viral-vector vaccine

myvac

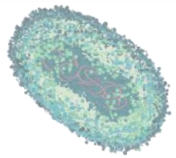


Local induction of immuno-stimulatory pathways

Expression of cancer antigens

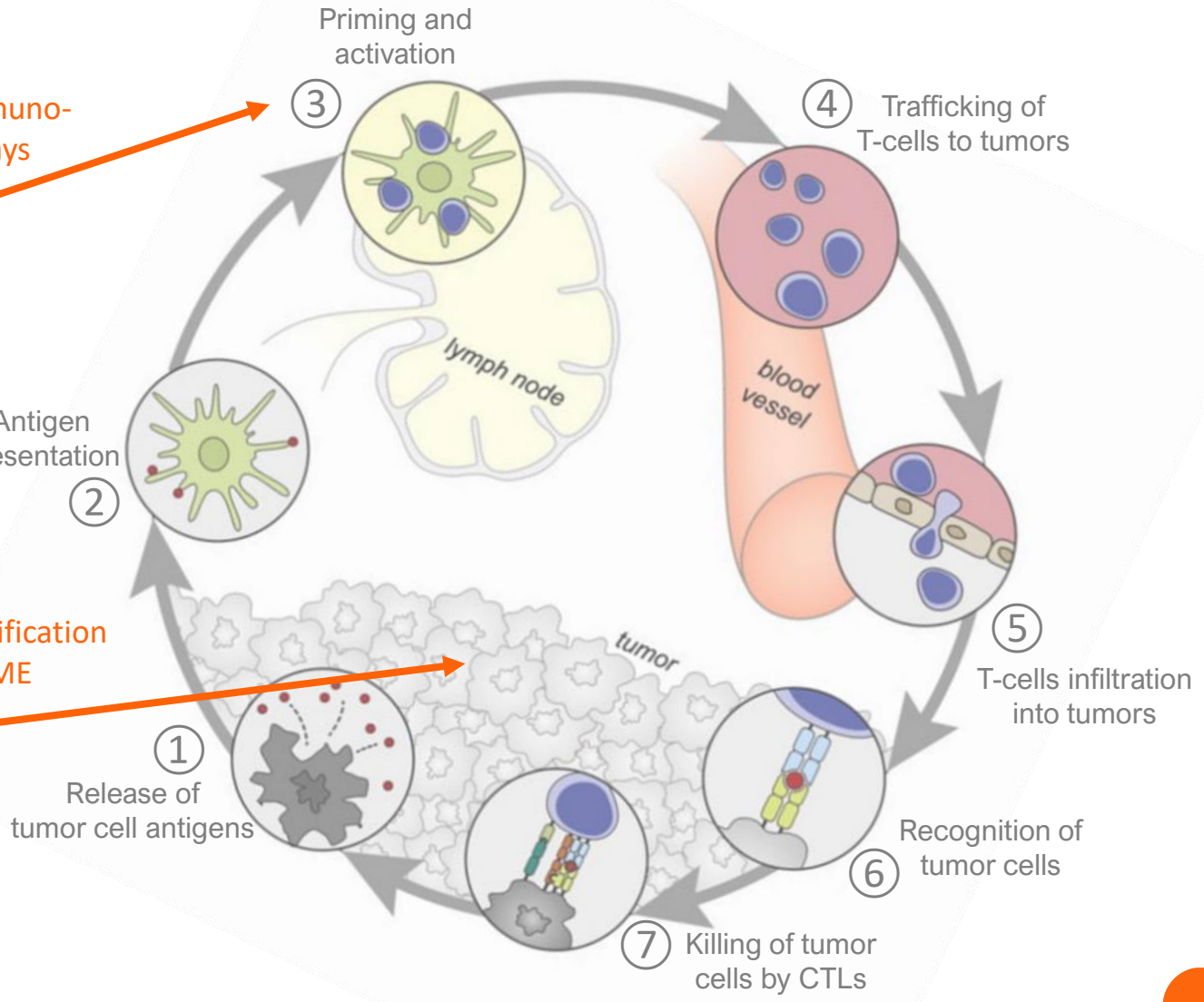
Oncolytic vector

invir io



Targeted modification of the TME

Immunogenic cell death

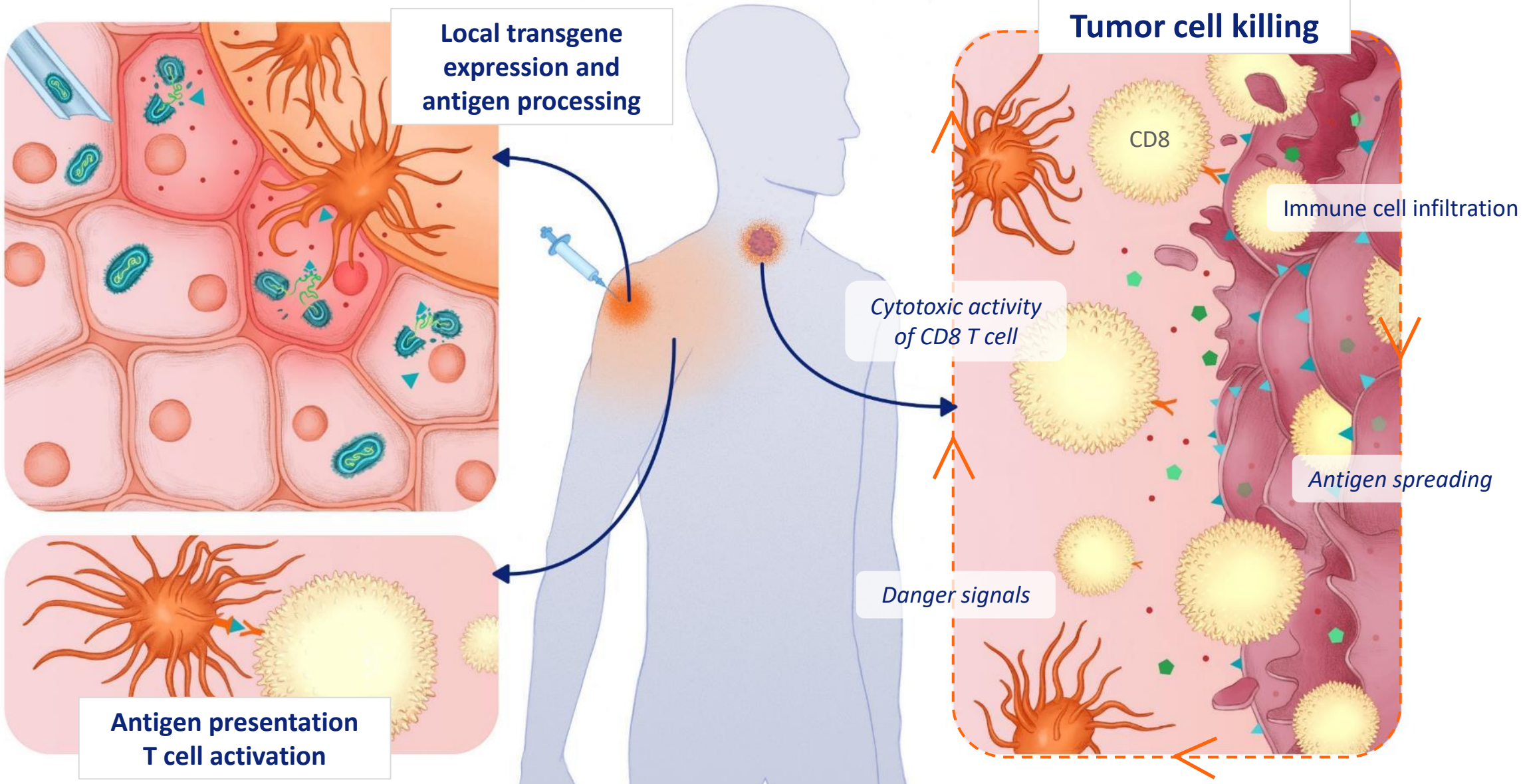


transgene

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

How Virus Powered Vaccines Treat Solid Tumors

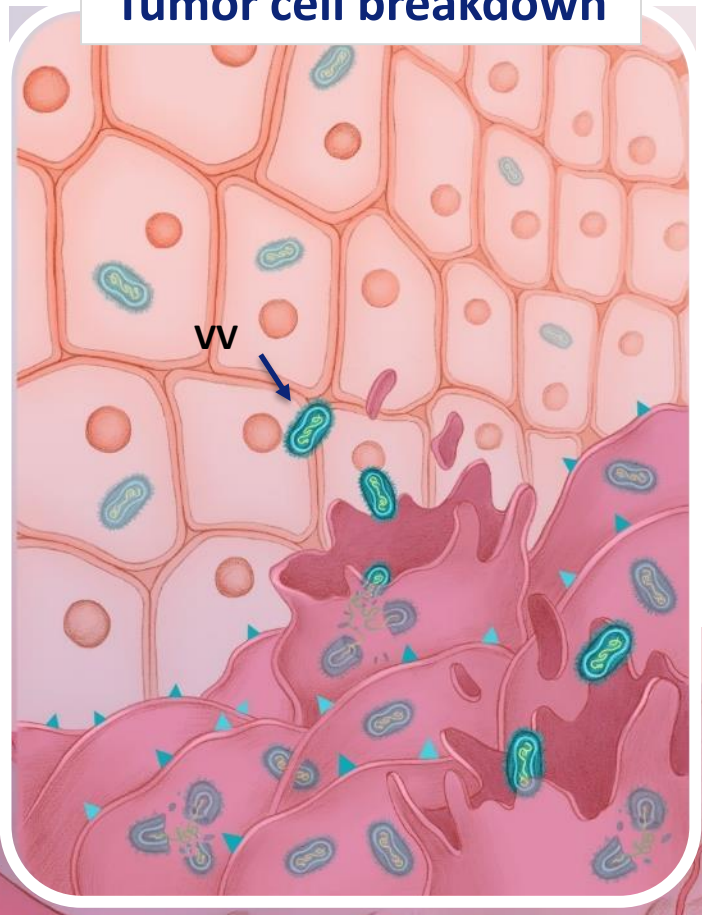
Our vaccines induce specific and strong immune response



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

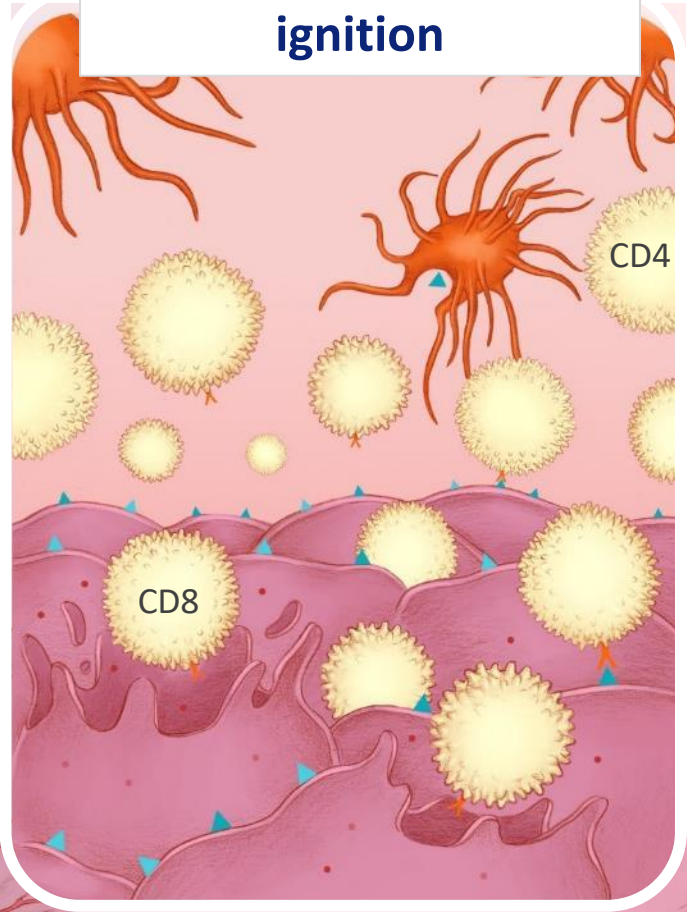
Armed oncolytics designed to improve the treatment of primary and secondary tumors

Tumor cell breakdown



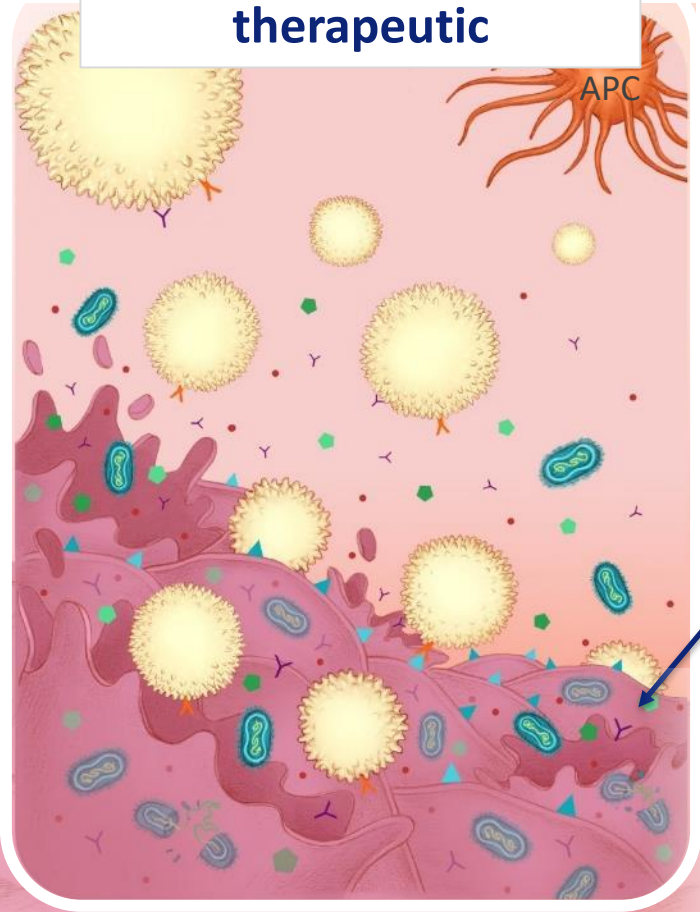
VV_{cop} TK^-RR^- selectively replicate in tumor cells and triggers apoptotic cell death

Immune system ignition



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

Local delivery of therapeutic



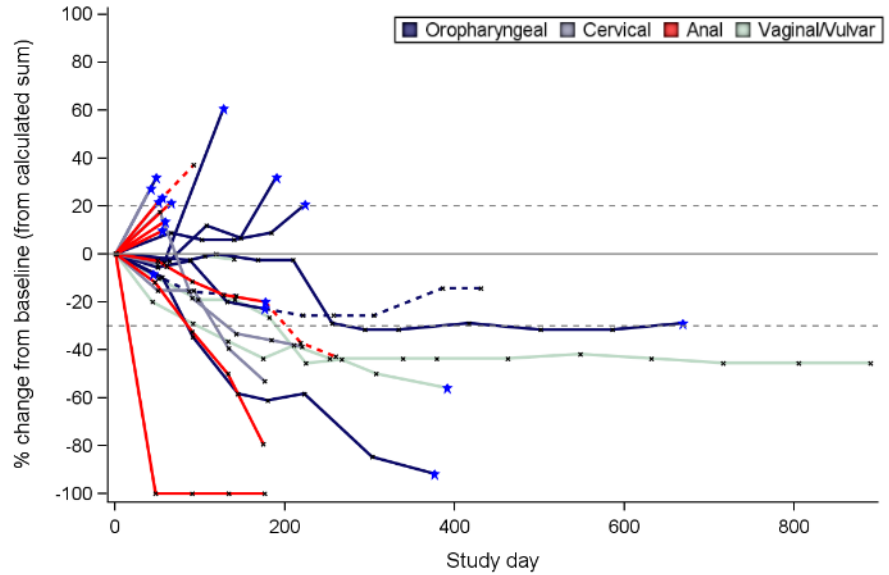
Secretion of modulators of the TME from infected tumor cells

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

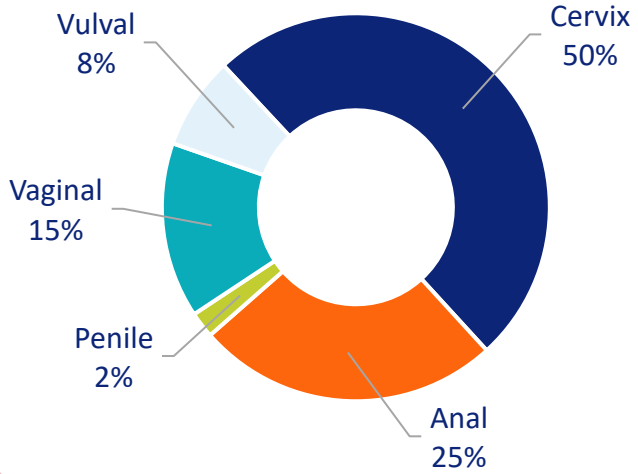
Significant Opportunity for TG4001 in Anogenital HPV16-Positive Cancers

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)

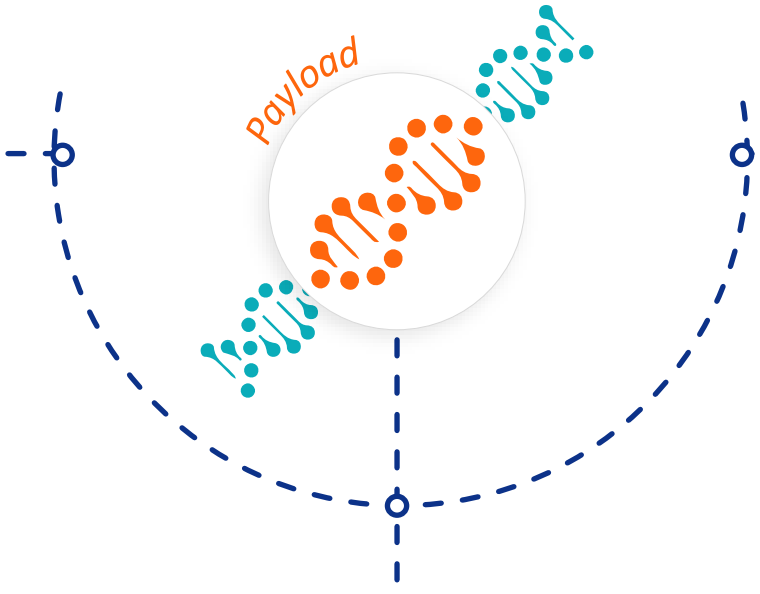
Estimated cancer cases (2025) based on: 1. ICO/IARC – HPV Information Center> Prevention at a glance // 2. HPV-positive cervical cancer: Globocan/IARC 2020 Cancer Fact Sheets: cervix uteri (C53); ICO/IARC – HPV Information Center Statistics // 3. HPV-positive vaginal cancer: Globocan/IARC 2020 Cancer 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

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

Ongoing Collaboration with AstraZeneca (AZ)

Invir.IO™ platform validation

AstraZeneca secured an access to Transgene's Invir.IO™ platform

Looking to augment in-house expertise in OVs

5 novel therapeutic payloads to be integrated in our VV_{COP}TK-RR- proprietary backbone

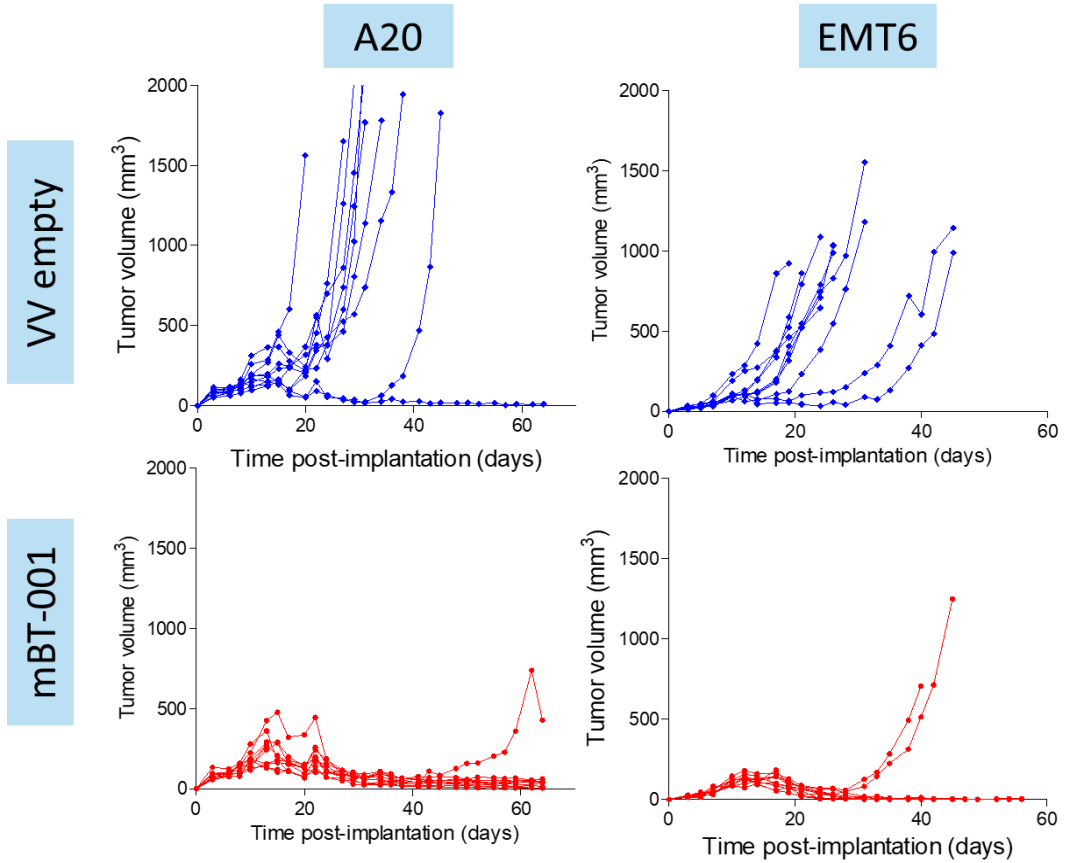
Possible option exercise by AZ on each candidate

- To continue development in the clinic
- Transgene in charge of GMP manufacturing of clinical batches

Could generate additional revenues for Transgene and further validate Invir.IO™ in the clinic

BT-001 - Exciting Preclinical Data

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

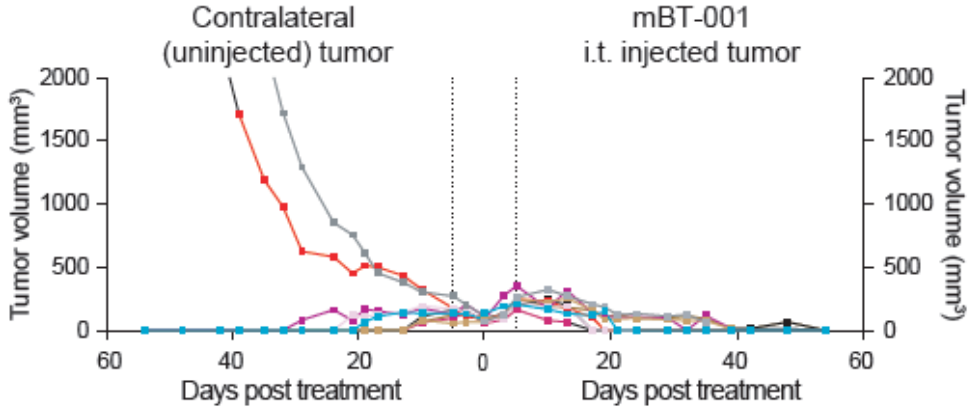


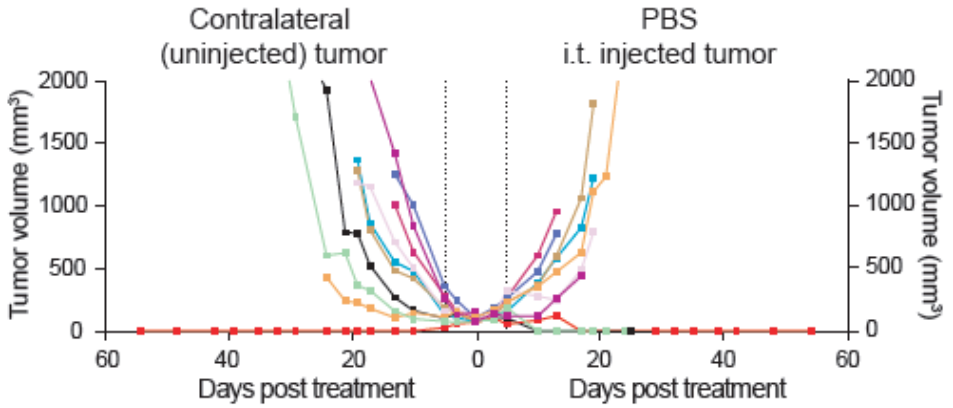
Marchand et al., "BT-001, an oncolytic Vaccinia virus armed with a Treg-depletion-optimized recombinant human anti-CTLA4 antibody and GM-CSF to target the tumor microenvironment", AACR, June 2020

BT-001 | Exciting Preclinical Data

Strong abscopal effect
(impact on distant lesions)

CT26

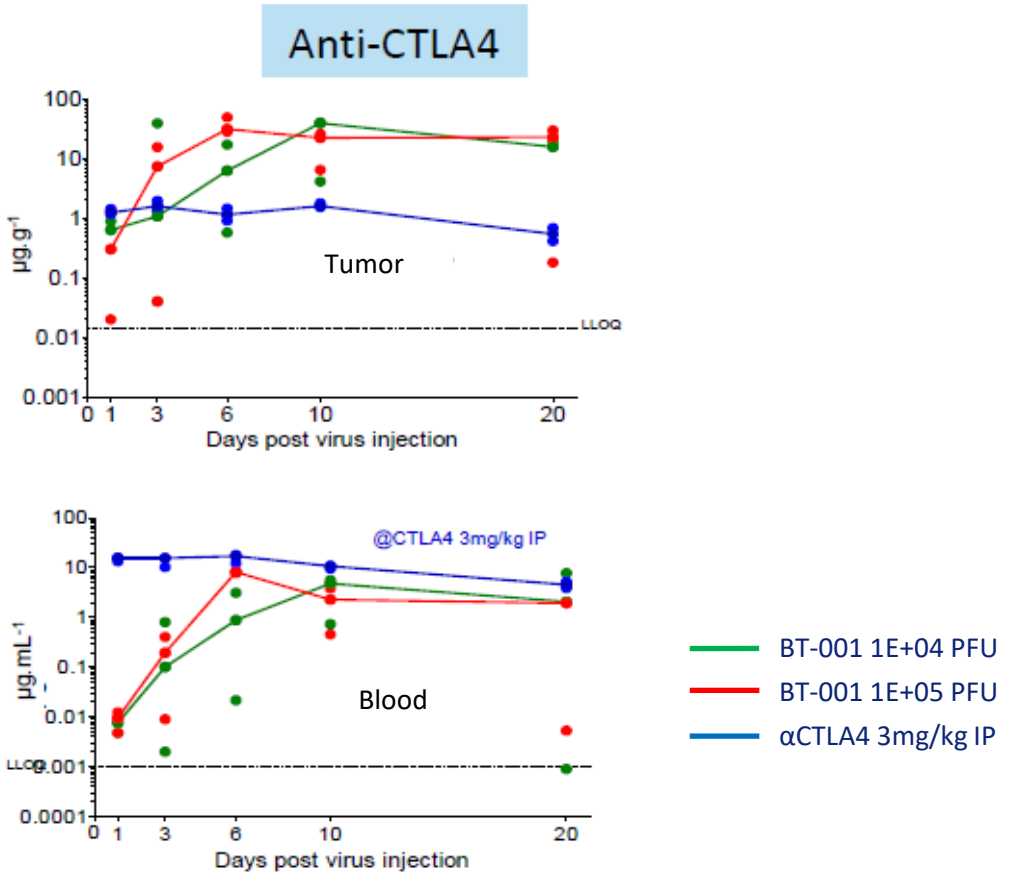




Semmrich et al., BT-001, an oncolytic vaccinia virus armed with a Treg-depleting human recombinant anti-CTLA4 antibody and GM-CSF to target the tumor microenvironment, SITC, Nov. 2020

BT-001 - Exciting Preclinical Data

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



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transgene

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