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Immunotherapies against cancer

March 2020
FY 2019 results

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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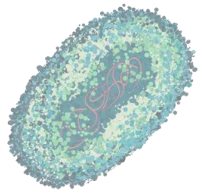
Transgene |Company overview



Virus-based immunotherapies against solid tumors

- Clinical trials active in **Europe** and in **the US**
- Integrated **R&D manufacturing unit (GMP)**
- **Collaborations** with

Orchestrating a brighter world NEC AstraZeneca MERCK Pfizer BioInvent

- **150** employees
- Listed on **the Paris stock exchange**

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Transgene | Virus-based immunotherapeutics

4 clinical-stage products and 2 novel platforms

Therapeutic Vaccines

Oncolytic Viruses

- ✓ **Large transgene capabilities**
- ✓ **Good safety profile**
- ✓ **Stimulate innate and adaptive immune response**

HPV16 therapeutic vaccine

TG4001

Individualized therapeutic vaccines

myvac **TG4050**

CT production in the tumor

TG6002

Multifunctional oncolytic viruses

invir io **BT-001**

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Major R&D milestones achieved in 2019
Strong clinical activity

			# trials
New Generations	myvac	**Two clinical trials with TG4050 authorized in Europe + USA** **Trials started in January 2020 - Collaboration with NEC**	**2**
	invirio	**Collaboration** agreement signed with **AstraZeneca** **BT-001:** CTA submitted - entering clinic in 2020	**1** *submitted*
Clinical Results	TG4001	**First efficacy results of the trial presented @ESMO –** **3/6 patients treated with the Ph2 dose are durable responders**	**1**
	TG6002	**IV route - Last dose levels currently evaluated** **IHA route – First patient dosed in Feb. 2020**	**2**
Finance	€43.3 million	**Cash available at year-end 2019**	

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Objectives for the coming 12 months

Portfolio to deliver significant news flow

2Q 2020

- **TG4001 HPV+ cancers:** Planned interim analysis (Phase 2)
- **TG6002 CRC - IV route:** First Phase 1 clinical readout
- ***myvac®*** and **Invir.IO™:** Scientific presentations

2H 2020

- **BT-001:** First clinical trial approval and launch of the first-in-human trial
- ***myvac®*** and **Invir.IO™:** Scientific presentations
- **Invir.IO™:**
  - **Collaboration with AstraZeneca**: Delivery of OVs – Possible option exercise
  - **Select proprietary preclinical candidate** and submit clinical trial application

1H 2021

- **TG4050:** First Phase 1 trials readout
- **TG6002 CRC – IHA route:** First Phase 1 data

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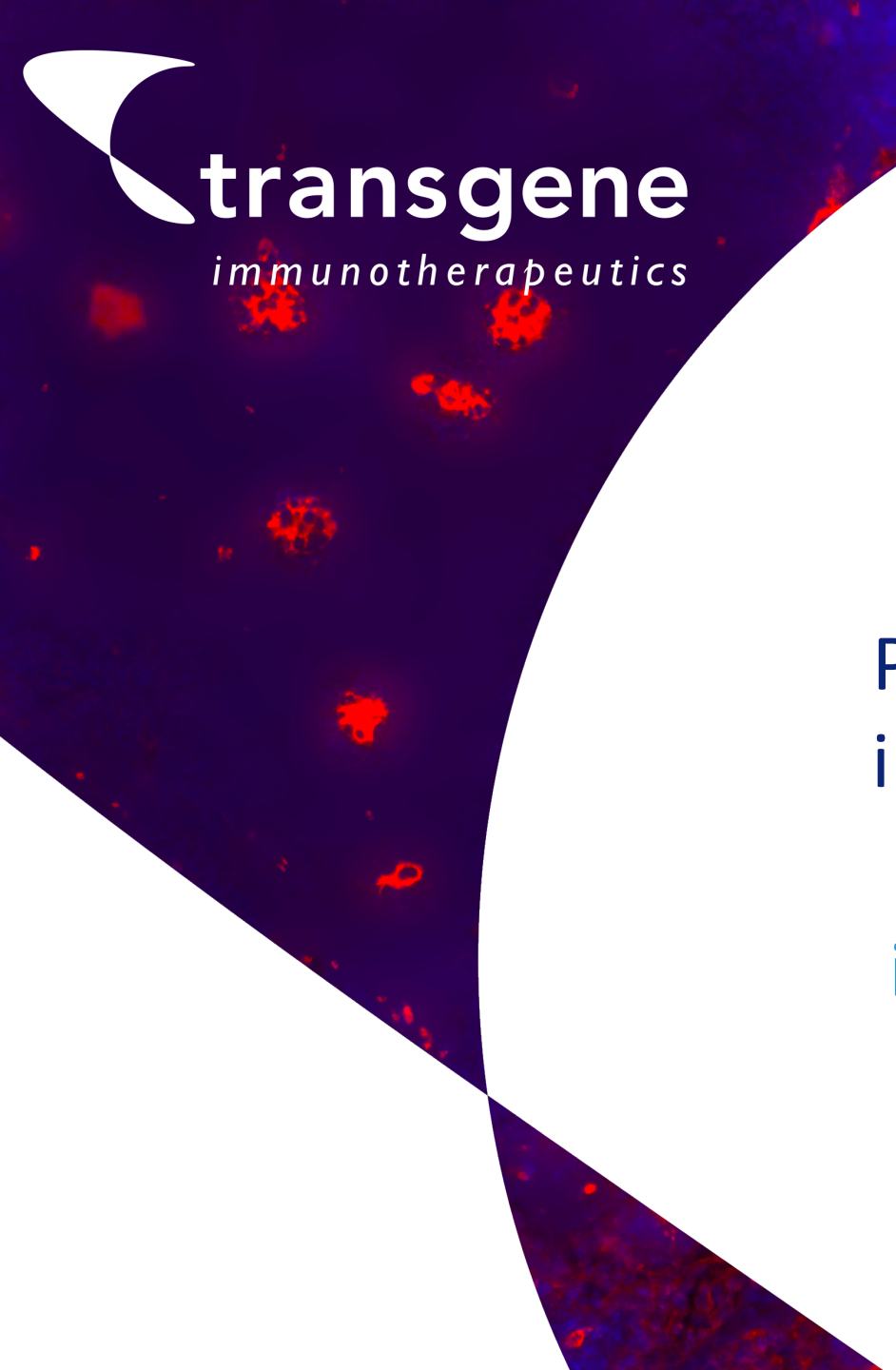
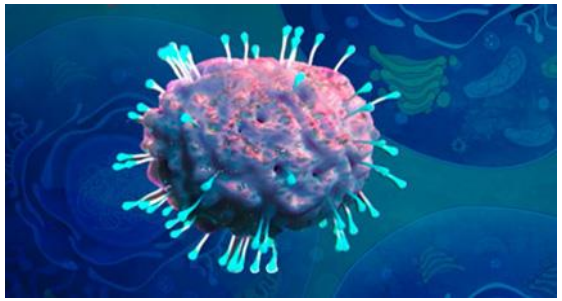


Promising Phase 1b Results with TG4001, in combination with avelumab

in HPV16-Positive Cancers

TG4001 | Therapeutic vaccine targeting HPV-positive cancers



Optimized virus

- **Attenuated MVA**

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- **HPV16 E6&7 antigens**
- **Human IL2**

➲ Designed to boost the patient's immune system against the tumor

1. **Targeted response against tumor cells carrying the HPV16 E6 & E7 antigens***
2. **Stimulate the infection-clearing activity** of the immune system*
3. **Good combination candidate** thanks to established **safety profile**

➲ Strong rationale for testing TG4001 in advanced stage HPV-positive cancers

➔ **High unmet medical need** ➔ **Target population: ~ 25,000 patients/year** (EU28 + USA)

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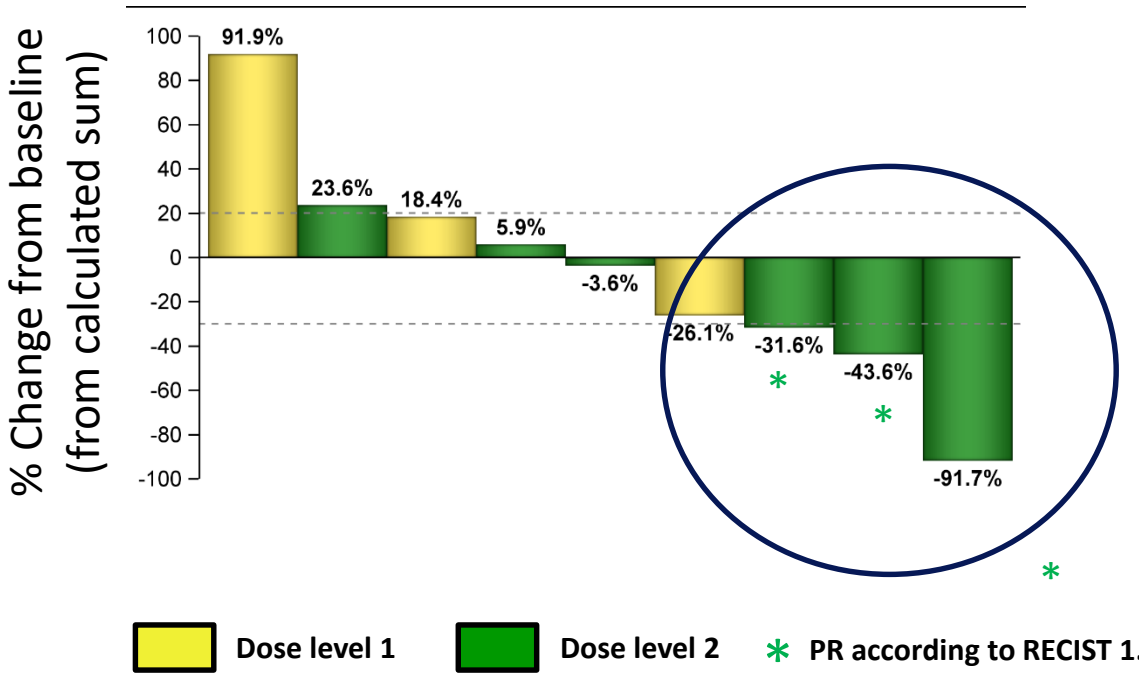
* Harper et al., *The efficacy and safety of Tipapkinogen Sovacivec therapeutic HPV vaccine in cervical intraepithelial neoplasia grades 2 and 3: Randomized controlled phase II trial with 2.5 years of follow-up*, Gynecologic Oncology, April 2019

Promising Phase 1b efficacy data presented @ESMO 2019

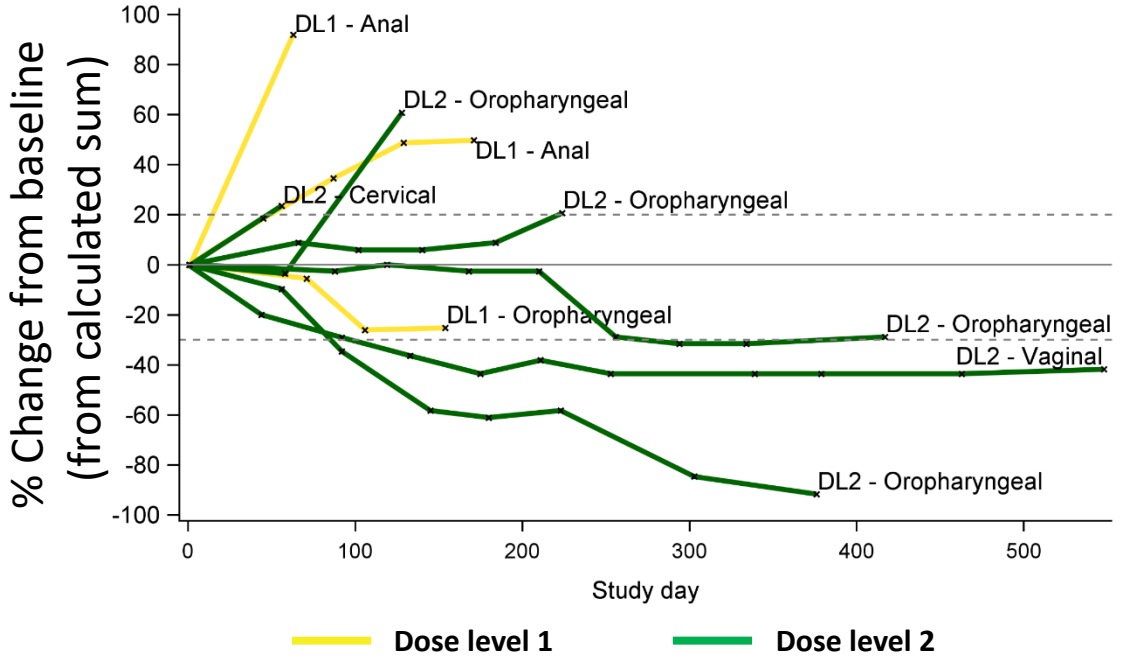
RECIST 1.1 evaluation:
Partial response: 3
Stable disease: 3

- **Heavily pretreated patients – 1 to 3 prior systemic chemo lines**
- **100% with distant metastases**

Best change in tumor size



Individual patient data



TG4001 + Avelumab in HPV16+ cancers - Key takeaways

Landmark data: First PoC efficacy data for the combination of a MVA-based therapeutic vaccine with an immune checkpoint inhibitor (ICI)

- ✓ 3 patients with durable responses out of the 6 patients treated with the Phase 2 dose
- ✓ Very challenging population (PFS < 4 months) – heavily pre-treated – 100% distant metastases
- ✓ Phase 1b data further confirm safety and biological activity of the combination regimen

Phase 2 ongoing - Interim analysis planned for 2Q 2020

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myvac

- Creating individualized immunotherapies based on our molecular virology expertise
- First product TG4050 in two ongoing clinical trials

Orchestrating a brighter world
NEC

bpifrance

TG4050 | Individualized immunotherapy already in the clinic

➲ Targets the patient's own neoantigens

MVA-based immunotherapy

- MVA vector: safe and immunogenic
  - Expected to induce **broader and stronger T cell response**
  - **Prime/boost patient's immune system** to overcome the immunosuppressive environment
- Based on the patient's own cancer mutations; **neoantigens are more immunogenic**
- GMP manufacturing unit ready

NEC: a partner committed to develop AI in the IO field

- NEC brings state-of the-art **AI technologies** to generate individualized immunotherapies
- Will **cover 50% of the cost** of the first two clinical trials of TG4050

TG4050 | Process for individualized neoantigen vaccination

➲ Combines bioengineering and digital transformation

Routine tumor biopsy

Patient

Treatment administration

Gene sequencing

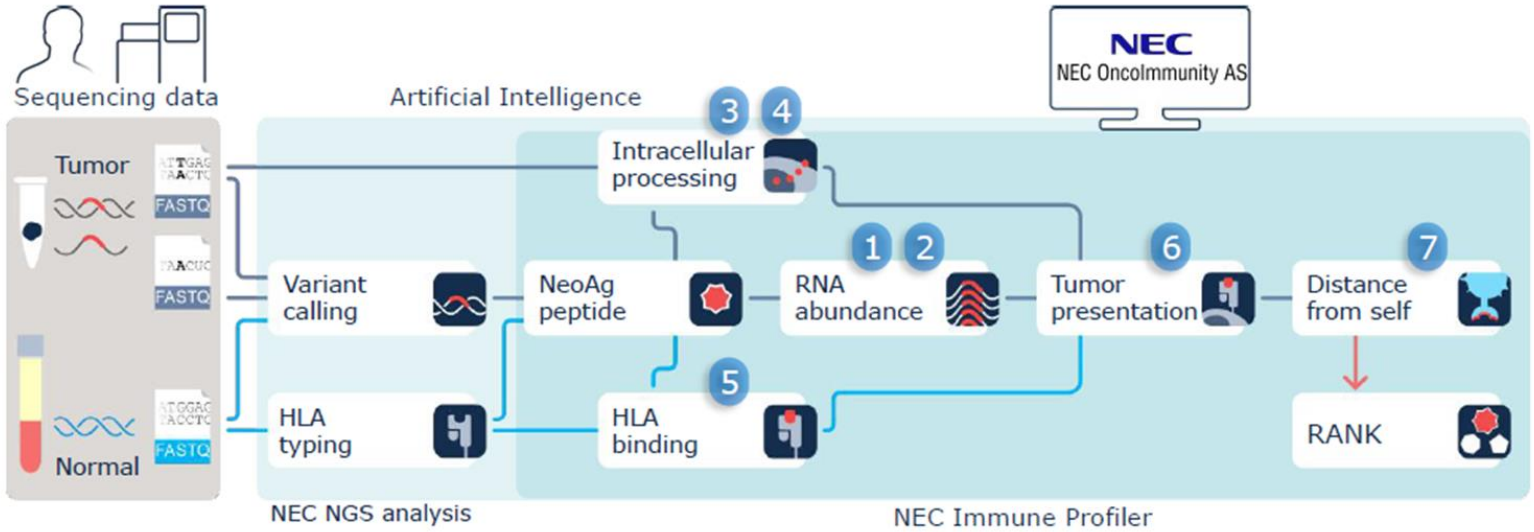
Next generation sequencing

Data processing, Artificial intelligence

Selection of 30 neoantigens

Gene editing, Manufacturing

Vaccine generation and manufacturing



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TG4050 | Proof-of-concept Phase 1 ongoing

Ovarian cancer after surgery and adjuvant chemotherapy

Lead investigator:
Matthew S. Block, MD, PhD
Mayo Clinic (Rochester)

Study

- Single arm, open label Phase 1 trial (NCT: 03839524)
- Sites in the USA and in France
- 13 patients

Protocol

- Patients receive TG4050 monotherapy after complete response to platinum-based chemotherapy

Endpoints

- Primary: safety and immunogenicity

First patients enrolled in January 2020

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TG4050 | Proof-of-concept Phase 1 ongoing

HPV negative head and neck cancers
after surgery and adjuvant therapy

This trial builds upon a long-term research collaboration between Transgene and the University of Southampton. I believe such personalized vaccine approaches are the next paradigm in cancer care.

Study

- Randomized two-arm, open label Phase 1 trial (NCT: 04183166)
- Sites in France and in the UK
- 30 patients

Lead investigator: Pr. Christian Ottensmeier, University of Southampton

Protocol

- Patients receive either TG4050 monotherapy after completion of the adjuvant therapy or in combination with SoC at the time of recurrence

Endpoints

- Primary: safety and immunogenicity

First patients enrolled in January 2020

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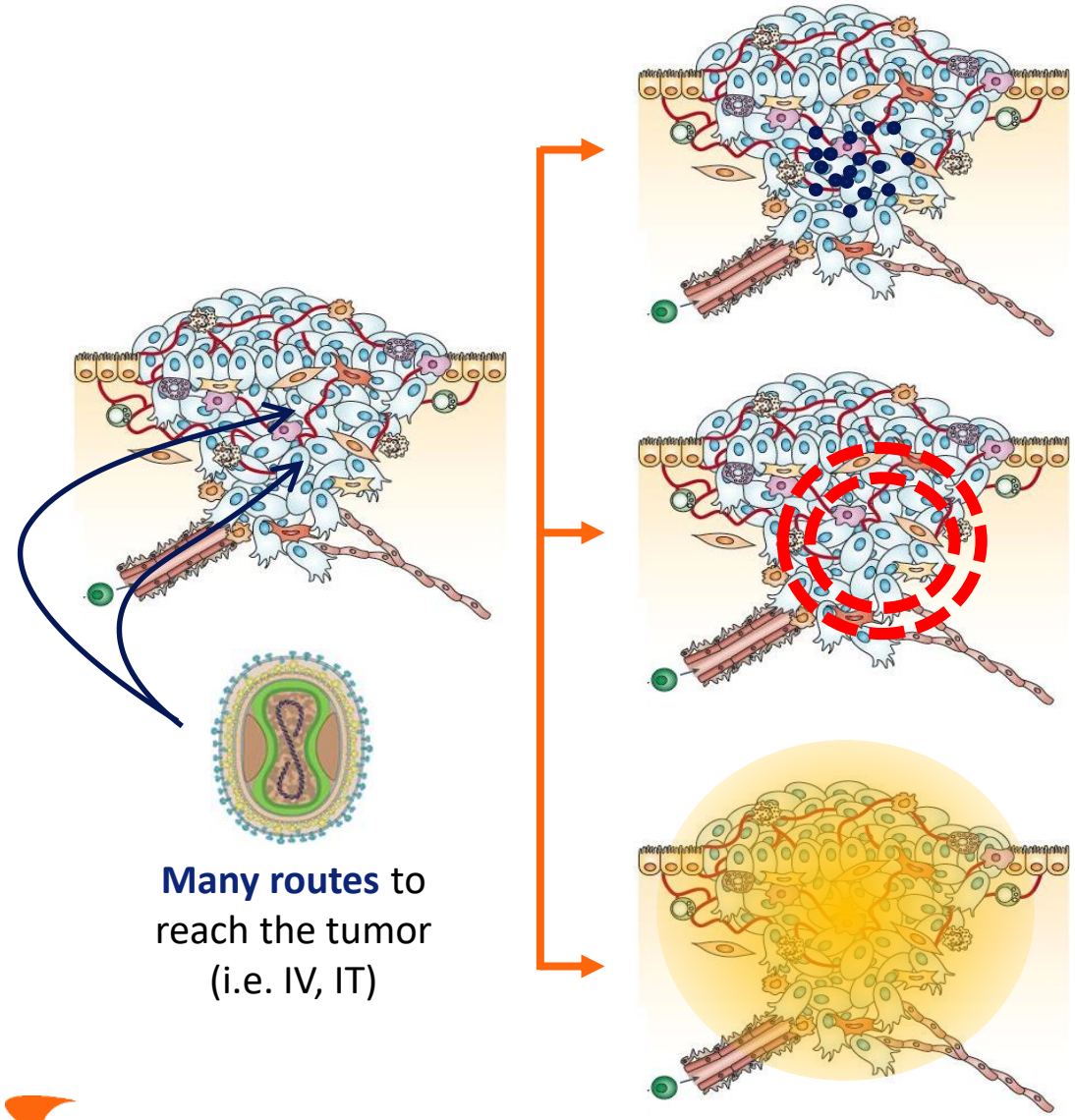
Our next generation multifunctional oncolytic virus (OV) platform

TG6002

invir io

Invir.IO® | Optimized OVs (VV_{Cop} TK^-RR^-) tumor attacked on multiple fronts



Many routes to reach the tumor (i.e. IV, IT)

Superior oncolysis

- ✓ Direct lysis of infected cells
- ✓ More specific replication in tumor cells

OncoImmunology Delaunnay et al., 2018

Increased and durable immune response

- ✓ Induction of immunogenic cell death
- ✓ Engagement of innate and adaptive anti-tumor immunity

Cancer Research Fend et al., 2017

Molecular Therapy Oncolytics Foloppe et al., 2019

High capacity and efficient immuno-modulating payloads delivery

- ✓ Targeted delivery of anti-tumor modalities
- ✓ Synergistic with other MOAs (e.g. targeted CT or immune modulation of TME)

OncoImmunology Kleinpeter et al., 2016

sitc Marchand et al., 2018

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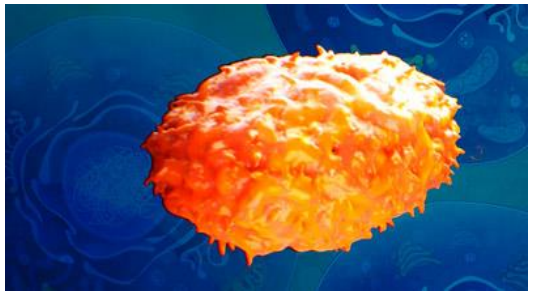
TG6002 | First multifunctional OV in the clinic



Expected increased efficacy without CT-associated side effects

1. **Excellent oncolytic properties**
2. **Production of chemotherapy (5-FU) in the tumor** with **FCU1 gene**

Optimized virus

- **Optimized and patented VV_{Cop} TK-RR- OV**

FCU1 gene

- **Unique** and **proprietary**
- **Oral 5-FC conversion into 5-FU**
- Preclinical results confirm **potency**

Chinese rights sold to Tasly Biopharmaceuticals (July 2018)

Two ongoing Phase 1/2a clinical trials
Evaluating TG6002 in colorectal cancer patients
(IV and IHA administration)

TG6002 | Two Phase 1/2a trials in 5-FU sensitive GI indications

➲ Two novel administration routes - IV and IHA

Gastro-intestinal adenocarcinoma with liver metastasis (colon cancer) - *IV route*

Protocol
- Phase 1 part (dose escalation): up to 24 patients
- Phase 2a part (efficacy) in CRC: 35 patients

Regimen
- TG6002 IV + oral 5-FC
- Additional cycles until disease progression

Principal investigator
- Prof Cassier, centre Léon Bérard (Lyon, France)
- INDs granted in Belgium, Spain, France

Continued dose escalation
First clinical readout 2Q 2020

Colorectal cancer patients with unresectable liver metastases (CRLM) – *IHA route*

Protocol
- Up to 75 patients

Regimen
- TG6002 IHA + oral 5-FC
- Additional cycles until disease progression

Principal investigator
- Dr. Adel Samson, MB ChB PhD, St. James' University Hospital (Leeds, UK)
- IND granted in the UK

First patient dosed in February 2020
First clinical readout 1H 2021

Collaboration and license option agreement with AstraZeneca

➲ Invir.IO® platform validation

5 novel oncolytic immunotherapies will be developed, integrating:

- Transgene Invir.IO® based oncolytic viruses (improved VV_{COP}TK-RR- proprietary viral vector)
- Potent therapeutic payloads to be encoded in the OV

Conduct of the project:

- Transgene designs the OVs and conduct *in vitro* preclinical development
- AstraZeneca leads *in vivo* preclinical development

Transgene has received $10 million at signing

Possible option exercise in 2H 2020

invir.io | BT-001 expresses GM-CSF and anti-CTLA4 mAb

BT-001

transgene BioInvent

- **Collaboration with BioInvent** : Transgene's Invir.IO® OV + BioInvent's full length human recombinant Treg depleting anti-CTLA4 mAb

Transgene's VV_{COP} TK-RR- can express mAbs in the tumor

OncoImmunology Kleinpeter et al., 2016

BioInvent's anti-CTLA4 Abs promotes depletion of intratumoral Treg cells

Cancer Cell Vargas F. et al., 2018

Combination of ICI and oncolytic VV treatments are additive

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

Outstanding preclinical data

- **Strong antitumor activity** in several **immunocompetent mice models**
- **Higher concentration** and **prolonged activity** of the anti-CTLA4 antibody vs. IV mAb administration
- **Expected improved tolerability** owing to lower systemic antibody exposure in peripheral non-tumor compartments

- **Presentations at scientific meetings**
- **Clinical trial application filed in 1Q 2020**
- **Trial expected to start before end of 2020**

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2019 Financial results

2019 FINANCIAL RESULTS

P&L

in € million	2019	2018	*Var.*
Revenue	**13.7**	**42.9**	***(29.2)***
Research and development expenses	(31.4)	(27.3)	(4.1)
General and administrative expenses	(7.1)	(7.0)	(0.1)
Other expenses	(0.7)	(1.2)	0.5
Net operating expenses	**(39.2)**	**(35.5)**	**(3.7)**
Operating income/(loss)	**(25.5)**	**7.4**	**(32.8)**
Interest income (expenses), net	6.7	(2.0)	8.7
Income from equity consolidated expenses	-	2.7	(2.7)
Total net income/(loss)	**(18.8)**	**8.0**	**(26.8)**
Net income/(loss) per share (in €)	(0.23)	0.13	(0.36)

- €39.2 million in net operating expenses compared with €35.6 million in 2018
- €18.8 million in net loss compared with €8.0 million net profit in 2018

2019 FINANCIAL RESULTS

Revenue

→ **€13.7 million in revenue compared with €42.9 million in 2018**

	In € million	2019	2018
1	Revenue from collaborative and licensing agreements	6.7	1.3
2	Government financing for research expenditures	6.6	5.7
3	Other revenue	0.4	35.8
	Revenue	**13.7**	**42.9**

1

- R&D Services: **€6.6 million in 2019** (€1.3 million in 2018) with €5.3 million booked from AstraZeneca collaboration
- Licenses: €0.06 million vs. €0.03 million in 2018

2

- Research tax credit: **€6.5 million in 2019** vs. €5.7 million in 2018

3

- Other revenue: in 2018, €35.6 million from the sale of rights in TG1050 for Greater China to Tasly Biopharmaceuticals

2019 FINANCIAL RESULTS

R&D expenses

→ **€31.4 million in R&D expenses compared with €27.3 million in 2018**

	In € million	2019	2018
1	Staff costs	11.2	11.2
1	Share-based payments	0.9	0.3
	External IP and licensing costs	0.8	0.9
2	External expenses on clinical projects	10.9	7.9
	External expenses on other projects	1.6	1.5
3	Operating expenses	4.2	3.7
	Depreciation and amortization	1.8	1.8
	R&D expenses	**31.4**	**27.3**

1 Staff costs & share-based payments

- **Stability in FTE in R&D** (112FTE, 78% of total FTE)

2 External expenses on clinical projects

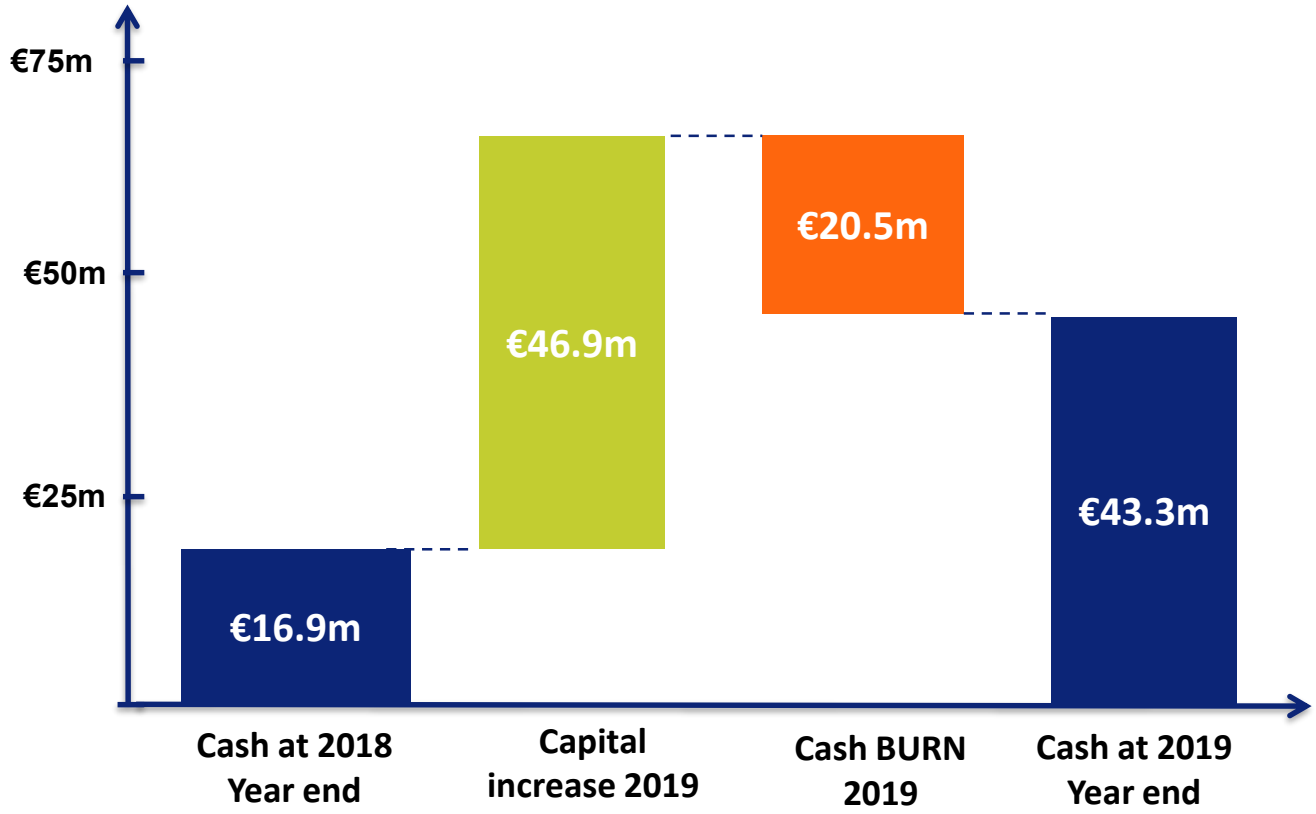
- **Increase due to strong clinical activity: €10.9 million in 2019** vs €7.9 million in 2018

3 Operating expenses

- **Consumables: +€0.5 million in 2019** due to the new manufacturing unit and Invir.IO® program in Research

2019 FINANCIAL RESULTS

Key Figures – Cash and cash equivalents



- €43.3 million in cash and cash equivalents at year end 2019
- €20.5 million of cash burn compared with €24.5 million in 2018
  - €8.9 million received in cash from AZ in 2019, but increase of R&D expenses (+€4 million)

Expected cash burn for 2020: approx. €25 million

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Outlook

Strong clinical activity in 2020

Current pipeline

Product	Indication	Partner	Preclinical	Clinical Phase: Phase 1	Clinical Phase: Phase 2	Next step
THERAPEUTIC VACCINES						
TG4001	Recurrent HPV positive cancers	Merck Pfizer *	+ avelumab (ICI)			Interim analysis in 2Q 2020
TG4050	Ovarian cancer Head & neck cancers	myvac; Orchestrating a brighter world NEC *				1st trials readouts in 1H 2021
ONCOLYTIC VIRUSES						
TG6002	Colorectal cancer – IV Route Colorectal cancer – IHA Route	**				First data 2Q 2020 First data 1H 2021
BT-001	Solid tumors	invir io	BioInvent *			Trial initiation 2H 2020
Proprietary OVs	Solid tumors	invir io				Candidate selection CTA filing 2H 2020
5 OVs	Confidential targets	invir io	AstraZeneca *			Potential option exercise

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* Research or clinical collaboration / ** Chinese rights sold to Tasly Biopharmaceuticals

Our priorities for 2020/2021

Clinical pipeline

- Progress our clinical portfolio to deliver readouts on TG4001 and TG6002

invir io

- Start clinical trial on BT-001 in 2H 2020
- Select second clinical candidate, based on our unique VV backbone
- Deliver all OVs to AstraZeneca – Potential option exercise

myvac

- TG4050 - progress two clinical trials and establish first clinical PoC

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