Viral-based immunotherapies to transform the fight against cancers and infectious diseases
Safe harbour statement

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 the Phase 2b part of the TIME trial will be predictive of future results with TG4010, (ii) regulatory authorities will agree with the Company’s further development plans for TG4010, or (iii) the Company will find a development and commercialization partner for TG4010 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. The Company’s ability to commercialize its products depends on but is not limited to the following factors: positive pre-clinical data may not be predictive of human clinical results, the success of clinical studies, the ability to obtain financing and/or partnerships for product development and commercialization, and marketing approval by government regulatory authorities.

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 Risque") section of the Document de Référence, 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.
A pioneer in developing viral vector-based immunotherapies for cancers and infectious diseases

2
Immunotherapy platforms
- Therapeutic vaccines
- Oncolytic viruses

5
Immunotherapy products in clinical trials o/w 3 at Phase 2 stage

Focus
Advanced cancer and chronic diseases

A high level of unmet medical needs remains despite new available treatments
Our combination focused strategy

Today
Demonstrate the power of our current immunotherapies by focusing on combination trials with the new standard of care (ICIs)

Tomorrow
Deliver a new cancer combination paradigm centered on our multifunctional oncolytic viruses
Management | Experienced team

Philippe Archinard, PhD
Chairman & Chief Executive Officer

Eric Quéméneur, PhD
Executive VP and Chief Scientific Officer

Christophe Ancel, PharmD
VP Quality and Qualified Person

Maud Brandely, MD, PhD
Chief Medical Officer

Jean-Philippe Del
VP Finance

Thibaut du Fayet, MBA
VP Marketing, Alliance and Project Mgt

John Felitti, JD, MBA
General Counsel and VP Legal

Hemanshu Shah, PhD, MBA
VP Corporate Development & Medical Affairs
## Recent Achievements | Validate Transgene’s strategy

| Exciting clinical product portfolio | Refocused clinical development on combi. trials with ICIs  
|  | • 3 clinical collaboration agreements for TG4010 and TG4001  
|  | • Actively working on 5 combination clinical trials, 4 already recruiting  
|  | 7 active clinical trials incl. Pexa-Vec Phase 3 (PHOCUS, HCC) and TG1050 in Phase 1/1b (HBV) |

| Cutting edge oncolytic viral pre-clinical developments | Prioritized research programs with new published preclinical developments  
|  | • Demonstrated efficacy of a new generation of oncolytic virus  
|  | Collaboration with Servier: develop new process for the fabrication of allogenic CAR-T cells |

| Finance | Company funded through the end of 2018  
|  | • Expected cash burn 2017: ~ €30 million  
|  | • Operating revenues: ~ €4 million as of June 30, 2017  
|  | • Cash and cash equivalents: €44 million as of June 30, 2017  
|  | • EIB loan (€10 million drawn down of €20 million facility) |
Anti-PD-1/PD-L1 | A new paradigm – need for improvement

Non-responders

ORR %

FDA approved agent available

ORR = approximate objective response rate %

Source: from ASCO Annual meeting 2017, by Gregory L. Beatty, MD PhD

Transgene’s indications of interest
Our strategy | Materialize the value of mature clinical assets & develop disruptive future innovation

Today | Combined with ICIs

Transgene’s immunotherapies
- Stimulate the immune response
- Create or boost T-cell proliferation
- Directly attack tumor cells
  - Boost the immune system

Immune Checkpoint Inhibitors (ICIs)
- Block a pathway that inhibits activated T-cells

Tomorrow | Optimized to deliver multi functional payloads

Engineered viruses that attack the tumor at multiple points
- Cellular
  - Improved replication in resistant tumor cells
  - Improved lytic activity + release of immunogenic components
- Tumor microenvironment
  - Attraction + infiltration of effector immune cells
  - Breakdown of immunosuppressive mechanisms
- Organism
  - Mobilization of innate + adaptive responses
  - Improved virus spreading to metastasis

Activated T-cells generated by Transgene’s products combined with ICIs have a better ability to destroy cancer cells
# Diversified portfolio of clinical-stage immunotherapies

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Clinical Phase</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td><strong>THERAPEUTIC VACCINES</strong></td>
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<tr>
<td>TG4010</td>
<td>Non-small cell lung cancer – 2nd line</td>
<td>+ nivolumab (ICI)</td>
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<tr>
<td></td>
<td>Non-small cell lung cancer – 1st line</td>
<td>+ nivolumab (ICI) + CT</td>
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<tr>
<td></td>
<td>Non-small cell lung cancer</td>
<td>Neo-adjuvant (translational)</td>
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<tr>
<td>TG4001</td>
<td>HPV positive cancers</td>
<td>+ avelumab (ICI)</td>
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<tr>
<td>TG1050</td>
<td>Chronic hepatitis B</td>
<td>+ antiviral</td>
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<tr>
<td><strong>ONCOLYTIC VIRUSES</strong></td>
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<tr>
<td>Pexa-Vec</td>
<td>Hepatocellular carcinoma – 1st line (PHOCUS)</td>
<td>+ sorafenib</td>
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<tr>
<td></td>
<td>Hepatocellular carcinoma – 1st line</td>
<td>+ nivolumab (ICI)</td>
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<tr>
<td></td>
<td>Other solid tumors</td>
<td>+ ipilimumab (ICI)</td>
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<td></td>
<td>Sarcoma – Breast cancer</td>
<td>+ cyclophosphamide</td>
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<td></td>
<td>Solid tumors</td>
<td>Neo-adjuvant (translational)</td>
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<tr>
<td>TG6002</td>
<td>Glioblastoma</td>
<td>About to start</td>
<td></td>
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*ICI*: Immunocore
*Neo-adjuvant (translational)*: Neo-adjuvant treatment for translational study.
Ideally Suited for Combination Immunotherapy Regimens
Our Therapeutic Vaccines platform

**Therapeutic vaccines** express tumor/viral antigens to stimulate a safe and specific immune response

- **Antigen (MUC1) expression** leading to maturation of Antigen Presenting Cell (APC)
- Mature APCs present MUC1 antigen to naive T-cells
- T-cells multiply, get activated and reach the blood stream
- Activated T-cells **infiltrate into the tumor**, recognize and kill MUC1+ tumor cells

Therapeutic vaccines have shown important benefits when combined with chemotherapy and/or ICIs

Applications in cancers and infectious diseases
TG4010 Targeting NSCLC

Modified Virus Ankara (MVA) expressing MUC1 antigen & interleukin 2

Supported by

Bristol-Myers Squibb
TG4010 | Strong clinical data
Well positioned for further development in NSCLC

SUCCESSFUL PHASE 2B TRIAL (RANDOMIZED, PLACEBO-CONTROLLED, 222 PATIENTS)
TG4010 in combination with chemotherapy for 1st line NSCLC

- Significant improvements in PFS and OS in patients with non-squamous tumors
- Clinical efficacy in both PD-L1 negative and PD-L1 positive patients

Source: The Lancet Oncology, Dec. 2015, Quoix, E. et al.
TG4010 | Strong clinical data

Improved response rate & duration of response

Source: The Lancet Oncology, Dec. 2015, Quoix, E. et al.
TG4010 | Clinical positioning
A very large population in NSCLC, stage IV, non-squamous patients

- Eligible Population (US, EU, JP), in thousands of patients
  - STAGE IV: 710 K
  - NON-SQUAMOUS: 532 K
  - NON-MUTATED (ALK, EGFR, ...): 441 K
  - LOW PD-L1 - 1ST LINE: 331 K
  - 2ND LINE (INDEPENDENT OF PD-L1 STATUS): 265 K

1L - TG4010 positioning
2L - TG4010 positioning
**TG4010 | Combination with ICIs**

**Scientific Rationale**

**TG4010**
(Therapeutic vaccine)

- Demonstrated mechanism of action: induction of CD8+ T cell response
- Activity shown in patients with no/low PD-L1 expression*

**Immune Checkpoints Inhibitors**
(ICIs)

- Block the signal that prevents activated T-cells from attacking cancer cells
  - Enhance the efficacy of anti-tumor T-cell response

**Increased response rate, longer duration of response, extended OS**

Positive effects of the combination of TG4010 with ICIs have been demonstrated in preclinical tumor models*

* The Lancet Oncology, Dec. 2015, Quoix, E. et al.
**TG4010 | Clinical development plan (non sq. NSCLC)**

Generate additional data in combination with ICIs

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3 trials to position TG4010 in all settings of advanced NSCLC

- **NSCLC - 1st line**
  - Patients with no or low level of PD-L1 expression
  - TG4010 + chemotherapy + PD-1 Inhibitor
  - Multi-center Phase 1/2 trial in US and Europe
  - BMS to supply nivolumab
  - US FDA IND approval granted (Sept. 2017)
  - FPI expected to be enrolled end 2017

- **NSCLC - 2nd line**
  - TG4010 + PD-1 Inhibitor
  - Multi-center Phase 2 trial in the US
  - PI: Dr Karen Kelly (UC Davis)
  - BMS to supply nivolumab
  - First results expected beginning of 2018

- **Resectable NSCLC**
  - Neo-adjuvant chemotherapy ± TG4010
  - Translational research study in the neoadjuvant setting
  - PI: Prof. Quoix at University of Strasbourg
  - FPI expected to be enrolled around the end of 2017
TG4010 | Non-Small Cell Lung Cancer (NSCLC) - 2nd line Phase 2 in combination with Opdivo® (Nivolumab)

**Support of**

[Images of UC Davis Comprehensive Cancer Center and Bristol-Myers Squibb]

- Principal Investigator: Dr Karen Kelly
- Collaborative agreement
  - with UC Davis Medical Center (USA)
  - and Bristol-Myers Squibb (supply of nivolumab)
- First patient treated in March 2017
- First results expected at the beginning of 2018

**Protocol**

- Up to 33 patients
- Multi-center, single-arm, open label study
- Stage IV non-squamous NSCLC who have progressed after one line of systemic therapy

**Endpoints**

- Primary endpoint: Objective response rate (ORR)
- Secondary endpoints: progression-free survival (PFS), overall survival (OS), duration of response and safety

**Participating centers**

- UC Davis
- UC San Francisco
- City of Hope
- UC San Diego
TG4010 | Non-Small Cell Lung Cancer (NSCLC) - 1st line
Phase 1/2 in combination with Opdivo® + Chemotherapy (CT)

Support of
Bristol-Myers Squibb

• Collaborative agreement with BMS (supply of nivolumab)
• US FDA IND Approval (Sept. 2017)
• First patient expected to be enrolled by the end of 2017

Study regimen
• TG4010 10⁸ PFU weekly for 6 weeks then every 3 weeks by SC route
• Nivolumab 360 mg every 3 weeks by IV route
• Pemetrexed-carboplatin (or cisplatin) every 3 weeks for 4 cycles

Protocol
• Up to 39 patients
• Multi-center, single-arm, open label study
• Stage III B-IV or delayed relapse, tumors with low or undetectable PD-L1 expression

Endpoints (Phase 2 part)
• Primary endpoint: Objective response rate (ORR)
• Secondary endpoints: progression-free survival (PFS), overall survival (OS), duration of response and safety

Participating countries
• USA
• Belgium
• Denmark
• France
TG4001 targeting HPV-positive head and neck cancer

MVA expressing HPV16 E6 & E7 antigens & interleukin 2
Dismal prognosis
Better therapeutic options needed

~60% of oropharyngeal HNSCC are HPV-positive
Increasing incidence in western countries → 25 000 patients

First-line therapy
- For patients with good performance status: historically platinum-based doublet (eg. Cisplatin/5-FU or carboplatin/paclitaxel)
  - ORR: 30% to 40%; median OS: 6-9 months regardless of specific drug
- For patient with poor performance status: use single agent CT or cetuximab

Second-line therapy
- Nivolumab, pembrolizumab
  - ORR: 16% to 19%; median OS: 7-8 months
TG4001 | HPV-positive Head & Neck Cancers (HNSCC)
Phase 1/2 in combination with avelumab (Bavencio®)

Support of

Collaborative agreement
• With the alliance of Merck KGaA and Pfizer (supply of avelumab)

Principal Investigator
• Prof Christophe Le Tourneau, Institut Curie

Protocol
• Up to 50 patients (France)
• Multi-center, single-arm, open label trial
• Metastatic or refractory/recurrent HPV-16+ head & neck cancers, after failure of standard therapy

Endpoints (Phase 2 part)
• Primary endpoint: Objective response rate (ORR)
• Secondary endpoints: progression-free survival (PFS), overall survival (OS), duration of response and safety

First patient expected to be treated shortly
TG1050 targeting chronic hepatitis B

Modified Adenovirus 5
that expresses 3 different HBV
(Hepatitis B Virus) antigens
TG1050 | Phase 1/1b in HBV patients close to completion
Combination with standard antivirals

Only ~3% of patients treated with antivirals are cured

High risk of developing cirrhosis and hepatocellular carcinoma

Large unmet medical need: cure rate is extremely low
Need to improve clinical outcome

• ~500,000 eligible patients currently controlled with lifelong treatment*

IP secured until 2032
First data readout in H2 2017

Protocol
• Up to 48 patients
• International, randomized safety and dose-finding study
• Patients currently being treated with standard-of-care antiviral therapy (tenofovir or entecavir)

Primary objectives
✓ Evaluate safety and tolerability of TG1050 administered in single and multiple doses (3 injections at one week interval)
✓ Determine dose and schedule of administration for further development

* Sources: Decision Resources: expert opinions, Company estimates, USA, Europe, Japan, 2015
Oncolytic Viruses

A New Promising Therapeutic Class
Our Oncolytic Virus platform

Next generation of cancer immunotherapies

- Act by directly attacking tumor cells
- And by stimulating immune response

Oncolytic viruses (OV) selectively cause cell lysis in the primary tumor and boost the immune response in the tumor micro-environment.

1. OV infect tumor cells where they selectively replicate. This replication leads to cell lysis and virus propagation in neighboring cells.
2. Active payloads are secreted in the tumor micro-environment.
3. Cytotoxic T-cells enter into the tumor, attracted by local inflammation and danger signals.
4. Infiltrated T-cells kill tumor cells and boost anti-tumor response by active release of tumor antigens.

Preclinical models show OV’s ability to reduce tumor burden and have an abscopal effect on distant metastasis via induced immunogenic cell death mechanism.
Pexa-Vec in hepatocellular carcinoma (HCC)

Vaccinia Virus expressing GM-CSF
Pexa-Vec | 3 complementary mechanisms of action

1. **Cancer cell oncolysis** *(Kirn D 2009)*: Infection, cell lysis and viral spread

2. **Tumor vascular shutdown** *(Breitbach C 2013)*: Infection and cell lysis

3. **Active immunotherapy** *(Kim MK, 2013)*: Tumor-specific immune response stimulation (GM-CSF)

Pexa-Vec | Large unmet medical need in HCC

First-line therapy
- Sorafenib is currently the only approved product - modest activity
  - ORR: 2%; median OS: 10.7 months
- Nivolumab likely to become a new therapeutic option: Promising activity in Phase 2
  - ORR: 14% to 16%; median OS: 14 to 15 months

Second-line therapy
- Regorafenib
  - ORR: 10%; median OS: 10.6 months

Dismal prognosis
Better therapeutic options needed
25,000 eligible patients in Europe
Pexa-Vec | Clinical development plan

Pivotal Phase 3 and three complementary studies

1. **Complete the Phase 3 Trial in 1st Line HCC in Combination with Sorafenib**

   **Advanced HCC 1st line**
   
<table>
<thead>
<tr>
<th>Pexa-Vec + sofarifenib</th>
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</thead>
<tbody>
<tr>
<td>• Multi-center <strong>Phase 3 trial</strong> in Europe, US, Asia</td>
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<tr>
<td>• Randomized, two arm trial</td>
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<tr>
<td>• Ongoing recruitment – Results expected in 2019</td>
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</table>

2. **Conduct three Phase 2 Trials in combination with ICI and other agents based on supportive preclinical data**

   **Advanced HCC 1st line**
   
<table>
<thead>
<tr>
<th>Pexa-Vec + Opdivo® (nivolumab)</th>
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</thead>
<tbody>
<tr>
<td>• Multi-center <strong>Phase 2 trial</strong> in France, Italy, US</td>
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<tr>
<td>• Sponsor: Transgene</td>
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<tr>
<td>• Open label, single arm trial / 1st patient dosed in July 2017</td>
</tr>
</tbody>
</table>

   **Solid tumors**
   
<table>
<thead>
<tr>
<th>Pexa-Vec + Yervoy® (ipilimumab)</th>
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<tbody>
<tr>
<td>• Multi-center <strong>Phase 2 trial</strong> in France</td>
</tr>
<tr>
<td>• Sponsor: Léon Bérard (France)</td>
</tr>
<tr>
<td>• 1st patient dosed in February 2017 / 1st results around the end of 2017</td>
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</table>

   **Breast cancer STS**
   
<table>
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<tr>
<th>Pexa-Vec + cyclophosphamide</th>
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<tbody>
<tr>
<td>• Multi-center <strong>Phase 2 trial</strong> in France</td>
</tr>
<tr>
<td>• Sponsor: Bergonié (France), funded by INCA</td>
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<tr>
<td>• 1st patient dosed in April 2017</td>
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</table>
**Pexa-Vec | Ongoing Phase 3 clinical trial (PHOCUS trial)**

1st line advanced hepatocellular carcinoma

Phase 3 study in combination with sorafenib (Kinase inhibitor)

**Design**
- Pexa-Vec + sorafenib versus sorafenib (only approved drug for advanced HCC)
- N=600 patients (Europe, North America and Asia), 140 clinical centers
- 1:1 randomized trial

**Endpoints**
- Primary: overall survival (OS)
- Secondary: safety, time to progression, progression-free survival, overall response rate and disease control rate

- ✓ Orphan drug designation granted
- ✓ SPA with FDA
- ✓ SFDA autorisation (July 2017)

- Conducted by SillaJen BioTherapeutics

- First patient enrolled in January 2016
- Recruitment ongoing
- 1st patient recently treated in Europe
- First results expected in 2019
Engineering oncolytic viruses

Creating next generation of immunotherapies
Oncolytic viruses | Transgene’s roadmap for success

**Imlygic/T-Vec, Pexa-Vec**
- Oncolytic activity
- IT administration
- Indirect immune stimulation, via non-specific immune modulators (e.g. GM-CSF)

**NEW GENERATION**
- Oncolytic activity
- Systemic (IV) administration
- Better tumor selectivity (double gene deletion)
- Additional functionality - targeted chemotherapy
  *e.g. TG6002*

**FUTURE GENERATIONS**
- Oncolytic activity
- Systemic (IV) administration
- Better tumor selectivity (double gene deletion)
- “Armed” – targeted immune modulators expressed in tumor microenvironment
- e.g. Oncolytic virus Immunotherapy

**Innovative content**
- Time to market
TG6002 | First product from our new generation platform
Improved backbone and advanced therapeutic payload

Superior oncolytic properties with local production of chemotherapy

- Proprietary backbone
- Double gene deletion TK- RR-
- Viral oncolysis
- Targeted chemotherapy

- Phase 1 trial in glioblastoma, open label, dose escalation, IV administration
- PI: Prof J-Y. Delattre (Pitié Salpêtrière)
- INCA Grant

First-in-human trial FPI in coming weeks
Development in GI cancers in active preparation
Immuno-armed oncolytic strategy
A multifunctional design

1. Validated backbone
   - Oncolytic activity
   - Immunogenic properties
   - Tumor targeting from the IV route

2. Differentiating Targets
   - Key effectors of the tumor microenvironment
   - Very effective mechanisms but toxic when administered systemically, and benefiting from local delivery

3. Additional Targets
   - Complementary effectors of the tumor microenvironment, Might be already commercially available but expensive (e.g. anti-PD1)

- VV TK::RR
- Enzyme
- Antibody
- Cytokines / Chemokines
- Receptor ligands
- 2nd antibody
Research collaboration with Servier
Development of a novel method for allogenic CAR-T preparation

**transgene**

- Large collection of viral vectors for therapeutic applications
- Competence in genome engineering

**SERVIER**

- Developing cell therapies since November 2015
- Exclusive rights to UCART-19 (Cellectis partnership)

**Application of viral vectors technology to the engineering of allogenic CAR-T**

**Objectives**

- Evaluate and select innovative vectors for targeted modification of T-cells
  - simpler, faster and more effective preparation methods
  - evolve towards multiple deletion beyond TCR, or insertion to improve immune tolerance, and efficiency of the cell therapy
Outlook

On Track to Deliver
Multiple Value-Enhancing
Clinical Data Read-Outs
Significant news flow in the next 12-18 months

- TG4010: Lung cancer (NSCLC) (Bristol-Myers Squibb)
- TG4001: HPV+ head & neck cancer (HNSCC) (Merck, Pfizer)
- TG1050: Chronic hepatitis B (HBV)
- Pexa-Vec: Liver cancer (HCC) (Sillajen)
- TG6002: Glioblastoma & gastro-intestinal tumors
## 2017 - A year of significant progress

<table>
<thead>
<tr>
<th>Product</th>
<th>Events</th>
</tr>
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</table>
| **TG4010** | 1st line:  
  - Collaboration agreement ✔  
  - US FDA IND Approval ✔  
  - 1st patient of the Phase 2 trial  
2nd line:  
  - 1st patient treated ✔ |
| **TG4001** | First patient treated (H2 2017)                                        |
| **TG1050** | First results (H2 2017)                                               |
| **Pexa-Vec** | Phase 3, HCC, 1st line: 1st patient treated in Europe (Q2 2017) ✔  
  Phase 2, HCC, 1st line: 1st patient treated (Q2 2017) ✔  
  Phase 1, solid tumors:  
    - 1st patient treated ✔  
    - First results around the end of 2017 |
| **TG6002** | First patient treated in the Phase 1 trial (coming weeks)               |
Transgene Ownership

Key Shareholders
As of June 30, 2017

- 56.4 million shares outstanding + 1.1 million options and free shares
- Market capitalization: ~ €200 million as of September 12, 2017
- Listed on Euronext Paris
- ISIN: FR0005175080
- Ticker: TNG
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