

## First Patient Dosed in a Phase 1/2 Trial of Transgene's Oncolytic Virus TG6002 Administered Intravenously in Patients with Advanced Gastrointestinal Tumors

*TG6002 Has Multiple Mechanisms of Action for Enhanced Anti-Tumor Activity: Oncolysis, Local Production of Chemotherapy in Tumor and Cell-Mediated Immune Response*

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Strasbourg, France, October 17, 2018, 6:00 p.m. CET - Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies, today announced that the first patient of a Phase 1/2 clinical trial evaluating TG6002 in patients with advanced gastrointestinal tumors, such as colon cancers, has been dosed at Centre Léon Bérard (France). This multicenter trial has already been approved in France, Belgium and Spain and will enroll up to 59 patients.

**TG6002 is a next-generation oncolytic virus (OV), which can be administered intravenously and has multiple mechanisms of action.** It has been engineered to combine the killing of cancer cells (oncolysis), the production of 5-FU, a widely used chemotherapy agent, in the tumor site, and the induction of immunogenic cell death by eliciting an immune response against tumor cells. TG6002 expresses the proprietary *FCU1* gene in the cancer cells it has infected, leading to local conversion of the pro-drug 5-FC (administered orally) into 5-FU. This is particularly important as most gastrointestinal tumors are 5-FU sensitive.

TG6002 has been shown to induce both response in the primary tumor and an immune-mediated regression of distant metastases (immunogenic cell death) in preclinical experiments.

Dr. Philippe Cassier, M.D., PhD, principal investigator of the trial and head of the early-phase trials unit at Centre Léon Bérard, explained: *"Even if patient outcomes have improved over the last 20 years, the median overall survival of patients with metastatic colorectal cancers (CRC) remains less than 3 years. Despite patients typically receiving up to four lines of treatments, some are associated with significant side effects. The majority of patients with metastatic CRC are refractory to immune checkpoint inhibitors. For this reason, 5-FU-based chemotherapy remains a reference treatment in this disease. TG6002, an oncolytic virus that lyses cancer cells and produces 5-FU where it is needed, represents a promising opportunity to provide patients with a more efficacious and better tolerated option."*

Dr. Maud Brandely, M.D., PhD, Chief Medical Officer of Transgene, added: *"With its multiple mechanism of action, TG6002 is a very promising oncolytic virus that is administered intravenously in this trial. Lysis of the cancer cells, production of chemotherapy in the tumor and induction of a targeted immune response are complementary approaches to better attack the disease. We look forward to progressing this trial and delivering clinical results for this promising new generation of oncolytic virus."*

This trial is a European single-arm open-label Phase 1/2 trial evaluating the safety and tolerability of multiple ascending doses of TG6002 administered intravenously in combination with oral 5-FC, a non-cytotoxic pro-drug that can be converted in 5-FU. The trial has safety as primary endpoint for the Phase 1 part and efficacy for the Phase 2 part. The trial will also evaluate pharmacokinetic properties and biodistribution of TG6002, along with immune modulation of the tumor micro-environment. The study will enroll up to 59 patients suffering from advanced gastrointestinal carcinomas who have failed and/or are intolerant to standard therapeutic options in the Phase 1 part and will enroll patients with colon cancer and liver metastases in the phase 2 part.

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## Notes to editors

### Contacts

#### Transgene:

##### Lucie Larguier

Director Corporate Communications & IR  
+33 (0)3 88 27 91 04  
[investorrelations@transgene.fr](mailto:investorrelations@transgene.fr)

#### Media contacts:

##### Citigate Dewe Rogerson

David Dible/Marine Perrier/Sylvie Berrebi  
+44 (0)20 7638 9571  
[transgene@citigatedewerogerson.com](mailto:transgene@citigatedewerogerson.com)

### About TG6002

TG6002 is a next generation oncolytic immunotherapy. It has been designed to induce the breakdown of cancer cells (oncolysis) and allow the local production of chemotherapy (5-FU) in the tumor. TG6002 is a modified *Vaccinia* virus, with double gene deletion (TK-RR-), and expressing the proprietary FCU1 gene in the cancer cells it has infected, leading to the local conversion of the non-cytotoxic pro-drug, flucytosine (5-FC), into 5-FU, a widely used cancer chemotherapy. The oncolytic virus TG6002 has shown efficacy and good safety profile in several preclinical models. Transgene believes that TG6002 may represent a new therapeutic option in recurrent cancer patients.

Another Phase 1/2 trial using TG6002 is ongoing in France in patients with glioblastoma.

### About gastrointestinal tumors

Gastrointestinal (GI) cancer is a term for a group of cancers that affect the digestive system. This includes cancers of the esophagus, gallbladder, liver, pancreas, stomach, small intestine, colon, rectum, and anus. Colorectal cancer is the second most commonly diagnosed cancer in Europe and a leading cause of death both in Europe and worldwide. In 2012, there were 447,000 new cases of CRC in Europe with 215,000 deaths and worldwide, there were 1.4 million new cases with 694,000 deaths (Ferlay J. *et al.*, 2013, Ferlay J. *et al.*, 2015). Over the last decade, the clinical outcome for patients with metastatic CRC (mCRC) has improved. Today, the median overall survival (OS) for patients with mCRC is ~30 months.

### About Transgene

Transgene (Euronext: TNG) is a publicly traded French biotechnology company focused on designing and developing targeted immunotherapies for the treatment of cancer and infectious diseases. Transgene's programs utilize viral vector technology with the goal of indirectly or directly killing infected or cancerous cells. The Company's lead clinical-stage programs are: TG4010, a therapeutic vaccine against non-small cell lung cancer, Pexa-Vec, an oncolytic virus against liver cancer, and TG4001, a therapeutic vaccine against HPV-positive head and neck cancers. The Company has several other programs in clinical development, including TG1050 (a therapeutic vaccine for the treatment of chronic hepatitis B) and TG6002 (an oncolytic virus for the treatment of solid tumors).

With its proprietary Invir.IO™, Transgene builds on its expertise in viral vectors engineering to design a new generation of multifunctional oncolytic viruses.

myvac™, an individualized MVA-based immunotherapy platform designed to integrate neoantigens, completes this innovative research portfolio.

Additional information about Transgene is available at [www.transgene.fr](http://www.transgene.fr).

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