

First Patient Treated in a Phase 1/2a Trial (Oncovirac) of Novel Oncolytic Virus TG6002 in Recurrent Glioblastoma

*TG6002 has a Double Mechanism of Action (Oncolysis and Local Delivery of Chemotherapy)
for Enhanced Anti-Tumor Selectivity and Activity*

First Readouts Expected in H2 2018

Strasbourg, France, October 26, 2017, 5:45 p.m. CET - Transgene (Euronext Paris: TNG), a biotech company that designs and develops viral-based immunotherapies, today announced that the first patient with recurrent glioblastoma has been treated at La Pitié-Salpêtrière hospital, Greater Paris University Hospitals, AP-HP (Paris), in the first-in-human clinical trial (Oncovirac trial) of TG6002, a novel oncolytic virus. TG6002 represents the next generation of oncolytic virus (OV), which is administered intravenously and has multiple functions. It has been engineered to combine oncolysis (the breakdown of cancer cells) with the local production of 5-FU chemotherapy agent in the tumor. It is also expected to induce an immune response following the antigen spreading that is caused by the cancer cells' breakdown.

TG6002: a novel oncolytic virus allowing the targeted production of chemotherapy in the tumor

TG6002 is a next generation oncolytic immunotherapy, which has a double mechanism of action. It has been designed by Transgene to:

1. induce the breakdown of cancer cells (oncolysis) by tumor-selective viral replication. In preclinical experiments, TG6002 was able to induce response in the primary tumor and an immune-mediated regression of distant metastases (immunogenic cell death);
2. allow the local production of chemotherapy (5-FU), a widely used cancer chemotherapy, in the tumor. TG6002 expresses the proprietary Fcu1 gene in the cancer cells it has infected, leading to the local conversion of the 5-FC into 5-FU.

First-in-human trial to deliver first readouts in H2 2018

Oncovirac is an open-label Phase 1/2a 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, flucytosine, that can be converted in 5-FU. The anti-tumor activity of this novel oncolytic virus will also be monitored. The study will enroll patients suffering from recurrent glioblastoma, who have failed standard of care treatment.

Dr. Ahmed Idbaih, M.D., PhD, neuro-oncologist at La Pitié-Salpêtrière Hospital (Paris, France), is the principal investigator of the study. He is involved in several clinical trials dedicated to primary brain tumor patients. He also coordinates "GlioTex", a research group focused on glioblastoma and experimental therapeutics at ICM (The Institut du Cerveau et de la Moelle épinière – Brain & Spine Institute). AP-HP Paris Greater Hospitals, is the sponsor of Oncovirac, a trial also supported by INCa (French National Cancer Institute). More information on the trial is available on [clinicaltrials.gov \(NCT03294486\)](https://clinicaltrials.gov/NCT03294486). The first readouts of the study are expected in the second half of 2018.

Maud Brandely, M.D., PhD, Chief Medical Officer of Transgene, added: *"TG6002 is a very promising new generation of oncolytic virus, which has the potential to be administered intravenously. Based on our compelling preclinical data, we have established that its replication induces immunogenic cell lysis and the local production of chemotherapy. We are excited to see this novel immunotherapy with multiple modes of action enter the clinic and look forward to obtaining results that will allow further development of TG6002 in several solid tumors indications."*

Dr. Ahmed Idbaih, M.D., PhD, neuro-oncologist at La Pitié-Salpêtrière hospital, AP-HP, and principal investigator of the trial, added: *“Current treatments of recurrent glioblastoma are insufficient. By combining the immunogenic lysis of cancer cells with the targeted production of chemotherapy in the tumor, TG6002 has the potential to show anti-tumor efficacy and to avoid systemic side effects of chemotherapy. We are very pleased to be conducting this first in human clinical trial evaluating this novel immunotherapy that we believe could improve the overall survival of recurrent glioblastoma patients while preserving their quality of life.”*

Contacts

Transgene:

Lucie Larguier

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

Media contacts:

Citigate Dewe Rogerson

David Dible/Marine Perrier
+ 44 (0)20 7638 9571
transgene@citigatedr.co.uk

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 of glioblastoma *in vitro* (i.e. cell line) and *in vivo* (i.e. xenografts in Swiss/Nude mice). Transgene believes that TG6002 may represent a new therapeutic option in recurrent glioblastoma patients. TG6002 could also be investigated in other solid tumors.

About Glioblastoma

Glioblastoma is the most common and the most aggressive primary brain cancer in adults. Approximately 70,000 new cases are diagnosed each year in Europe 28 and in the USA (Globocan 2012). Despite very intensive treatments (i.e. maximal safe surgery, radiotherapy, and several lines of cytotoxic chemotherapy), inducing significant adverse events, the prognosis of glioblastoma patients remains poor. More efficient and less toxic therapies are urgently needed to improve survival and quality of life of glioblastoma patients.

About Transgene

Transgene (Euronext: TNG), part of Institut Mérieux, 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 (chronic hepatitis B) and TG6002 (solid tumors). Transgene is based in Strasbourg, France, and has additional operations in Lyon, as well as a joint venture in China. Additional information about Transgene is available at www.transgene.fr.

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Transgene undertakes no obligation to update these forward-looking statements, even if new information becomes available in the future.

About AP-HP

AP-HP (Greater Paris University Hospitals) is a European world-renowned university hospital. Its 39 hospitals treat 10 million people every year: in consultation, emergency, during scheduled or home hospitalizations. The AP-HP provides a public health service for everyone, 24 hours a day. This mission is a duty as well as great source of pride. AP-HP is the leading employer in the Greater Paris area: 100, 000 staff members – doctors, researchers, paramedical staff, administrative personnel and workers – work there. <http://www.aphp.fr>