

First Patient Dosed with Transgene's Oncolytic Virus TG6002, Administered by Intrahepatic Artery Infusion in Colorectal Cancer with Liver Metastases

The Phase 1/2a trial evaluates a novel route of administration for TG6002, an oncolytic virus that allows the production of chemotherapy agent directly in the tumor

Strasbourg, France, February 20, 2020, 5:45 p.m. CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer, today announces that the first patient has successfully received TG6002, via an intrahepatic artery (IHA) infusion, as a locoregional treatment for unresectable liver metastases from colorectal cancer (CRLM). This procedure was performed at the NHS St James's University Hospital in Leeds (United Kingdom). Dr. Adel Samson, Academic Medical Oncologist at The Leeds Teaching Hospitals NHS Trust and The University of Leeds, is the Chief Investigator of this trial. TG6002 is a next-generation oncolytic virus **which has multiple mechanisms of action, both directly in the tumor micro-environment and systemically.**

The oncolytic virus TG6002 has been engineered to directly kill cancer cells (oncolysis), to enable the production of a chemotherapy agent (5-FU) within the tumor, and to elicit an immune response by the body against the tumor cells. In preclinical experiments, TG6002 has been shown to induce the shrinkage of the primary tumor as well as the regression of distant metastases¹.

TG6002 has been designed to achieve a better anti-tumor effect with limited chemotherapy-induced side effects, by enabling the production of a chemotherapy agent in the tumor.

- TG6002 enables the production of 5-FU by the expression of the proprietary FCU1 gene in the cancer cells TG6002 has infected, leading to local conversion of the pro-drug 5-FC (administered orally) into 5-FU.
- 5-FU is a common chemotherapy for patients with CRLM. However, it is associated with side effects that can lead to treatment discontinuation. With TG6002, 5-FU is produced within the tumor where it is expected to be present at a high concentration level in contrast to the very low levels anticipated in the rest of the patient's body.

In this trial, TG6002 is administered via the intrahepatic artery (IHA).

- This administration route is routinely used to deliver therapeutic agents into patients with liver tumors. The IHA route will efficiently deliver a higher concentration of TG6002 to the liver metastases (visible or not visible with CT scan).
- The IHA trial is a single-arm open-label Phase 1/2a trial evaluating the safety, pharmacokinetics, biodistribution and efficacy of repeated and ascending doses of TG6002 in combination with oral 5-FC. The study will enroll up to 75 patients.

TG6002 is also being evaluated in another Phase 1/2a clinical trial where it is being given via intravenous administration in advanced GI cancer patients. The first clinical data from this trial will be reported during the second quarter of 2020.

¹ *The Enhanced Tumor Specificity of TG6002, an Armed Oncolytic Vaccinia Virus Deleted in Two Genes Involved in Nucleotide Metabolism*, J. Foloppe, et al., Molecular Therapy Oncolytics, <https://doi.org/10.1016/j.omto.2019.03.005>

“The start of this trial evaluating the safety and activity of TG6002 administered via an IHA infusion in patients with CRLM will enable us to further strengthen the data package for this novel oncolytic virus. IHA infusion is a novel administration mode for oncolytics and we believe it will help broaden the scope of potential indications that could be targeted by vaccinia-based oncolytics. Our on-going trial with TG6002 administered by the intravenous route is proceeding well. No safety signals have been observed so far and the dose-escalation phase is ongoing. We expect the first clinical data from this IV study to be reported during the second quarter of 2020.” said **Dr. Maud Brandely, MD, PhD, Chief Medical Officer of Transgene.**

Dr. Samson added: *“Previous trials with vaccinia-based oncolytic viruses have shown that these novel immunotherapeutics can modulate the tumor micro-environment. The addition of the local production of chemotherapy offers new perspectives in the treatment of CRLM patients. The use of IHA infusion should enable a higher concentration of TG6002 in the liver tumors allowing it to become an additional effective and well tolerated treatment modality. I hope that this study will demonstrate that the multiple mechanisms of action of TG6002 are able to achieve better outcomes for the patients whilst limiting systemic exposure to 5-FU.”*

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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.

About Colorectal cancer

Colorectal cancer (CRC) is the second most commonly diagnosed cancer in Europe and a leading cause of death both in Europe and worldwide. In 2018, there were approximately 500,000 new cases of CRC in Europe with 242,000 deaths and worldwide, there were 1.8 million new cases with 881,000 deaths (Globocan 2018). Approximately half of all CRC patients develop liver metastases, only a small proportion of whom being suitable for potentially curative hepatic resection (Leporrier J, 2006). 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 clinical-stage programs are TG4001, a therapeutic vaccine against HPV-positive cancers, TG6002, an oncolytic virus for the treatment of solid tumors, and TG4050, the first individualized therapeutic vaccine based on the *myvac*® platform.

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

Additional information about Transgene is available at: www.transgene.fr.

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