



Positive initial data from a Phase 1 trial with Transgene's oncolytic virus TG6002

Intravenous administration of TG6002 is well tolerated and induces the production of a chemotherapy agent (5-FU) via its replication in tumor cells

Strasbourg, France, September 8, 2020, 5:45 pm CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer, announces first positive data from the Phase 1 clinical trial evaluating the intravenous administration of TG6002 in patients with advanced gastrointestinal tumors.

The trial aims at confirming the good tolerability of ascending doses of intravenous TG6002 and at providing the first translational data from this novel route of administration.

- **The independent safety review committee met and recommended that the trial be continued and that the dose level be increased** to a 3×10^9 pfu in the absence of dose-limiting toxicity of TG6002 at the 10^9 pfu dose.
- **The first translational data show that, when administered intravenously, TG6002 circulates transiently in the patient's bloodstream and induces the production of 5-FU at therapeutic doses.** The production of 5-FU results from the expression of the FCU1 gene, integrated into the TG6002 genome, as the virus replicates selectively in the tumor cells.

TG6002 has been engineered to combine the oncolytic and immunogenic actions of the virus with the intra-tumoral production of 5-FU, a chemotherapeutic agent. This production is achieved by converting the pro-drug 5-FC (administered orally) into 5-FU, which is expected to reach high concentrations within the tumor. This mechanism of action is based on the expression of the proprietary FCU1 gene that has been integrated with the genome of TG6002.

"This is the first clinical study demonstrating that Transgene's Vaccinia Virus from the Invir.IO™ platform is able to reach the tumor when administered intravenously. Importantly, through the production of 5-FU at therapeutic doses, we have also demonstrated the functionality of the FCU1 transgene integrated into the genome of TG6002. These positive initial translational data, combined with a satisfactory tolerability profile, have allowed us to continue this Phase 1 clinical trial and evaluate higher doses of this promising new drug candidate," said **Dr. Maud Brandely, MD, PhD, Chief Medical Officer of Transgene.**

With this clinical trial, Transgene aims to demonstrate the benefits of intravenous administration of next generation oncolytic viruses such as TG6002 and the candidates derived from the Invir.IO™ platform, in order to extend the use of these therapies to many solid tumors, including gastrointestinal cancers. This broad utility contrasts with first-generation oncolytic viruses that have only been approved to be given via intra-tumoral administration, which restricts their use to easily accessible tumors.

TG6002 is also being evaluated in another Phase 1/2a clinical trial where it is being given by Intrahepatic Artery Infusion in patients with advanced colorectal cancer with liver metastases (CRLM). In order to respond to the Covid-19 pandemic, the trial's clinical site had temporarily suspended patient inclusion; recruitment resumed in early September 2020.

About the trial

This trial is a 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-FU, a non-cytotoxic pro-drug that can be converted in 5-FU, its active metabolite. Based on the safety profile of TG6002, several dose levels have been added to the initial Phase 1 clinical protocol. At the end of this Phase 1 part, Phase 2 patients will receive the recommended dose of TG6002. The trial has safety as primary endpoint for the Phase 1 part and efficacy for the Phase 2 part. The trial also evaluates pharmacokinetic properties and biodistribution of TG6002, along with immune modulation of the tumor micro-environment. This European study will enroll up to 40 patients suffering from advanced gastrointestinal carcinomas who have failed and/or are intolerant to standard therapeutic options in the Phase 1 part. Patients with colon cancer and liver metastases will be enrolled in the phase 2 part.

Dr. Philippe Cassier, M.D., PhD, head of the early-phase trials unit at Centre Léon Bérard (Lyon, France) is the principal investigator of the trial.

About TG6002

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.

The production of 5-FU directly in the tumor aims at achieving a better anti-tumor effect with limited chemotherapy-induced side effects.

- TG6002 induces the production of 5-FU in the cancer cells it has infected, by enabling the local conversion of the pro-drug 5-FU (administered orally) into 5-FU. 5-FU is a common chemotherapy for patients with CRLM. This mechanism of action is based on the expression of the proprietary FCU1 gene that has been integrated with the genome of TG6002, as the virus replicates selectively in the tumor cells.
- 5-FU 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.

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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>

About Transgene

Transgene (Euronext: TNG) is a publicly traded French biotechnology company focused on designing and developing targeted immunotherapies for the treatment of cancer. Transgene's programs utilize viral vector technology with the goal of indirectly or directly killing cancer cells.

The Company's clinical-stage programs consist of two therapeutic vaccines (TG4001 for the treatment of HPV-positive cancers, and TG4050, the first individualized therapeutic vaccine based on the *myvac*[®] platform) as well as two oncolytic viruses (TG6002 for the treatment of solid tumors, and BT-001, the first oncolytic virus based on the Invir.IO[™] platform).

With Transgene's *myvac*[®] platform, therapeutic vaccination enters the field of precision medicine with a novel immunotherapy that is fully tailored to each individual. The *myvac*[®] approach allows the generation of a virus-based immunotherapy that encodes patient-specific mutations identified and selected by Artificial Intelligence capabilities provided by its partner NEC.

With its proprietary platform Invir.IO[™], Transgene is building on its viral vector engineering expertise to design a new generation of multifunctional oncolytic viruses. Transgene has an ongoing Invir.IO[™] collaboration with AstraZeneca.

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

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