PRESS RELEASE

Transgene - First Patient Dosed in Phase I Trial Evaluating TG6050, a Novel IL-12-Armed Oncolytic Virus Administered Intravenously, in Non-Small Cell Lung Cancer

TG6050 is an oncolytic virus derived from Transgene's Invir.IO® platform encoding interleukin-12 (IL-12) and an anti-CTLA4 antibody, with the potential to trigger a powerful antitumor immune response.

The Phase I Delivir trial will evaluate the intravenous (IV) administration of this novel multi-armed immunotherapy in patients with recurrent metastatic advanced non-small cell lung cancer.

Intravenous administration extends the use of oncolytic viruses to a much wider range of solid tumors compared to intratumoral administration, broadening TG6050's potential addressable markets.

Strasbourg, France, May 10, 2023, 8:00 a.m. CET – **Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer, announced that the first patient has been dosed in Delivir, a Phase I clinical trial evaluating TG6050. This multi-mechanism oncolytic immunotherapy is administered intravenously in patients with recurrent metastatic advanced non-small cell lung cancer (NSCLC)**.

TG6050 seeks to overcome tumor resistance by initiating an antitumor response through multiple mechanisms of action that include oncolysis, the induction of an immune response together with high intra-tumoral concentrations of IL-12 and anti-CTLA4 antibody.

The Delivir trial will enroll up to 36 patients with advanced NSCLC who have failed standard therapeutic options, including immune checkpoint inhibitors. The IV route is considered the most appropriate route of administration for this patient population with disseminated disease and multiple overt and occult metastases. Completion of the trial is expected in H2 2024.

The potential for IV administration of Transgene's patented Invir.IO® platform has been seen in the data presented for TG6002. TG6050 will build on the safety profile of Transgene's backbone while enhancing the therapeutic potential of its two highly immunogenic payloads – IL-12 and a full length anti-CTLA-4 antibody – while limiting exposure to their systemic toxicity.

"We are pleased to initiate this first-in-human trial of TG6050 administered intravenously in patients with recurrent/metastatic advanced non-small cell lung cancer in great need for effective new therapeutic options," said **Dr. Maud Brandely, MD, PhD, Chief Medical Officer of Transgene**. "*Intravenous administration of TG6050 aims at significantly enhance the therapeutic potential of this promising oncolytic virus as it allows a targeted approach to many internal cancer lesions and metastases inaccessible by intratumoral injection. With its multiple mechanisms of action – including oncolysis, the induction of an immune response together with high intra-tumoral concentrations of IL-12 and anti-CTLA4 antibody – and its ability to be administered intravenously, TG6050 has several competitive advantages. We look forward to progressing this trial and delivering clinical results for this promising new oncolytic virus."*

Efficacy and safety of TG6050 were demonstrated in preclinical and toxicology studies in non-human animal models. Initial data were presented at the American Association for Cancer Research (AACR) Annual Meeting, April 14 -19, 2023 and can be accessed here.

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About the Delivir trial (NCT: NCT05788926)

The Delivir trial is a multicenter, open label, dose-escalation Phase I trial evaluating TG6050 as a single agent. The trial will enroll up to 36 patients with metastatic/advanced non-small cell lung cancer (NSCLC), who have failed standard therapeutic options including immunotherapies such as immune checkpoint inhibitors. Patients will receive single and repeated escalating doses of TG6050 administered intravenously, to determine the recommended dose and best schedule of administration for subsequent clinical development.

About TG6050

TG6050 is an oncolytic virus developed with Transgene's Invir.IO® platform for intravenous administration. Invir.IO®'s viruses are based on the patented large capacity *Vaccinia virus* Copenhagen strain genetically modified with the double deletion TK^-RR^- ($VV_{COP}TK^-RR^-$). TG6050 has been engineered to encode human IL-12, a cytokine that triggers a powerful antitumor immune response and a full length anti-CTLA4 antibody. It has also been optimized with the deletion of the gene encoding for the M2L viral protein that targets CD80 and CD86, two ligands of CTLA4 [source: Kleinpeter et al., J Virol. 2019 Jun 1; 93(11): e00207-19]. The use of an oncolytic virus to deliver these immunotherapies locally and selectively in the tumor microenvironment allows high intratumoral concentrations of both therapeutic proteins eliciting a stronger and more effective antitumor response. By reducing systemic exposure to a very low level, this local therapeutic activity furthermore allows to increase the safety and tolerability profile of IL-12 and the anti-CTLA4 antibody.

It is evaluated in the Delivir trial, a Phase I trial conducted in advanced NSCLC patients.

A short video detailing TG6050's mechanism of action can be found here.

About Transgene

Transgene (Euronext: TNG) is a 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 a portfolio of therapeutic vaccines and oncolytic viruses:

TG4050, the first individualized therapeutic vaccine based on the *myvac*® platform, TG4001 for the treatment of HPV-positive cancers, as well as TG6002, BT-001 and TG6050, three oncolytic viruses based on the Invir.IO® viral backbone. 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. Additional information about Transgene is available at: www.transgene.fr
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