

Transgene - Preclinical Results Showing TG6050, a Novel Oncolytic Virus, induces Tumor Regression by Activating Innate and Adaptive immune responses presented at AACR

Invir.IO® based oncolytic virus TG6050, is armed with IL-12 and an anti-CTLA4 antibody. A Phase I trial (Delivir) recently started enrolling patients with advanced non-small cell lung cancer (NSCLC)

Strasbourg, France, April 17, 2023, 7:30 a.m. CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer, presented promising preclinical data on its novel oncolytic virus TG6050, at the American Association for Cancer Research (AACR) Annual Meeting, April 14-19, 2023.

These data demonstrate the ability of TG6050 to induce strong antitumor responses through the production of IL-12 and anti-CTLA4 antibody in the tumor and the induction of innate and adaptive immune responses.

TG6050 is a clinical-stage oncolytic virus that has been engineered to encode human IL-12 and a full length anti-CTLA4 antibody. It is derived from the Invir.IO® platform and its patented VV_{copTKRR} viral vector which was shown to be well tolerated in humans and to replicate and express payloads in tumor tissues.

Key results of the poster are as follows:

- ✓ Sustained expression of IL-12 has been detected in tumors after intravenous and intratumoral administration of the murine version of TG6050 (mTG6050). The levels of functional IL-12 found in the tumor reach active concentrations. They are associated with low systemic exposure.
- ✓ mTG6050 treatment increased T cell responses capable of killing cancer cells.
- ✓ Transcriptomic and immunological analyses clearly show a remodeling of the tumor micro-environment and the activation of numerous innate and adaptive immune pathways.
- ✓ In several mice models, mTG6050 displayed a very strong anti-tumor activity.

Hedi Ben Brahim, Transgene's CEO said, *"We have designed TG6050, a novel oncolytic virus encoding the IL-12 and an anti-CTLA4, to generate both innate and adaptive immune responses. These outstanding pre-clinical findings clearly support the clinical development of TG6050, which has recently started the Phase I Delivir trial in patients with non-small cell lung cancer. We are confident that by generating similar effects in humans, TG6050 could become a new standard of care in patients with solid tumors."*

The Phase I Delivir trial has been initiated in 2023 and is currently enrolling patients with metastatic and recurring NSCLC.

Transgene will present a total of eight posters at AACR 2023 which all demonstrate the potential of the Company's viral vectors in the treatment of solid tumors.

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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 will be 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 the Delivir trial (NCT: 05788926)

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 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. Transgene has an ongoing Invir.IO® collaboration with AstraZeneca. Additional information about Transgene is available at: www.transgene.fr

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