PRESS RELEASE

Transgene Receives Approval to Start a Phase I Trial of TG6050, a Novel IL-12-Armed Oncolytic Virus Given by Intravenous Administration

TG6050 is a proprietary oncolytic virus derived from Transgene's Invir.IO™ platform encoding interleukin-12 (IL-12) and an anti-CTLA4 antibody.

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

Strasbourg, France, January 6, 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, today announces it has received clinical trial application (CTA) approval from the French National Agency for the Safety of Medicines and Health Products (ANSM) to proceed with a Phase I clinical trial of TG6050, a novel oncolytic virus (OV) that will be administered intravenously in patients with advanced non-small cell lung cancer (NSCLC)**.

TG6050 has been generated using Transgene's patented Invir.IO™ platform. It has been engineered to express human IL-12, a cytokine that triggers a powerful antitumor immune response, and a full length anti-CTLA4 antibody.

By selectively targeting tumor cells and expressing IL-12 and the anti-CTLA4 antibody in the tumor microenvironment, **TG6050 is expected to elicit a powerful and multi-pronged antitumor response**. A short video detailing the mechanism of action can be found here.

TG6050 has been designed to be administered intravenously, a route of administration that has been demonstrated to be safe and feasible with an Invir.IO™ based OV. Intravenous administration will significantly enhance the therapeutic and market potential of this OV as it allows a more targeted approach to many internal cancer lesions and metastases inaccessible by intratumoral injection. Intratumoral injection, where the drug is injected directly into the tumor, is currently the only approved route of administration for an oncolytic virus. IV administration would represent a significant advantage.

The Delivir trial will enroll up to 36 patients with advanced NSCLC who have failed standard therapeutic options, including immune checkpoint inhibitors (ICIs). TG6050 is expected to overcome tumor resistance by the initiation of an antitumor response through multiple mechanisms of action that include oncolysis, the induction of an immune response and high intra-tumoral concentrations of IL-12 and anti-CTLA4 antibody. The IV route is considered the most appropriate route of administration for this patient population with disseminated disease and multiple overt and occult metastases.

Hedi Ben Brahim, CEO of Transgene commented: *"TG6050 is an exciting new asset within Transgene's growing oncolytic virus pipeline, and further demonstrates the ability of our Invir.IO™ platform to generate highly targeted immuno-oncology drugs. These multi-armed drug candidates are expected to have significant advantages over existing therapies. Acting like a Trojan horse, they induce the production of potent therapies such as IL-12 directly in the tumor. The goal: to achieve high concentrations of these drugs only in the tumor, for improved efficacy and fewer side effects compared to systemic administration of these drugs. Intravenous administration addresses a broader range of patients with solid tumors who are not suitable for intratumoral administration. IV administration has the potential to improve the outcomes of patients with advanced lung cancer patients who are in great need of new treatment options.*
This CTA approval is an important milestone for Transgene, and we look forward to the first patient being recruited and providing further updates on TG6050's clinical development."

The first patient is expected to be enrolled in this multicenter trial in the first half of 2023.

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About the Delivir trial

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 ICIs. 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 will be evaluated in the Delivir trial, a Phase I trial conducted in advanced NSCLC patients.

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 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 three oncolytic viruses based on the Invir.IO™ viral backbone (TG6002, BT-001 and TG6050).
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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