PRESS RELEASE

Transgene — Preclinical Proof-of-Concept Data of Oncolytic Virus TG6050 Published in *JITC*

These data, published in The Journal for ImmunoTherapy of Cancer (JITC), demonstrate that TG6050 induces tumor regression and profound remodeling of the tumor microenvironment

TG6050 has also shown to avoid toxicity associated with systemic administration of IL-12 and anti-CTLA-4

TG6050 is currently being evaluated in a Phase I clinical trial (Delivir) for non-small cell lung cancer

Strasbourg (France), August 27, 2024, 7:30 am CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer, **announces the publication in the Journal for ImmunoTherapy of Cancer (*JITC*) of a peer-reviewed article which illustrates that TG6050 induces profound immune remodeling of the tumor microenvironment in animal models. The paper highlights TG6050's potential to induce sustained intratumoral expression of interleukin-12 (IL-12) and anti-cytotoxic T-lymphocyte associated antigen-4 (CTLA-4) antibody at active concentrations without the toxicity observed with systemic administration.**

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 localized antitumor immune response.

The *JITC* paper reports that in addition to consistent multiplication and propagation of TG6050 in tumor cells, functional transgenes are expressed in the tumor with a sustained intratumoral accumulation of IL-12 and anti-CTLA-4 antibody. The three components of TG6050 (oncolytic viral backbone, IL-12 and anti-CTLA-4 antibody transgenes) act together to induce tumor regression in numerous "hot" and "cold" murine tumor models investigated in these studies. This antitumoral activity was further amplified when TG6050 was combined with an anti-PD1.

Moreover, these studies show that TG6050 triggers a strong adaptive antitumoral immune response, accompanied by a profound modification of the tumor microenvironment based on infiltration of both innate and adaptive immune cells, altering it to a more inflamed state (from "cold" to "hot").

TG6050 was also shown to be safe. Upon intravenous administration in non-human primates for toxicology evaluation, it did not induce any of the IL-12 related adverse effects that are associated with systemic administration. TG6050 has now progressed into Phase 1 clinical development (the *Delivir* trial) in metastatic non-small cell lung cancer (NCT05788926).

"*These strong preclinical data demonstrate the ability of our invir.IO® oncolytic virus platform to generate promising candidates for further development and support our decision to advance TG6050 into the clinic in metastatic non-small cell lung cancer. We have thoroughly explored the mechanism of action of TG6050, with local delivery of functional IL-12 and anti-CTLA-4 resulting in strong antitumor activity. Moreover, in toxicology studies after repeated intravenous administrations in non-human primates, TG6050 did not display any observable adverse effects,*" commented **Dr. Maud Brandely, MD, PhD, Chief Medical Officer of Transgene.**

The *JITC* paper is titled "*TG6050, an oncolytic vaccinia virus encoding interleukin-12 and anti-CTLA-4 antibody, favors tumor regression via profound immune remodeling of the tumor microenvironment*" and can be accessed here.

***

About TG6050

TG6050 is an oncolytic virus developed with Transgene's invir.IO® platform for intravenous administration. invir.IO® 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 CD28 [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 an increase in the safety and tolerability profile of IL-12 and the anti-CTLA4 antibody.
TG6050 is being evaluated in the Deliver trial, a Phase I trial conducted in advanced non-small cell lung cancer (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 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 BT-001 and TG6050, two 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 invir.IO® platform, 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
Follow us on social media: X (formerly Twitter): @TransgeneSA – LinkedIn:@Transgene

Contacts

Transgene Contacts:
Media:
Caroline Tosch
Corporate Communications Manager
+33 (0)3 68 33 27 38
communication@transgene.fr

Lucie Larguier
Chief Financial Officer

Nadege Bartoli
IR Analyst and Financial Communications Officer
+33 (0)3 88 27 91 00/03
investorrelations@transgene.fr

Transgene Media Contact:
MEDiSTRAVA
Frazer Hall/Sylvie Berrebi
+ 44 (0)203 928 6900
transgene@medistrava.com

Disclaimer

This press release contains forward-looking statements, which are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated. The occurrence of any of these risks could have a significant negative outcome for the Company's activities, perspectives, financial situation, results, regulatory authorities' agreement with development phases, and development. The Company's ability to commercialize its products depends on but is not limited to the following factors: positive pre-clinical data may not be predictive of human clinical results, the success of clinical studies, the ability to obtain financing and/or partnerships for product manufacturing, development and commercialization, and marketing approval by government regulatory authorities. For a discussion of risks and uncertainties which could cause the Company's actual results, financial condition, performance or achievements to differ from those contained in the forward-looking statements, please refer to the Risk Factors ("Facteurs de Risque") section of the Universal Registration Document, available on the AMF website (http://www.amf-france.org) or on Transgene's website (www.transgene.fr). Forward-looking statements speak only as of the date on which they are made, and Transgene undertakes no obligation to update these forward-looking statements, even if new information becomes available in the future.