PRESS RELEASE

Transgene Confirms the Potential of the Intravenous Route of its Invir.IO™ Oncolytic Viruses against Solid Tumors with TG6002 Phase I Data Presented at ESMO Congress 2022

Additional positive TG6002 Phase I data show that the oncolytic virus is able to reach the tumor, replicate and express its payload in all patients when administered intravenously

Strasbourg, France, September 12, 2022, 8:00 am CEST – **Transgene (Euronext Paris: TNG),** a biotech company that designs and develops virus-based immunotherapeutics against cancer, today announces **positive confirmatory data from the Phase I trial evaluating TG6002 administered intravenously (IV) in combination with oral 5-FC in patients with advanced gastrointestinal carcinomas.**

TG6002 is based on Transgene's double deleted $VV_{cop}TK^{-}RR^{-}$ patented virus backbone, which forms the basis of the company's Invir.IO™ platform, and is generating a pipeline of multi-armed therapeutic OV drug candidates.

These updated data generated on 37 patients treated at the highest dose levels of the Phase I demonstrated that the therapy is well tolerated and confirmed the mechanism of action of TG6002 administered IV. They were presented on September 11, 2022, in a poster presentation at the European Society for Medical Oncology (ESMO) meeting taking place in Paris (France) from September 9-13, 2022.

The findings are as follows:

- **TG6002 demonstrated good tolerability** when administered weekly or on days 1,3 and 5. No major toxicities limiting the dose escalation process or the intensification of the schedule of administration were observed. Transient fever is the most common adverse event.
- TG6002 is able to reach the tumor, replicate, and express its payload after IV administration.
- Onset of a neutralizing antibody response is not associated with a decreased biological activity of the product.
- **These data further confirm the mechanism of action of the Invir.IO™-based oncolytic viruses in humans.**
- **The two IV administration schedules display different characteristics, that can both be leveraged in upcoming clinical trials.** Three doses given once a week resulted in higher levels of expression of the payload than the more intensive schedule (3 injections within 5 days). The intensive schedule allowed for a longer lasting expression of the payload.

These findings support the potential of IV administration of Invir.IO™-based oncolytic viruses, extending the use of these therapies to a broad range of solid tumors.

The overall Phase I program with TG6002 was aimed at establishing the tolerability and the potential different doses and administration schedules for further development. Additional data will be produced from the Phase I program and will be presented at a scientific congress in H1 2023.

- **Title of the poster:** "Updated data of biodistribution and activity of oncolytic virus TG6002 after intravenous administration in patients with advanced gastrointestinal carcinomas"
- **Authors**: Victor Moreno, Philippe Cassier, Bernard Doger, Emiliano Calvo, Maria De Miguel, Rocio Garcia-Carbonero, Carlos Gomez-Roca, Christiane Jungels, Sophie Sainte-Croix, Philippe Erbs, Alain Sadoun and Kaïdre Bendjama
- **Abstract Number:** #4886
- **Poster Number**: 392P

The abstract and the e-poster are available on the ESMO congress website here and the e-poster can be downloaded on the Transgene website here as well.

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Contacts

Transgene:
Lucie Larguier
Director Corporate Communications & IR
+33 (0)3 88 27 91 04
investorrelations@transgene.fr

Media Transgene:
MEDiSTRAVA Consulting
David Dible/Sylvie Berrebi
+44 (0)203 928 6900
transgene@medistrava.com

About the trial (NCT03724071)

This trial is a single-arm open-label Phase I/II trial evaluating the safety and tolerability of multiple ascending doses of TG6002 administered intravenously in combination with oral 5-FC, 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 and administration schedules have been added to the initial Phase I clinical protocol. The trial has safety as primary endpoint for the Phase I. The trial also evaluates pharmacokinetic properties and biodistribution of TG6002, along with immune modulation of the tumor micro-environment. This European study enrolled patients suffering from advanced gastrointestinal carcinomas who have failed and/or are intolerant to standard therapeutic options in the Phase I part.
Dr. Philippe Cassier, M.D., Ph.D., 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. Its satisfactory safety profile after intravenous administration and its mechanism of action has been shown in human in a Phase I trial.
In preclinical experiments, TG6002 has been shown to induce the shrinkage of the primary tumor as well as the regression of distant metastases (Foloppe, et al., *Molecular Therapy Oncolytics*, https://doi.org/10.1016/j.omto.2019.03.005).
The production of 5-FU directly in the tumor aims to achieve a better anti-tumoral 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-FC (administered orally) into 5-FU. 5-FU is a common chemotherapy agent for patients with gastrointestinal cancers. This mechanism of action is based on the in-tumor expression of the proprietary FCU1 gene that has been encoded in the genome of TG6002, taking advantage of the virus selective replication in the tumor cells.

When administered systemically, 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.

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 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. Follow us on Twitter: @TransgeneSA

Transgene 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.