PRESS RELEASE

Transgene presents data from Phase I clinical trial confirming the potential of the oncolytic virus TG6002

- *Initial Phase I data will be presented at ESMO Congress 2021 (poster presentation) starting today*
- *Clinical Proof of Concept for the feasibility of the intravenous administration of Transgene's patented oncolytic virus backbone behind the Invir.IO™ platform*

Strasbourg, France, September 16, 2021, 8:30 am CEST – **Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapeutics against cancer, today announces the presentation of data from a Phase I study combining intravenous (IV) oncolytic virus TG6002 and oral 5-FC in patients with advanced gastrointestinal carcinomas at the European Society for Medical Oncology (ESMO) virtual meeting taking place from September 16-21, 2021.**

These important data further confirm that Transgene's double deleted $VV_{cop}TK^{-}RR^{-}$ patented virus backbone, which forms the basis of the company's Invir.IO™ platform, has the potential to be given intravenously. After IV administration, TG6002 is able to selectively replicate and persist in tumor cells leading to the local expression of its functional payload (the *FCU1* gene).

INTRAVENOUS ADMINISTRATION COULD ALLOW ONCOLYTIC VIRUSES FROM TRANSGENE'S INVIR.IO™ PLATFORM TO BE USED TO TREAT A BROAD RANGE OF SOLID TUMORS

To date, the only oncolytic virus to have received regulatory approval has to be given via intra-tumoral administration, restricting its use to superficial lesions. Transgene's ambition is to significantly enlarge the number of solid tumors, such as gastro-intestinal tumors, that could be addressed by an oncolytic virus, by developing oncolytics administered intravenously.

TG6002 has been designed to combine multiple mechanisms of action: the lysis of tumor cells, the production of a chemotherapy agent 5-FU directly in the tumor and the induction of an immune response against cancer cells. This concept is presented in a short video available by clicking here.

The Phase I data that will be presented at the ESMO congress further demonstrate that TG6002 persists selectively in cancer cells while expressing its transgene of interest. This finding supports the potential of IV administration of Invir.IO™-based oncolytic virus, extending the use of these therapies to a broad range of solid tumors.

DATA CONFIRM THE PERSISTENCE OF THE CHEMOTHERAPY AGENT 5-FU IN PATIENTS' TUMORS AFTER INTRAVENOUS ADMINISTRATION

The data also demonstrate that the chemotherapy agent 5-FU is produced in the tumor across the three dose-level cohorts ($3x10^8$ pfu, $1x10^9$ pfu and $3x10^9$ pfu). 5-FU results from the local conversion of the pro-drug 5-FC (administered orally) allowed by the in-tumor expression of the proprietary *FCU1* gene that has been integrated within the genome of TG6002.

5-FU and its final metabolite F-BAL were detected in tumor tissue and in peripheral blood at days 5, 7 and 14 in most of the evaluable patients across the three dose-level cohorts. Interestingly, patients with the highest levels of 5-FU in blood and tumor were patients for which there was direct evidence of TG6002 in the tumor.

As of today, dose escalation has been completed. The trial is currently enrolling patients in additional cohorts assessing several administration schedules.

- **Title of the poster:** "Bioavailability and activity of oncolytic virus TG6002 after intravenous administration in patients with advanced gastrointestinal carcinomas"
- **Authors**: Philippe Cassier, Victor Moreno, Bernard Doger, Emiliano Calvo, Maria De Miguel, Christiane Jungels, Kaïdre Bendjama, Philippe Erbs, Damien Carpentier, and Alain Sadoun
- **Abstract Number:** #3550
- **Poster Number**: 486P

Detailed results:

- ✓ Direct evidence of TG6002 in the tumor, after intravenous administration, which remains active and effectively express *FCU1* gene selectively in tumor tissue;
- ✓ Detection of 5-FU and its final metabolite F-BAL in tumor tissue and in peripheral blood in most of the evaluable patients across the three dose-level cohorts;
- ✓ Replication of TG6002 is concentrated in tumor cells as suggested by the absence of widespread virus distribution in the body and the clear association of FCU1 activity with high virus concentration in tumor tissue;
- ✓ TG6002 is well tolerated and no major toxicities limiting the dose escalation process were observed.

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.

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. At the end of this Phase I part, Phase II patients will receive the recommended dose of TG6002. The trial has safety as primary endpoint for the Phase I part and efficacy for the Phase II part. The trial also evaluates pharmacokinetic properties and biodistribution of TG6002, along with immune modulation of the tumor micro-environment. This European study will enroll up to 40 patients suffering from advanced gastrointestinal carcinomas who have failed and/or are intolerant to standard therapeutic options in the Phase I part. Patients with colon cancer and liver metastases will be enrolled in the Phase II 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. 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 gastro-intestinal 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

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