PRESS RELEASE

Transgene presents initial Phase I data of TG6002, highlighting the potential of the intravenous administration of its oncolytic viruses

- *Detailed results to be presented at AACR 2021 Annual Congress*
- *Intravenous administration could allow oncolytic viruses from Transgene's Invir.IO™ platform to be used to treat a broad range of solid tumors*

Strasbourg, France, April 9, 2021, 7:30 am CET – **Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapeutics against cancer, today announces initial promising results from a Phase I study combining intravenous (IV) oncolytic virus TG6002 and oral 5-FC in patients with advanced gastrointestinal carcinomas. These data provide a clinical proof of concept for Transgene's double deleted $VV_{cop}TK^{-}RR^{-}$ patented virus backbone: after IV administration, TG6002 reached the tumor, multiplied within tumor cells, and induced the local expression of its payload (the *FCU1* gene).**

These results will be presented at the American Association for Cancer Research (AACR) virtual meeting taking place from April 10-15, 2021.

DATA CONFIRM THAT THE CHEMOTHERAPY AGENT 5-FU IS PRODUCED IN PATIENTS' TUMORS AFTER INTRAVENOUS ADMINISTRATION

TG6002 is a novel oncolytic virus that has been engineered to combine multiple mechanisms of action. It has been designed to:

- selectively replicate within cancer cells. This is due to the deletion of the viral genes encoding TK and RR, which reduces the virus's ability to grow in normal cells. This selective viral replication leads to the breakdown of the infected tumor cells in a process called oncolysis,
- prime an immune response against the primary tumor and metastases,
- and to induce the local expression of a biologically active enzyme able to convert 5-FC into its active cytotoxic metabolite 5-FU, directly in the tumor.

The data demonstrate that high concentration and continuous production of 5-FU chemotherapy can be obtained within the tumors through the local conversion of the pro-drug 5-FC (administered orally). This mechanism of action is based on the in-tumor expression of the proprietary *FCU1* gene that has been integrated within the genome of TG6002.

In this study, extensive analyses are being performed including metastasis biopsy with synchronous blood sampling, assessment of virus presence, quantification of 5-FC and 5-FU and assessment of neutralizing antibody titers.

These analyses have allowed Transgene to document TG6002's pharmacokinetics (PK) and biodistribution, and the functioning of the *FCU1* gene when given by IV administration.

Detailed results:

- ✓ TG6002 infects tumors after intravenous administration, remains active and effectively express *FCU1* gene selectively in tumor tissue;
- ✓ Absence of widespread virus distribution in the body and association of FCU1 activity with high virus concentration in tumor tissue suggest that the replication of TG6002 is concentrated in tumor cells;
- ✓ None of the patients presented clinical signs of extra-tumoral dissemination of the virus suggesting a high tumor specificity of the viral replication;
- ✓ The study is continuing with escalating dosing of TG6002.

CLINICAL PROOF OF CONCEPT OF THE FEASIBILITY OF THE IV ADMINISTRATION OF TRANSGENE'S PROPRIETARY ONCOLYTIC VIRUS

To-date, the only oncolytic virus that has received regulatory approval is only approved for intra-tumoral administration, restricting its use to superficial lesions.

Transgene aims to enlarge the number of solid tumors, such as gastro-intestinal tumors, that could be addressed by an oncolytic virus, by developing oncolytics that can be administered intravenously.

The findings that will be presented at AACR demonstrate the relevance of intravenous administration of Transgene's next generation oncolytic viruses including TG6002.

These data also suggest that candidates derived from Transgene's unique Invir.IO™ platform could also be given intravenously, extending the use of these therapies to a broad range of solid tumors.

- **Title of the poster:** "Oncolytic virus TG6002 locates to tumors after intravenous infusion and induces tumor-specific expression of a functional pro-drug activating enzyme in patients with advanced gastrointestinal carcinomas"
- **Authors**: Kaidre Bendjama, Philippe Cassier, Victor Moreno, Bernard Doger, Emiliano Calvo, Maria De Miguel, Christiane Jungels, Philippe Erbs, Damien Carpentier, Alain Sadoun.
- **Abstract/Poster Number**: LB179
- **Session**: PO.IM02.11 - Vaccines

The e-poster presentation will be available on the AACR website beginning at 8:30 am US EDT on Saturday, April 10, until Monday, June 21. The text of this abstract will be posted at 12:01 am US EDT on Friday, April 9 on the AACR website.

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 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., PhD, 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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