PRESS RELEASE

Transgene Presented Additional Phase I Data with TG4050 (*myvac*® platform) at ASCO 2022

Strasbourg, France, June 6, 2022, 8:00 am CEST - **Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer, today announced that it presented updated preliminary Phase I data on TG4050, its individualized neoantigen cancer vaccine, in a poster session at the American Society of Clinical Oncology (ASCO) annual meeting. TG4050 is based on Transgene's *myvac*® platform and powered by NEC's cutting-edge AI capabilities.**

These additional positive initial data, including molecular (ctDNA) response, have been generated from the first patients with ovarian cancer and HPV-negative head and neck cancer enrolled in the two ongoing Phase I trials assessing TG4050. They were presented in-person in Chicago, IL, June 5, 2022.

"*These new results, though early, are very encouraging" said* **Dr. Maud Brandely, MD, PhD, Chief Medical Officer of Transgene.** *"So far we accumulated promising preliminary data with TG4050: good tolerability, consistent immunogenicity and encouraging molecular response. We are particularly impressed by the effective priming of the immune system and the early signs of clinical activity. These results suggest that our individualized vaccine, TG4050, has the potential to extend the remission period, thus providing a new hope for cancer patients. In addition, the information we gather from the two ongoing Phase I studies will be pivotal in designing the Phase II trial of TG4050 which could start as early as 2023."*

Prof. Jean-Pierre Delord, MD, PhD, General Manager of IUCT Oncopole of Toulouse and first author of the poster, added: "*Neoantigen vaccination such as TG4050 is a relevant strategy for the treatment of patients with high risk of cancer relapse for whom the medical need is particularly high. In this setting, the vaccine is expected to deliver clinical benefit by controlling the residual disease. To date, this non-invasive treatment is well tolerated by the patients and although preliminary, the data presented at ASCO clearly suggest that TG4050 could become a new treatment option for cancer patients. I am looking forward to seeing this potential game-changing therapy moving forward."*

For the first time, ctDNA data were generated following treatment with TG4050

Liquid biopsies were performed to measure the circulating tumor DNA (ctDNA) levels. ctDNA is an emerging modality that is used to detect subclinical disease or asymptomatic relapse in an increasing number of indications. Use of such highly sensitive and specific marker seeks to identify patients whose disease is very likely to relapse in the near future, before their disease becomes detectable with current standard methods such as imaging. Moreover, it allows a non-invasive monitoring of treatment effectiveness. For instance, in at least one ovarian cancer patient in the study, a decline in ctDNA was concomitant with CA-125 normalization and disease control. Analyses are ongoing in more recently included patients.

Clinical follow-up data continue to demonstrate the potential of TG4050 in ovarian and head and neck cancer patients

In the head and neck cancer trial, patients were randomized to immediately receive vaccination with TG4050 (early treatment arm, arm A) or at relapse (delayed vaccination arm, arm B). **All evaluable patients randomized to arm A (n=8) are still in complete response** as of mid-May 2022. In arm B (n=8), two patients have experienced relapse.

In the ovarian cancer trial (n=5), a fifth patient initiated her treatment with TG4050 recently. One patient treated after an elevation of CA-125 experienced a normalization of CA-125 without clinical progression for 9 months until death from an unrelated chronic illness. Another patient was treated upon onset of radiological evidence of relapse and remained stable for 11.4 months.

To date, the vaccine has been well tolerated and no related Serious Adverse Events have been reported across the two studies.

In both clinical studies, enrollment and patient dosing are progressing in line with our expectations. Overall, Transgene plans to treat 13 patients in the ovarian cancer trial and 30 patients in the head and neck cancer trial.

Immune cell response data demonstrated an effective priming of the immune system which is associated with disease regression

Transgene presented a comprehensive set of immunological data at ASCO. Circulating immune cells quantification (in particular monocytes, DC, NK cells, subcells of CD8, CD4, Treg) and expression of immune checkpoints (ICOS and PD1) suggest that the vaccine is able to effectively induce innate and adaptive immune responses in patients.

In an ovarian cancer patient, clinical resolution and biological responses (CA-125 and ctDNA responses) were concomitant to an immune response against multiple epitopes and to the onset of markers of an effective immune response (switch in circulating CD4 and CD8 cells toward an effector phenotype, increase in CD16neg NK cells; peak in circulating cytokines).

All evaluable patients developed a robust T-cell response against multiple targeted neoantigens (median of 10 positive responses per patient). T-cell responses were observed for class I and class II epitopes, they consisted of *de novo* responses and amplifications of preexisting responses.

The poster can be downloaded from the ASCO and Transgene websites.

Poster title: ***Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OC) and head and neck carcinoma (HNSCC)***

- Abstract number: 2637
- Session title: Developmental Therapeutics—Immunotherapy
- Authors: J.P. Delord, M. Block, C. Ottensmeier, G. Colon-Otero, C. Le Tourneau, A. Lalanne, O. Lantz, KL. Knutson, G. Lacoste, A. Tavernaro, M. Brandely, N. Silvestre, B. Grellier, Y. Yamashita, O. Kousuke, N. Yamagata, Y. Tanaka, B. Malone, E. Quemeneur, K. Bendjama

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About the clinical trials

TG4050 is being evaluated in two Phase I clinical trials for patients with ovarian cancer (NCT03839524) and HPV-negative head and neck cancers (NCT04183166).

In a first Phase I trial, TG4050 is being administered to patients with HPV-negative head and neck cancer. A personalized treatment is created for each patient after they complete surgery and while they receive an adjuvant therapy. Half of the participants receive their vaccine immediately after they complete their adjuvant treatment. The other half is given TG4050 as an additional treatment at the time of recurrence of the disease as an additional treatment to SoC. This randomized study is evaluating the treatment benefits of TG4050 in patients who have a high risk of relapse. Up to 30 patients will receive TG4050 in France, in the UK and in the USA. The principal investigator of the trial is Prof. Christian Ottensmeier, MD, PhD, Consultant Medical Oncologist at the Clatterbridge Cancer Centre and Professor of Immuno-Oncology at the University of Liverpool. In France, the clinical trial is being conducted at Institut Curie, Paris by Prof. Christophe Le Tourneau, MD, PhD, Head of the Department of Drug Development and Innovation (D3i), and at the IUCT-Oncopole, Toulouse by Prof. Jean-Pierre Delord, MD, PhD. In the USA, the trial is being led by Yujie Zhao, MD, PhD, at the Mayo Clinic. Endpoints of the trial include safety, feasibility and biological activity of the therapeutic vaccine.

In parallel, a Phase I clinical trial of TG4050 is enrolling patients with ovarian cancer. This second trial is including patients at the time of asymptomatic relapse after surgery and first-line chemotherapy. Matthew Block, MD, PhD, Consultant Medical Oncology, Consultant Immunology and Associate Professor of Oncology at the Mayo Clinic (USA) is the principal investigator of the trial; in France, the trial is being conducted by Prof. Le Tourneau, MD, PhD, at Institut Curie and by Alexandra Martinez, MD, Associate Head of Surgical Department, at IUCT-Oncopole. Endpoints of the trial include safety, feasibility and biological activity of the therapeutic vaccine.

The first preliminary clinical data generated from the first patients treated with TG4050 were very encouraging.

About *myvac®*

myvac® is a viral vector (MVA – *Modified Vaccinia Ankara*) based, individualized immunotherapy platform that has been developed by Transgene to target solid tumors. *myvac*®-derived products are designed to stimulate the patient's immune system, recognize and destroy tumors using the patient's own cancer specific genetic mutations. Transgene has set up an innovative network that combines bioengineering, digital transformation, established vectorization know-how and unique manufacturing capabilities. Transgene has been awarded "Investment for the Future" funding from Bpifrance for the development of its platform *myvac*®. TG4050 is the first *myvac*®-derived product being evaluated in clinical trials.
Click **here** to watch a short video on *myvac*®.

About TG4050

TG4050 is an individualized immunotherapy being developed for solid tumors that is based on Transgene's *myvac*® technology and powered by NEC's longstanding artificial intelligence (AI) expertise. This virus-based therapeutic vaccine encodes neoantigens (patient-specific mutations) identified and selected by NEC's Neoantigen Prediction System. The prediction system is based on more than two decades of expertise in AI and has been trained on proprietary data allowing it to accurately prioritize and select the most immunogenic sequences.
TG4050 is designed to stimulate the immune system of patients in order to induce a T-cell response that is able to recognize and destroy tumor cells based on their own neoantigens. This individualized immunotherapy is developed and produced for each patient.

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

About IUCT-Oncopole

The IUCT-Oncopole, a cancer care, research and training center in Toulouse, combines the expertise of 1,800 professionals on a single site labeled "Comprehensive Cancer Center". It combines several state-of-the-art clinical facilities for the treatment of cancer with a world-class research infrastructure, on an integrated campus that brings together public and private stakeholders, including industrial partners. The IUCT-Oncopole, which includes the Claudius Regaud Institute (ICR) and several teams from the Toulouse University Hospital, treats more than 10,000 new patients every year, and more than one in eight patients is enrolled in clinical studies.
www.iuct-oncopole.fr

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.