

## Transgene Announces Positive Interim Analysis Results of Phase II Trial Evaluating TG4001 + Avelumab vs Avelumab in HPV-Positive Anogenital Cancers

Based on promising progression-free survival (PFS) interim analysis, trial to continue and an optimized number of patients to be randomized in the trial

Management to host webcast presentation of the interim results today, November 2, 2022 at 6 p.m. CET / 1 p.m. EST

Strasbourg, France, November 2, 2022, 5:45 pm CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapeutics against cancer, today announces that following an interim analysis of its randomized controlled Phase II clinical study comparing TG4001 in combination with avelumab to avelumab alone in patients with HPV16-positive anogenital tumors ([NCT: 03260023](#)), the Independent Data Monitoring Committee (IDMC) has recommended the study continue.

Based on positive signals observed in the interim analysis, the trial is now expected to enroll an additional 66 patients, for a total trial size of 120 patients compared to the previously announced target of 150 patients. Transgene anticipates the last patient to be randomized in the trial in H1 2024.

Hedi Ben Brahim, CEO, and Dr. Maud Brandely, Chief Medical Officer, MD, PhD, will host an analyst and investor call to discuss the interim analysis at 6:00 pm CET (1:00 pm EST) today (see details below).

The Phase II study is evaluating TG4001, an investigational therapeutic cancer vaccine, in combination with avelumab compared to avelumab alone in patients with HPV16-positive anogenital tumors without liver metastases, through a continuing collaboration with the alliance of Merck KGaA, Darmstadt, Germany, and Pfizer, which is supplying avelumab.

“We are very pleased with the outcome of this interim analysis,” said **Hedi Ben Brahim, Chief Executive Officer of Transgene**. “The IDMC’s recommendation to continue the study reinforces our confidence in TG4001, which follows promising data from our earlier Phase Ib/II trial. This also enables us to reduce the number of patients randomized in the trial. We are looking forward to completing this trial in H1 2024 and communicating its results when they are available. We expect that positive final results from this trial will allow us to launch a registration trial to further confirm

the benefit of our therapeutic vaccine candidate. TG4001 aims to provide a new solution to patients who currently have very limited treatment options.”

The interim analysis was triggered per protocol, by a predefined number of PFS events. Based on the interim results, the IDMC’s objective was to provide a recommendation on the continuation of the trial and on the final sample size using adaptive sample size re-estimation modeling approach.

To date, the treatment has been well tolerated. Adverse events are consistent with previous observations made in the Phase Ib/II trial.

TG4001 is based on a MVA (Modified Vaccinia Ankara) vector, which is engineered to express HPV16 antigens (E6 & E7) and interleukin 2 (IL-2). TG4001 is designed to alert the immune system specifically to cells presenting the HPV16 E6 and E7 antigens that can be found in HPV16-related tumors and to induce a specific cellular immune response against these cancer cells.

## Phase II trial aims to show superiority of TG4001 + avelumab over avelumab monotherapy

The trial is enrolling patients in the USA and in Europe (France and Spain). It focuses on patients with recurrent or metastatic HPV16-positive anogenital cancer without liver metastases, including cervical, vulvar, vaginal, penile, and anal cancer. Patients are randomized to either receive the combination regimen of the therapeutic vaccine TG4001 and avelumab or avelumab alone.

The primary endpoint of the trial is progression-free survival (PFS) according to RECIST 1.1. Secondary endpoints include objective response rate (ORR), disease control rate (DCR), overall survival (OS) and a series of immunological parameters.

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A conference call in **English** is scheduled today, on November 2, 2022, at 6 p.m. CET / 1 p.m. EST.

### **Webcast link to English language conference call:**

[https://channel.royalcast.com/landingpage/transgene/20221102\\_1/](https://channel.royalcast.com/landingpage/transgene/20221102_1/)

### **Participant telephone numbers:**

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A replay will be available on the Transgene website ([www.transgene.fr](http://www.transgene.fr)) following the live event.

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### **About the trial**

The multi-center, open label, randomized Phase II trial (NCT03260023) is designed to compare the efficacy of the combination of TG4001 and avelumab versus avelumab alone in patients with advanced, recurrent and/or metastatic HPV16-positive anogenital cancers who have disease progression after a maximum of one line of systemic treatment, or who are not eligible for first-line chemotherapy.

Prof. Christophe Le Tourneau, M.D., PhD, Head of the Department of Drug Development and Innovation (D3i) at the Curie Institute, is the Principal Investigator of the study. The trial is being conducted in collaboration with Merck KGaA, Darmstadt, Germany, and Pfizer Inc. (NYSE: PFE), which are providing avelumab for the trial. Avelumab is co-developed and co-commercialized by Merck KGaA, Darmstadt, Germany and Pfizer Inc. Transgene will continue to be the sponsor of the trial and conduct the trial. Avelumab is not approved alone or in combination for the treatment of HPV16-positive anogenital tumors in any region.

Patients will receive TG4001 at the dose of  $5 \times 10^7$  pfu, SC, weekly for 6 weeks, every 2 weeks up to six months, and every 12 weeks thereafter, in combination with avelumab or avelumab alone at 800 mg, IV every two weeks, until disease progression. The primary endpoint of the trial is progression-free survival (PFS) according to RECIST 1.1. Secondary endpoints include objective response rate (ORR), disease control rate (DCR), overall survival (OS) and other immunological parameters. The trial will enroll 120 patients.

#### ***About the Phase Ib/II data of TG4001 + avelumab (single arm trial)***

**The combination of TG4001 and avelumab demonstrated anti-tumor activity (22% ORR) in patients with previously treated recurrent and/or metastatic HPV-related cancers (including patients with oropharyngeal cancers and anogenital cancers). Presence of liver metastases had a profound impact on the outcome in terms of ORR and PFS. In patients without liver metastases, an ORR of 32%, a median PFS of 5.6 months and a median OS of 13.3 months were achieved.** The treatment induced HPV-specific T-cell responses and was associated with increased levels of immune cell infiltration in the tumors and expression of genes associated with activation of the immune system. The results from the Phase Ib/II parts of the trial combining TG4001 with avelumab in HPV16-positive recurrent and/or metastatic malignancies have been updated in a R&D day held in September 2022 by Transgene. A first set of data had been presented at SITC 2020 and ESMO IO 2020 <sup>[1,2]</sup>.

#### ***About TG4001***

TG4001 is an investigational therapeutic vaccine based on a non-propagative, highly attenuated Vaccinia vector (MVA), which is engineered to express HPV16 antigens (E6 & E7) and an adjuvant (IL-2). TG4001 is designed to have a two-pronged antiviral approach: to alert the immune system specifically to cells presenting the HPV16 E6 and E7 antigens, that can be found in HPV16-related tumors, and to further stimulate the infection-clearing activity of the immune system through interleukin 2 (IL-2). TG4001 has been administered to more than 350 individuals, demonstrating good safety and promising efficacy results <sup>[1,2]</sup>. Its mechanism of action and good safety profile make TG4001 an excellent candidate for combinations with other therapies in HPV-mediated solid tumors.

#### ***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*<sup>®</sup> 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<sup>™</sup> platform).

With Transgene's *myvac*<sup>®</sup> platform, therapeutic vaccination enters the field of precision medicine with a novel immunotherapy that is fully tailored to each individual. The *myvac*<sup>®</sup> 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<sup>™</sup>, Transgene is building on its viral vector engineering expertise to design a new generation of multifunctional oncolytic viruses. Transgene has an ongoing Invir.IO<sup>™</sup> collaboration with AstraZeneca. Additional information about Transgene is available at: [www.transgene.fr](http://www.transgene.fr). Follow us on Twitter: [@TransgeneSA](https://twitter.com/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](http://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.

## References

- [1] Le Tourneau et al. “TG4001 (Tipapkinogene sovavivec) and avelumab for recurrent/metastatic (R/M) Human Papilloma Virus (HPV)-16+ cancers: clinical efficacy and immunogenicity.” 2020 [SITC Annual Meeting](#), 9-11 November 2020, Poster presentation
- [2] Le Tourneau et al. “TG4001 therapeutic vaccination combined with PD-L1 blocker avelumab remodels the tumor microenvironment (TME) and drives antitumor responses in Human PapillomaVirus (HPV)+ malignancies.” 2020 ESMO IO meeting, 12 December 2020, mini-oral presentation