

## Transgene Reports First Promising Efficacy Results with TG4001 in Combination with Avelumab in HPV-Positive Cancer at ESMO 2019

- ✓ *Three of six patients showed durable responses (patients treated with the recommended Phase 2 dose)<sup>1</sup>*
- ✓ *Combination therapy results in changes in tumor microenvironment shifting immune status from “cold” to “hot”*
- ✓ *Clinical trial conducted in collaboration with Merck KGaA, Darmstadt, Germany, and Pfizer*

*Conference call scheduled on October 3, 2019 at 2:30 p.m. CET*

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Strasbourg, France, September 30, 2019, 5:45 p.m. CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapeutics against cancer, today presented promising safety and efficacy data of TG4001 in combination with avelumab (BAVENCIO®), a human anti-programmed death ligand (PD-L1) antibody, in HPV-16+ recurrent or metastatic malignancies (including oropharyngeal cancers). These Phase 1b data have been presented in a poster (#1210P) at the European Society for Medical Oncology (ESMO) 2019 Congress in Barcelona, Spain. TG4001 is a therapeutic vaccine based on a *Vaccinia* vector (MVA), which is engineered to express HPV-16 antigens (E6 & E7). It has been administered to more than 300 individuals in previous trials, demonstrating good safety, significant HPV clearance rate and promising efficacy results.

In the Phase 1b part of the trial, 9 heavily pretreated patients received either one of the two tested doses of TG4001 combined with a fixed dose of avelumab. The Phase 2 part of the trial started in October 2018 and will enroll 40 patients.

### Key results of the Phase 1b trial are:

- **3 of the 6 patients treated with the higher dose of TG4001 showed durable partial responses<sup>1</sup>.**
- **No dose-limiting toxicity** was observed, confirming a good safety profile of the combined regimen.
- **T cell responses against the HPV-16 E6 and E7 antigens** were detected in patients' blood at day 43.
- **The combination regimen was able to prime the immune system** and modified positively the tumors microenvironment. Patients displayed **increased immune cells infiltrates** (including CD8 T cells) and an increased expression of genes associated with **innate and adaptive immune response**.
- An **increase in PD-L1 expression** in the tumor cells was seen.

**Dr. Maud Brandely, MD, PhD, Chief Medical Officer of Transgene,** commented, *“These Phase 1b results with a combination treatment regimen containing TG4001 are promising. In this heavily pretreated population, the quality of the responses, in particular the duration of the responses, and the immune changes in the tumor, give us great confidence that we will see a positive outcome from the ongoing Phase 2 part of the trial. The results also confirm our conviction that a HPV-16 targeted therapeutic vaccine would be able to stimulate the immune response, and can advantageously be combined with an immune*

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<sup>1</sup> These data compare favorably with current treatments in HPV-16 associated indications for patients with metastatic diseases receiving a second line of treatment. With immune checkpoint inhibitors, median overall survival remains inferior to 11 months and median progression free survival is between 2 and 4 months. In this heterogeneous group of malignancies, overall response rates are around 10-15%.

checkpoint inhibitor. Based on these results, I believe that the combination of TG4001 and an ICI could potentially offer a much-improved treatment option than single agent immune checkpoint inhibitor for patients with HPV-16+ recurrent or metastatic malignancies. Patient accrual in the Phase 2 part of the trial is in line with our expectations and the next clinical readout is expected in 1H 2020."

Poster presentation - September 30, 2019, 12:00-13:00 - Poster Area Hall 4

**Title: Phase Ib/II trial of TG4001 (Tipapkinogene sovavivec), a therapeutic HPV-vaccine, and Avelumab in patients with recurrent/metastatic HPV16 positive cancers (ID 2536)**  
Poster #1210P | Presenter: Christophe Le Tourneau (Institut Curie, Paris, France)

The abstract is available on [the ESMO website](#).

The poster is available on Transgene's website (Publication section) [www.transgene.fr](http://www.transgene.fr).

### **About the trial**

This multi-center, open-label trial is assessing the safety and tolerability, as well as the anti-tumor activity of this immunotherapy combination regimen (TG4001 + avelumab) in approximately 50 patients with HPV-16 positive cancers who had failed at least one line of systemic treatment for R/M disease (NCT03260023). Prof. Christophe Le Tourneau, M.D., PhD, Head of the Department of Drug Development and Innovation (D3i) at the Curie Institute, and a world expert in head and neck cancers, is the Principal Investigator of the study. The trial is conducted in collaboration with Merck KGaA, Darmstadt, Germany, a leading science and technology company which in the US and Canada operates its biopharmaceutical business as EMD Serono, and Pfizer Inc (NYSE: PFE).

**In the Phase 1 part**, 9 patients were enrolled to either one of the two doses of the vaccine ( $5 \times 10^6$  and  $5 \times 10^7$  pfu). TG4001 was administered SC weekly for 6 weeks, every 2 weeks up to M6, and every 12 weeks thereafter. Avelumab was given IV at 10 mg/kg every 2 weeks. Tumor response was assessed by RECIST 1.1. For translational and immunological assessments, PBMC samples were collected longitudinally and tissue samples were collected at baseline and D43.

**The Phase 2 part** of the trial started in October 2018. 40 patients will be enrolled. They will receive the highest TG4001 dose tested in the Phase 1b part of the trial ( $5 \times 10^7$  pfu), in combination with avelumab at 10 mg/kg. The primary endpoint of the Phase 2 part is overall response rate. Secondary endpoints include progression free survival, overall survival, disease control rate and other immunological parameters. **The interim readout is expected in 1H 2020.**

More information on the trial is available on [clinicaltrials.gov](http://clinicaltrials.gov).

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**A conference call in English is scheduled on October 3, 2019, at 2:30 p.m. CET.**

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

[https://channel.royalcast.com/webcast/transgene/20191003\\_1/](https://channel.royalcast.com/webcast/transgene/20191003_1/)

### **Participant telephone numbers:**

France: +33 (0) 1 7037 7166

Confirmation code: Transgene

United Kingdom: +44 (0) 20 3003 2666

United States: +1 212 999 6659

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

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### **About HPV-Positive Cancers**

HPV-positive cancers comprise a variety of malignancies, including head and neck cancers and anogenital cancers. Squamous cell carcinoma of the head and neck (SCCHN) is a heterogeneous group of cancers that can affect the oral cavity, pharynx, and larynx. The incidence of HPV16-related SCCHN has significantly increased in recent years. HPV16 infection is associated with more than 85% of oropharynx squamous cell carcinomas (Kreimer et al., 2005), i.e. approximately 10,000 patients at metastatic stage and receiving a second line of treatment. Other HPV16-positive cancers include cervical, vaginal, vulvar and penile cancers, i.e. approximately 15,000 cancers at metastatic stage and eligible for a second line of treatment. (Source: meta-analysis, IARC, Globocan, SEER – EU28, USA, 2022).

Current treatments include surgical resection with radiotherapy, chemoradiotherapy or immune checkpoint inhibitors. However, better options are needed for advanced and metastatic HPV+ cancers. It is thought that immunotherapy combined with immune checkpoint inhibitors could provide a promising potential treatment option that would address this strong medical need. With immune checkpoint inhibitors, median overall survival remains inferior to 11 months and median progression-free survival is between 2 and 4 months. In this heterogeneous group of malignancies, overall response rates are around 10-15%.

### **About TG4001**

TG4001 is an investigational therapeutic vaccine based on a non-propagative, highly attenuated *Vaccinia* vector (MVA), which is engineered to express HPV-16 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 HPV-16-infected cells that have started to undergo precancerous transformation (cells presenting the HPV-16 E6 and E7 antigens) and to further stimulate the infection-clearing activity of the immune system through interleukin 2 (IL-2). TG4001 has been administered to more than 300 individuals, demonstrating good safety, significant HPV clearance rate and promising efficacy results (Harper et al., [Gynecologic Oncology](#), 2019). Its mechanism of action and good safety profile make TG4001 an excellent candidate for combinations with other therapies in HPV-mediated solid tumors.

### **Avelumab Approved Indications**

Avelumab (BAVENCIO®) in combination with axitinib is indicated in the US for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

The US Food and Drug Administration (FDA) also granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Avelumab is currently approved for patients with MCC in 50 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

### **Avelumab Important Safety Information from the US FDA-Approved Label**

The warnings and precautions for avelumab (BAVENCIO®) include immune-mediated adverse reactions (such as pneumonitis and hepatitis [including fatal cases], colitis, endocrinopathies, nephritis and renal dysfunction and other adverse reactions [which can be severe and have included fatal cases]), infusion-related reactions, hepatotoxicity, major adverse cardiovascular events (MACE) [which can be severe and have included fatal cases], and embryo-fetal toxicity.

Common adverse reactions (reported in at least 20% of patients) in patients treated with BAVENCIO® monotherapy include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reaction, peripheral edema, decreased appetite/hypophagia, urinary tract infection and rash. Common adverse reactions (reported in at least 20% of patients) in patients receiving BAVENCIO® in combination with axitinib include diarrhea, fatigue, hypertension, musculoskeletal pain, nausea, mucositis, palmar-plantar erythrodysesthesia, dysphonia, decreased appetite, hypothyroidism, rash, hepatotoxicity, cough, dyspnea, abdominal pain and headache. Clinical chemistry and hematology laboratory value abnormalities reported in at least 10% of patients include hyponatremia, lymphopenia, GGT increased, blood triglyceride increased and lipase increased, and grade 3-4 lymphopenia, anemia, elevated cholesterol and liver enzymes.

For full Prescribing Information and Medication Guide for BAVENCIO®, please see [www.BAVENCIO.com](http://www.BAVENCIO.com).

### **About Transgene**

Transgene (Euronext: TNG) is a publicly traded French biotechnology company focused on designing and developing targeted immunotherapies for the treatment of cancer and infectious diseases. Transgene's programs utilize viral vector technology with the goal of indirectly or directly killing infected or cancerous cells. The Company's lead clinical-stage programs are: TG4010, a therapeutic vaccine against non-small cell lung cancer, TG4001, a therapeutic vaccine against HPV-positive cancers, and TG6002, an oncolytic virus for the treatment of solid tumors.

With its proprietary platform Invir.IO<sup>®</sup>, Transgene builds on its expertise in viral vectors engineering to design a new generation of multifunctional oncolytic viruses. *myvac*<sup>™</sup>, an individualized MVA-based immunotherapy platform designed to integrate neoantigens, completes this innovative research portfolio. TG4050, the first candidate selected from the *myvac*<sup>™</sup> platform, will enter the clinic for the treatment of ovarian cancer and head and neck cancer.

Additional information about Transgene is available at: [www.transgene.fr](http://www.transgene.fr).

Follow us on Twitter: [@TransgeneSA](https://twitter.com/TransgeneSA)

### **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 Document de Référence, 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.*