

## Transgene Completes Safety and Tolerability Assessment of TG4001 in Combination with Avelumab in Phase 1b Part of Trial in HPV-Positive Cancer Patients

- Objectives from the Phase 1b study successfully met
- On track with the Phase 2 part of the study: first patients enrolled
- Preliminary efficacy data expected in 2H 2019
- Clinical trial in collaboration with Merck KGaA, Darmstadt, Germany, and Pfizer

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Strasbourg, France, December 20, 2018, 5:45 p.m. CET - Transgene (Euronext Paris: TNG), a biotechnology company that designs and develops virus-based immunotherapies against cancers and infectious diseases, announces that the primary endpoint (safety and tolerability) was met in the Phase 1b part of a trial combining TG4001 and avelumab, a human anti-programmed death ligand (PD-L1) antibody, as a treatment for HPV-16<sup>+</sup> recurrent or metastatic malignancies, such as oropharyngeal squamous cell carcinoma of the head and neck (SCCHN).

In the Phase 1b part of the trial, 9 patients received escalating doses of TG4001 combined with a fixed dose of avelumab. No dose-limiting toxicity was observed, confirming a satisfactory tolerability profile for the combined regimen, allowing the trial to progress to the Phase 2 part.

The Phase 2 part of the trial will enroll 40 patients with HPV16+ recurrent or metastatic SCCHN. Patients will receive the highest TG4001 dose tested in the Phase 1b part of the trial, in combination with avelumab at 10 mg/kg, until disease progression. The first patients have already been enrolled.

The first data from this trial on the activity of the combination are expected during the second half of 2019.

### **About the trial**

This multi-center, open-label trial will assess the safety and tolerability, as well as the anti-tumor activity of this immunotherapy combination regimen (TG4001 + avelumab) in up to 50 patients (NCT03260023). Prof. Christophe Le Tourneau, M.D., PhD, Head of the Department of Drug Development and Innovation (D<sup>3</sup>i) 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).

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

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<sup>1</sup>Human papillomavirus type 16: HPV-16 is known to be one of the causing agents of a variety of cancers (see notes to the editors)

## Notes to editors

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### 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. Its mechanism of action and good safety profile make TG4001 an excellent candidate for combinations with other therapies in HPV-mediated solid tumors.

### About Avelumab

Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.<sup>1-3</sup> Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) *in vitro*<sup>3-5</sup>. In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

### Approved Indications

The US Food and Drug Administration (FDA) 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 more than 45 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

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

The warnings and precautions for avelumab (BAVENCIO®) include immune-mediated adverse reactions (such as pneumonitis, hepatitis, colitis, endocrinopathies, nephritis and renal dysfunction and other adverse reactions), infusion-related reactions and embryo-fetal toxicity.

Common adverse reactions (reported in at least 20% of patients) in patients treated with BAVENCIO® for mMCC and patients with locally advanced or metastatic UC include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reaction, peripheral edema, decreased appetite/hypophagia, urinary tract infection and rash.

For full prescribing information and medication guide for BAVENCIO®, please see [www.BAVENCIO.com](http://www.BAVENCIO.com).

### About HPV-Positive Head and Neck Cancer

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 HPV-related SCCHN has significantly increased in recent years. HPV-16 infection is associated with more than 85% of oropharynx squamous cell carcinomas in the US (Kreimer et al., 2005), i.e. more than 25,000 patients (Source: meta-analysis, IARC - De Martel et al., 2017, International Journal of Cancer).

Current treatments include surgical resection with radiotherapy, chemoradiotherapy or immune checkpoint inhibitors. However, better options are needed for advanced and metastatic HPV+ SCCHN. It is thought that immunotherapy combined with immune checkpoint inhibitors could provide a promising potential treatment option that would address this strong medical need.

### **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, Pexa-Vec, an oncolytic virus against liver cancer, and TG4001, a therapeutic vaccine against HPV-positive head and neck cancers. The Company has several other programs in clinical development, including TG1050 (a therapeutic vaccine for the treatment of chronic hepatitis B) and TG6002 (an oncolytic virus for the treatment of solid tumors).

With its proprietary Invir.IO™, Transgene builds on its expertise in viral vectors engineering to design a new generation of multifunctional oncolytic viruses.

*myvac*™, an individualized MVA-based immunotherapy platform designed to integrate neoantigens, completes this innovative research portfolio.

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

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### **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. There can be no guarantee that (i) the results of preclinical work and prior clinical trials will be predictive of the results of the clinical trials currently underway, (ii) regulatory authorities will agree with the Company's further development plans for its therapies, or (iii) the Company will find development and commercialization partners for its therapies in a timely manner and on satisfactory terms and conditions, if at all. The occurrence of any of these risks could have a significant negative outcome for the Company's activities, perspectives, financial situation, results and development.

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 Risques") 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.

### **References**

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