Acceptance of Late Breaking Abstract at Upcoming SITC 2020 Conference, on the detailed results from clinical study of TG4001 in combination with avelumab in advanced HPV-positive cancers

Strasbourg, France, October 19, 2020, 7:30 a.m. CET – Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapeutics against cancer, announced that detailed results of the data from the Phase 1b/2 trial combining TG4001, a HPV16 targeted therapeutic vaccine, with avelumab (BAVENCIO®), a human anti-PD-L1 antibody, in HPV16-positive recurrent and/or metastatic malignancies, will be presented in a poster presentation at the upcoming virtual meeting of the Society for Immunotherapy of Cancer (SITC) taking place November 9-14, 2020.

The principal investigator Professor Christophe Le Tourneau will present results from a pooled analysis of the Phase 1b/2 trial, including response rate, median progression-free survival, as well as the impact of patient/disease characteristics on outcome and immunogenicity.

As a reminder, the analysis of the trial data demonstrated clinical activity of the combination regimen and confirmed a manageable safety profile.
The purpose of this exploratory Phase 1b/2 trial was to evaluate the safety and efficacy of the combination of TG4001 and an immune checkpoint inhibitor in a heterogeneous group of patients with aggressive, recurrent and/or metastatic HPV16-positive cancer. Clinical activity was observed in the overall study population (34 evaluable patients with oropharyngeal, anal, cervical, or other HPV16-positive cancers).
In addition, Transgene has identified patient characteristics associated with promising clinical activity in this trial. For more than 50% of these patients, the disease had not progressed at 12 weeks, compared to an expected median progression-free survival (PFS) of 8 weeks for this population with current treatment regimens *. Consistent with data presented at ESMO 2019 [1], durable responses have been observed in most of the responder patients.

The trial was being conducted in collaboration with Merck KGaA, Darmstadt, Germany, and Pfizer.

About the trial

This multi-center, open-label trial is assessing the safety and efficacy of this immunotherapy combination regimen (TG4001 + avelumab) in patients with HPV16-positive cancers who have disease progression after at least one line of systemic treatment for recurrent/metastatic 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 drug development and head and neck cancers, is the Principal Investigator of the study. The trial is being 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).
Patients received TG4001 at the dose of $5x10^7$ pfu, SC, weekly for 6 weeks, every 2 weeks up to six months, and every 12 weeks thereafter, in combination with avelumab at 10 mg/kg, IV every two weeks, until disease progression.

* Current treatment regimens, including immune checkpoint inhibitors, for patients with metastatic disease receiving a second (or further) line of treatment for their HPV16 associated indications deliver very limited benefit. With immune checkpoint inhibitors, overall response rates are around 10–15% [2-6] in this heterogenous group of malignancies, while median overall survival is less than 11 months [2-6] and median progression-free survival is around 2 months [2-6].

The primary endpoint of the Phase 2 part is the overall response rate (ORR, using RECIST 1.1). Secondary endpoints include progression-free survival, overall survival, disease control rate and other immunological parameters.

More information on the trial is available on clinicaltrials.gov.

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About HPV-Positive Cancers

HPV-positive cancers comprise a variety of malignancies, including head and neck cancers and anogenital cancers [7]. Squamous cell carcinoma of the head and neck (SCCHN) is a heterogeneous group of cancers that can affect sites including the oral cavity, pharynx, and larynx [8]. The incidence of HPV16-related SCCHN has significantly increased in recent years [8]. HPV16 infection is associated with more than 85% of oropharynx squamous cell carcinomas [8], i.e. approximately 10,000 patients at metastatic stage and receiving a second line of treatment [9]. Other HPV16-positive cancers include cervical [10], vaginal [11], vulvar [12], anal [13] and penile [14] cancers, i.e. approximately 15,000 cancers at metastatic stage and eligible for a second line of treatment [15].

Current treatments include chemoradiotherapy, immune checkpoint inhibitors, or surgical resection with radiotherapy. However, better options are needed for advanced and metastatic HPV+ cancers. It is thought that this immunotherapy combined with other immunotherapeutic agents such as immune checkpoint inhibitors could provide a promising potential treatment option that would address this strong medical need [16,17]. With immune checkpoint inhibitors, median overall survival remains inferior to 11 months [2-6] and median progression-free survival is between 2 and 4 months [2-6]. In this heterogenous group of malignancies, overall response rates are around 10–15% [2-6].

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 HPV-16-infected cells that have started to undergo precancerous transformation (cells presenting the HPV16 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 [1; 18]. 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®) is indicated in the US for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy. BAVENCIO is also indicated for the treatment of patients with locally advanced or metastatic UC 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.

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

In the US, the FDA granted accelerated approval for BAVENCIO for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

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 other immune-mediated adverse reactions as a single agent or in combination with axitinib [which can be severe and have included fatal cases]), infusion-related reactions, hepatotoxicity in combination with axitinib, major adverse cardiovascular events (MACE) in combination with axitinib [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, 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. Grade 3-4 hematology laboratory value abnormalities reported in at least 10% of patients with Merkel cell carcinoma treated with BAVENCIO® monotherapy include lymphopenia; in patients receiving BAVENCIO® in combination with axitinib, grade 3-4 clinical chemistry abnormalities include blood triglyceride increased and lipase increased.

For full US Prescribing Information and Medication Guide for BAVENCIO®, please see http://www.BAVENCIO.com.

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About Transgene

Transgene (Euronext: TNG) is a publicly traded French 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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