Transgene to present Phase 1b/2 trial results of TG4001 in combination with avelumab in advanced HPV-positive cancers at ESMO IO 2020

Strasbourg, France, December 3, 2020, 06:45 pm CET – **Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapeutics against cancer, will present the Phase 1b/2 trial results of TG4001, a HPV16 targeted therapeutic vaccine, in combination with avelumab (BAVENCIO®), a human anti-PD-L1 antibody, in HPV16-positive recurrent and/or metastatic malignancies at ESMO Immuno-Oncology Virtual Congress 2020, December 9-12, 2020.**

These data will be presented by the principal investigator, Professor Christophe Le Tourneau, M.D., PhD, Head of the Department of Drug Development and Innovation (D3i) at the Institut Curie (Paris) in an oral presentation on December 12, 2020 at 12:40 pm CET.

Professor Christophe Le Tourneau added: *"Current treatments for HPV-16 positive cancer patients do not address the viral origin of the disease. These data are a very encouraging first step to hopefully provide patients with better treatment options, particularly for patients with advanced disease who have a devastating disease with poor prognosis."*

Number and title of the abstract and mini-oral presentation: (abstract #276, presentation #63 MO) *TG4001 therapeutic vaccination combined with PD-L1 blocker avelumab remodels the tumor microenvironment (TME) and drives antitumor responses in Human PapillomaVirus (HPV)+ malignancies*

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Session date and time: Mini Oral Session 2, December 12, 2020, 12:35-1:55 pm CET (Channel 1). The session consists of short oral presentations by authors, followed by expert discussion and perspectives.

Key results of the trial (n=34 evaluable patients):

- **The combination of TG4001 and avelumab demonstrated a clinically relevant anti-tumor activity (23.5% ORR)** in patients with previously treated recurrent and/or metastatic HPV-related cancers.
- **The presence of liver metastases has a notable impact on outcome in terms of ORR and PFS**. **In patients without liver metastases, an ORR of 34.8% and a median PFS of 5.6 months were achieved.**
- **The disease control rate (DCR) at 12 weeks was 56.6% in patients without liver metastasis**, against 9.1% in patients with liver metastasis.
- **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.
- **These results warrant further confirmation in a larger controlled randomized study.**

About the trial

The purpose of this exploratory, multi-center, open-label Phase 1b/2 trial is to evaluate the safety and efficacy of the combination of TG4001 and an immune checkpoint inhibitor (avelumab) in a heterogeneous group of patients with aggressive, recurrent and/or metastatic HPV16-positive cancers who have disease progression after at least one line of systemic treatment (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, and Pfizer Inc. (NYSE: PFE). Avelumab is co-developed and co-commercialized by Merck KGaA, Darmstadt, Germany and Pfizer Inc.

Thirty-four 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. 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.

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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 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 300 individuals, demonstrating good safety, significant HPV clearance rate and promising efficacy results [1, 2]. Its mechanism of action and good safety profile make TG4001 an excellent candidate for combinations with other therapies in HPV-mediated solid tumors.

About HPV-Positive Cancers

HPV-positive cancers comprise a variety of malignancies, including head and neck cancers and anogenital cancers [3]. 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 [4]. The incidence of HPV16-related SCCHN has significantly increased in recent years [4]. HPV16 infection is associated with more than 85% of oropharynx squamous cell carcinomas [4], i.e. approximately 10,000 patients at metastatic stage and receiving a second line of treatment [5]. Other HPV16-positive cancers include cervical [6], vaginal [7], vulvar [8], anal [9] and penile [10] cancers, i.e. approximately 15,000 cancers at metastatic stage and eligible for a second line of treatment [11].

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 [12,13]. With immune checkpoint inhibitors, median overall survival remains inferior to 11 months [14-20] and median progression-free survival is between 2 and 4 months [14-20]. In this heterogenous group of malignancies, overall response rates are around 10–15% [14-20].

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.

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

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