First Patient Treated in a Phase 1b/2 Trial of TG4001 in Combination with Avelumab in HPV-Positive Cancers

Clinical Trial in Collaboration with the Merck-Pfizer Alliance

First Results Expected in 2018

Strasbourg, France, September 19, 2017, 5:45 p.m. CET - Transgene (Euronext Paris: TNG), a biotech company that designs and develops viral-based immunotherapies, today announces that the first patient has been treated at the Curie Institute, Paris, France, in a Phase 1b/2 clinical trial evaluating the combination of TG4001 with avelumab*as a treatment for human papillomavirus type 16 positive (HPV-16+) recurrent or metastatic cancers, such as oropharyngeal squamous cell carcinoma of the head and neck (SCCHN). This subtype of cancer represents more than 80% of oropharynx cancers.

This multi-center, open-label trial will assess the safety and tolerability, as well as the anti-tumor activity and efficacy of this immunotherapy combination regimen in up to 50 patients (NCT03260023).

Prof. Christophe Le Tourneau, M.D., Head of the Early Phase Program at the Curie Institute, and a world expert in head and neck cancers, is the Principal Investigator of the study.

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

TG4001: an investigational viral-based therapeutic vaccine that has shown efficacy

TG4001 is an active immunotherapeutic designed by Transgene to express the coding sequences of the E6 & E7 tumor-associated antigens of HPV-16 and the cytokine, IL-2. This therapeutic vaccine, which is based on a non-propagative, attenuated vaccinia vector (MVA), has already been administered to more than 300 subjects in previous clinical trials. TG4001 has demonstrated promising activity in terms of HPV viral clearance and was well tolerated.

TG4001 + avelumab: a promising immunotherapy regimen

Avelumab is a human anti-PD-L1 IgG1 monoclonal antibody. Avelumab is designed to potentially engage both the adaptive and innate immune systems. By binding to PD-L1, avelumab is thought to prevent tumor cells from using PD-L1 for protection against white blood cells, such as T-cells, thereby exposing them to the anti-tumor responses.

Immunotherapeutic agents, and in particular the therapeutic vaccine TG4001 together with the PD-L1 blocker avelumab, by targeting two distinct steps in the immune response, are hoping to improve efficacy for patients who have not responded to or have progressed after first line treatment.

Commenting on the potential of this immunotherapy combination regimen, Maud Brandely, Chief Medical Officer of Transgene, added: "*The preclinical and clinical data obtained with TG4001 clearly indicate that this therapeutic vaccine can induce HPV clearance in patients with HPV-16 associated diseases. Avelumab has also demonstrated a promising preclinical and clinical efficacy in multiple tumor types, pointing to potential synergies with TG4001. We believe an immunotherapy combination regimen, such as the combination of TG4001 and avelumab shows significant promise for patients with*

recurring or resistant advanced HPV-16+ oropharyngeal cancers. We are very pleased to start this Phase 1b/2 trial with Merck and Pfizer as partners to assess the potential of this novel immunotherapy regimen in an effort to improve the outcomes of these patients."

Commenting on this novel immunotherapy regimen, Prof. Christophe Le Tourneau, MD, Head of the Early Phase Program at the Curie Institute, and Principal Investigator of the trial, added: "*HPV-positive cancer patients suffer from the lack of a specific treatment regimen that addresses the underlying etiology of their disease. I am confident that immunotherapy combination regimens, based around TG4001, could deliver better outcomes for patients who have not responded to or have progressed after a first line of treatment.*"

*Avelumab is under clinical investigation for treatment of HPV-16+ recurrent or metastatic cancers, such as oropharyngeal SCCHN in combination with TG4001 and has not been demonstrated to be safe and effective for these indications. There is no guarantee that avelumab will be approved for HPV-16+ recurrent or metastatic cancers, such as oropharyngeal SCCHN by any health authority worldwide.

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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). It is targeting HPV+ sub population. 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 subjects, 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 antibody specific for a protein called PD-L1, or programmed death ligand-1. Avelumab is designed to potentially engage both the adaptive and innate immune systems. By binding to PD-L1, avelumab is thought to prevent tumor cells from using PD-L1 for protection against white blood cells, such as T cells, exposing them to anti-tumor responses. Avelumab has been shown to induce antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro. In November 2014, Merck and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Indications

The US Food and Drug Administration (FDA) granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) metastatic Merkel Cell Carcinoma (mMCC) in adults and pediatric patients 12 years and older and (ii) patients with locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy, or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications were 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 (BAVENCIO®) was also granted marketing authorization by Swissmedic for the treatment of patients with mMCC, whose disease has progressed after at least one chemotherapy 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.

About HPV-Mediated 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. HPV-16 infection is recognized to participate in the development of a substantial proportion of head and neck cancers and is associated with a subset of SCCHN, especially those arising from the oropharynx (more than 80%)

The incidence of HPV-16-related head and neck cancer has significantly increased in recent years. Although there are more than 100 subtypes of HPV, HPV-16 accounts for 90% of all HPV-related head and neck cancers. Global spending on head and neck cancer indications amounted to $1 billion in 2010.

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), part of Institut Mérieux, 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 and preclinical development, including TG1050 (chronic hepatitis B) and TG6002 (solid tumors). Transgene is based in Strasbourg, France, and has additional operations in Lyon, as well as a joint venture in China. Additional information about Transgene is available at www.transgene.fr.
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