

Transgene Announces Collaboration with Merck and Pfizer to Evaluate the Combination of TG4001 with Avelumab in HPV-Positive Head & Neck Cancer in a Phase 1/2 Study

Strasbourg, France, October 11, 2016, 6:00 pm CET – Transgene (Euronext Paris: TNG), a company focused on designing and developing targeted immunotherapies for the treatment of cancer and infectious diseases, today announced it has entered a collaboration agreement with Merck, the science and technology company, and Pfizer (NYSE: PFE) under which Transgene will sponsor a Phase 1/2 study evaluating the potential of the therapeutic vaccine candidate TG4001 in combination with avelumab, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody, for the treatment of human papilloma virus- (HPV-) positive head and neck squamous cell carcinoma (HNSCC), after failure of standard therapy.

Philippe Archinard, Chairman and CEO of Transgene, commented: *“We are pleased to enter this collaboration with Merck and Pfizer to evaluate our therapeutic vaccine TG4001 in association with avelumab. In previous clinical trials, TG4001 has demonstrated promising activity in terms of HPV viral clearance and was well tolerated. TG4001 is one of the few drugs targeting HPV-associated cancers that can be combined with an immune checkpoint blocker such as avelumab. The preclinical and clinical data that have been generated with both TG4001 and avelumab individually suggest this combination could potentially demonstrate a synergistic effect, delivering a step up in therapy for HPV-positive HNSCC patients.”*

The combination of TG4001 and avelumab aims to target two distinct steps in the immune response to target cancer cells. This is an exclusive agreement between the parties to study the combination of these two classes of investigational agents in HPV-positive HNSCC.

Prof. Christophe Le Tourneau, M.D., Head of the Early Phase Program at Institut Curie, and a world expert in ENT cancers, will be the Principal Investigator of the Phase 1/2 study. This trial is expected to begin in France, with the first patient expected to be recruited in H1 2017. It will seek to recruit patients with recurrent and/or metastatic virus-positive oropharyngeal squamous cell carcinoma that have progressed after definitive local treatment or chemotherapy, and cannot be treated with surgical resection and/or re-irradiation.

Prof. Christophe Le Tourneau said: *“HPV-induced head and neck cancers are currently treated with the same regimen as non-HPV-positive HNSCC tumors. However, their different etiology clearly suggests that differentiated treatment approaches are needed for HPV-positive patients. Immunotherapy, and in particular the therapeutic vaccine TG4001 together with the PD-L1 blocker avelumab, by targeting two distinct steps in the immune response, could deliver improved efficacy for patients who have not responded to or have progressed after a first line of treatment.”*

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 patients with high grade cervical intra-epithelial neoplasia (CIN 2/3). It has demonstrated good safety, a significant HPV clearance rate and promising efficacy results. Its mechanism of action and good safety profile make TG4001 a particularly appropriate candidate for combinations with other therapies, such as avelumab.

Avelumab is an investigational, fully human antibody specific for a protein found on tumor cells called PD-L1, or programmed death ligand-1. As a checkpoint inhibitor, avelumab is thought to have a dual mechanism of action that may potentially enable the immune system to find and attack cancer cells. 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 is also thought to help white blood cells such as natural killer (NK) cells find and attack tumors in a process known as ADCC, or antibody-dependent cell-mediated cytotoxicity. In 2014, the science and technology company Merck and Pfizer signed a strategic alliance to co-develop and co-commercialize avelumab.

Alise Reicin, M.D., Head of Global Clinical Development in the biopharma business of Merck, commented: *“We believe combination regimens show significant promise in the development of novel and efficacious immuno-oncology treatments. Through this study, we hope to discover the potential of avelumab as a combination therapy with TG4001 for patients fighting this recurring cancer.”*

Chris Boshoff, M.D., Ph.D., Head of Immuno-Oncology, Early Development, and Translational Oncology at Pfizer, said: *“Through this collaboration, we hope to better understand how therapeutic vaccines may help support the clinical development program for avelumab as our end goal is to find the best treatment options for patients.”*

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About HPV-mediated Head and Neck Cancer

Head and neck squamous cell carcinoma (HNSCC) 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 HNSCC, especially those arising from the oropharynx (more than 80%), which are the most frequent, and the larynx (~70%).

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 or chemoradiotherapy. However, better options are needed for advanced and metastatic HPV+ HNSCC. 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 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 one of the few therapies 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 patients, 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 solid tumors.

About Avelumab

Avelumab (also known as MSB0010718C) is an investigational, fully human antibody specific for a protein found on tumor cells called PD-L1, or programmed death ligand-1. Avelumab is thought to have a dual mechanism of action which may enable the immune system to find and attack cancer cells. 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 is also thought to help white blood cells such as natural killer (NK) cells find and attack tumors in a process known as ADCC, or antibody-dependent cell-mediated cytotoxicity. In November 2014, Merck and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

About Transgene

Transgene S.A. (Euronext: TNG), part of Institut Mérieux, is a publicly traded French biopharmaceutical 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 two lead clinical-stage programs are: TG4010 for non-small cell lung cancer and Pexa-Vec for liver cancer. The Company has several other programs in clinical and pre-clinical development. Transgene is based in Strasbourg, France, and has additional operations in Lyon, as well as a JV in China with Tasly Group. Additional information about Transgene is available at www.transgene.fr.

Disclaimer

This press release contains forward-looking statements about the future development of TG4001. Although the Company believes its expectations are based on reasonable assumptions, these forward-looking statements 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 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 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, which is available on the AMF website (<http://www.amf-france.org>) or on Transgene's website (www.transgene.fr).