



## **Transgene Announces Topline Preliminary Results from Phase 2b Part of TIME Trial with TG4010 in Non-Small Cell Lung Cancer**

**Overall results support use of TrPAL predictive biomarker to select patients to receive treatment with TG4010 in combination with chemotherapy**

**Results warrant continuation into Phase 3 part of TIME study**

**Conference call scheduled for January 9, 2014 at 9:00 am CET**

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**Strasbourg, France, January 8, 2014** – Transgene SA (NYSE-Euronext: TNG) today announced topline preliminary results from the Phase 2b part of the Phase 2b/3 TIME trial evaluating TG4010 MUC-1 targeted immunotherapy in combination with chemotherapy versus placebo plus chemotherapy in the first-line treatment of MUC-1 positive advanced non-small cell lung cancer (NSCLC) patients. The primary objective of the Phase 2b part of the study was to validate the triple-positive activated lymphocytes (TrPAL) predictive biomarker<sup>1</sup>; the safety and efficacy of TG4010 in combination with various chemotherapy regimens in this patient population were also assessed.

The predictive value of the TrPAL biomarker, which was identified in an earlier Phase 2 study in advanced NSCLC patients (the TG4010.09 study)<sup>2</sup>, was assessed by comparing progression-free survival (PFS) between the two arms in two subgroups of patients according to their TrPAL level (normal or high) at the time they entered the trial (baseline). A total of 210 patients (170 normal TrPAL level, 40 high TrPAL level) were enrolled in the study, and the current analyses were conducted per protocol after 89 progression events had occurred in the normal TrPAL group. For the primary analysis, a patient's TrPAL level was determined using a threshold based on an assessment of TrPAL levels in healthy people, a so-called "upper limit of normal" (ULN) threshold. The study did not meet its primary endpoint when the ULN threshold was used.

However a second pre-planned PFS analysis, described below, was performed on the entire study population using a quartile approach similar to the one performed in the prior TG4010.09 study. This analysis and the data generated, which is discussed below, will lead to a refined threshold, which is different than the ULN threshold, for the Phase 3 part of the trial.

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<sup>1</sup> The TrPAL biomarker measures at baseline the level of triple positive (CD16+, CD56+, CD69+) circulating lymphocytes, a phenotype of activated NK cells.

<sup>2</sup> In the TG4010.09 study, for the normal TrPAL group, a better clinical outcome was noted with TG4010 plus chemotherapy compared with chemotherapy alone contrary to the high TrPAL group. *Lancet Oncol.* 2011 Nov;12(12):1125-33

With this threshold the quartile analysis showed that, in the 75% of patients having the lower baseline level of TrPAL (i.e., the three lowest quartiles) and who received TG4010, there was a clinically meaningful improvement in PFS, as indicated by a greater than 25% reduction in the risk of progression or death compared to placebo. Conversely, in the 25% of patients with the higher level of TrPAL (highest quartile) and who received TG4010 there was no improvement in PFS. These initial results are generally consistent with the results of the previous TG4010.09 study and support both the activity of TG4010 in this setting as well as the predictive value of the TrPAL biomarker. Additionally, in subgroup analyses using the quartile approach, an even larger improvement in PFS was obtained in patients with non-squamous tumors not treated with bevacizumab (73% of initial study population); in general this is a large and growing subgroup of NSCLC and so will warrant further investigation.

TG4010 was well tolerated, and the nature and incidence of adverse events in the TG4010 arm were consistent with previous Phase 2 clinical trials. The data from the trial continue to mature; detailed results are expected to be presented at major medical meetings during 2014.

The Company plans to meet with regulatory authorities to discuss plans for moving into the Phase 3 part of the TIME trial, including defining the threshold level for TrPAL cells for the predictive biomarker, which would be used to select the patient population for Phase 3.

Elisabeth Quoix, M.D., Head of the Department of Pulmonology at the University Hospital of Strasbourg and Coordinating Investigator of the TIME study said: *“Immunotherapy is a very active area in the development of innovative cancer therapies. The topline preliminary results from the Phase 2b part of the TIME study with TG4010, Transgene’s immunotherapy against lung cancer, show the same trend in PFS as the earlier Phase 2 study and are an encouragement to initiate the Phase 3 part of the trial with this product. They also support the use of the TrPAL biomarker for selecting the patient population for the Phase 3 part of the trial and will help to determine the best threshold cutoff separating normal and high TrPAL levels for the biomarker.”*

*“We are strongly encouraged by these promising initial results from the TIME trial and believe they provide a solid rationale for advancing into the Phase 3 part of the study,”* said Philippe Archinard, Chairman and Chief Executive Officer of Transgene. *“We believe these results support both the activity of TG4010, a novel targeted immunotherapy, in combination with chemotherapy in the first-line treatment of advanced non-small cell lung cancer patients, as well as the use of the TrPAL predictive biomarker for selecting the patient population for the Phase 3 part of the trial.”* Mr. Archinard added: *“As the leading cause of cancer-related deaths worldwide, lung cancer remains an area of major unmet medical need. We look forward to continuing to develop TG4010 in this important indication and will be meeting with regulatory authorities to advance our plans for the Phase 3 part of the study. The data and analyses from the TIME trial have been provided to Novartis, and we are working closely with them to ensure they have the information they need to make a decision on their option for TG4010.”*

Transgene has signed an exclusive option agreement with Novartis for the development and commercialization of TG4010 for the first-line treatment of NSCLC and other potential cancer indications.

**Conference call scheduled:**

The company will host a conference call and webcast in English on Thursday, January 9, 2014 at 9:00 am CET. The dial-in numbers are:

France: +33(0)1 76 77 22 21

United Kingdom: +44(0)20 3427 1907

United States: +1 646 254 3364

Confirmation Code: 3223282

The weblink for the webcast is: <http://www.media-server.com/m/p/ro5jtf93>

The replay will be available on Transgene's website at [www.transgene.fr](http://www.transgene.fr) following the live webcast.

For access to the live and on demand webcast from any IOS apple or Android mobile devices, please use the following QR code:



**About TG4010:**

TG4010, a novel MUC1 targeting immunotherapy, is in development as a first indication for the treatment of metastatic NSCLC in combination with first-line chemotherapy. TG4010 is a recombinant vaccinia virus of the Ankara strain (MVA) expressing the coding sequences of the MUC1 antigen and of the human cytokine, Interleukin-2 (IL2). In healthy cells, the MUC1 protein is normally found on the surface of epithelial cells in many types of tissue and works to protect these cells. In tumor cells, several modifications of MUC1 can occur: over expression, hypoglycosylation and changes in cellular localization. These changes transform the MUC1 protein into a highly immunogenic tumor associated antigen (TAA) and make it an attractive target for cancer immunotherapy. Thus, the strategy is to induce MUC1 antigen expression in a non-tumor environment, i.e., where the immune system is fully functional, in order to induce both innate and MUC1 specific adaptive immunity. The MUC1 TAA is expressed in many solid tumor types, such as lung, breast, colorectal, kidney and prostate cancers.

**About the TIME trial:**

The TIME trial is a randomized, placebo-controlled, global Phase 2b/3 trial evaluating TG4010 in combination with chemotherapy in patients with Stage IV MUC-1 positive NSCLC. The primary objective of the Phase 2b part of the study is to validate the predictive value of the TrPAL biomarker for the selection of the patient population for the Phase 3 portion of study. The

safety and efficacy of TG4010 in combination with various chemotherapy regimens in this patient population are also being assessed.

### **About non-small cell lung cancer:**

Lung cancer is one of the most common malignancies worldwide with an estimated incidence of 1.6 million people and is the leading cause of cancer-related deaths, accounting for an estimated 1.4 million deaths in 2008, the latest figures available. NSCLC represents approximately 80 per cent of all lung cancers. Recent statistics estimate that over 287,000 people in the European Union (EU) were diagnosed with lung cancer in 2008, and approximately 252,000 people in the EU died from this disease. In the U.S., deaths due to lung cancer are expected to account for about 27% of all cancer deaths in 2013, more than from colon, breast and prostate cancers combined. It is estimated that there will be over 228,000 new cases of lung cancer in the U.S. in 2013 and over 159,000 deaths due to this disease. Lung cancer remains one of the cancer types with the worst prognosis (five-year survival rate for NSCLC of 18% in the U.S.), underlining the unmet need in this disease.

Current treatments for lung cancer include surgery, chemotherapy, radiation and targeted molecular therapy, but only one third of patients present resectable (able to be removed by surgery) disease at diagnosis. The poor prognosis in patients with advanced disease is improved by platinum-based chemotherapies that produce longer survival times. However, the medical need for developing new treatments for NSCLC remains extremely high and new approaches are necessary to significantly change the outcome of the disease.

### **About Transgene:**

Transgene, a member of the Institut Mérieux Group, is a publicly traded French biopharmaceutical company focused on discovering, developing and manufacturing targeted immunotherapies for the treatment of oncology and infectious diseases. Transgene's programs utilize well-tolerated viruses with the goal of indirectly or directly killing infected or cancerous cells. The Company's four clinical-stage programs are: TG4010 for non-small cell lung cancer; Pexa-Vec for liver cancer; TG4001 for oropharyngeal cancer (under a collaboration agreement with the EORTC) and TG4040 for chronic Hepatitis C. Transgene has concluded corporate strategic agreements for the development of two of its immunotherapy products: an exclusive option agreement with Novartis for the development and commercialization of TG4010 and an in-licensing agreement with U.S.-based Jennerex, Inc. for the development and commercialization of Pexa-Vec in certain territories. The Company also has several programs in research and pre-clinical development that are based on its core viral vector technology. Transgene is based in Strasbourg, France, and has additional operations in Lyon, as well as satellite offices in China and the U.S. Additional information about Transgene is available at [www.transgene.fr](http://www.transgene.fr).

**Disclaimer:**

*This press release contains forward-looking statements about the future development of TG4010. 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. There can be no guarantee that (i) the results of the Phase 2b part of the TIME trial will be predictive of future results with TG4010, (ii) regulatory authorities will agree with the Company's plans for the Phase 3 part of the trial, or (iii) Novartis will exercise its option for TG4010. 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](http://www.transgene.fr)).*

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