

Peer Reviewed Scientific Publications Highlight TG4010's Ability to Induce Broad CD8+ Responses and its Synergistic Effects in Combination with Immune Checkpoint Inhibitors

*Transgene Is Currently Developing TG4010 in Advanced Lung Cancer (NSCLC)
in Combination Regimens with Immune Checkpoint Inhibitors (ICIs)*

Strasbourg, France, October 12, 2017, 5:45 p.m. CET - Transgene (Euronext Paris: TNG), a biotech company that designs and develops viral-based immunotherapies, recently published two papers supporting the efficacy and mechanism of action of its therapeutic vaccine TG4010. After successful completion of the phase 2b TIME trial for combination of TG4010 and chemotherapy (Quoix et al. *Lancet Oncol.*, 2015), these two peer-reviewed articles support the ongoing development of the product in combination with immune checkpoint inhibitors (ICIs) in advanced NSCLC. More generally, they confirm the interest in viral vectors as immunotherapeutics.

“Viral based vaccine TG4010 induces broadening of specific immune response and improves outcome in advanced NSCLC.” By Tosch et al., [Journal for ImmunoTherapy of Cancer](#), 2017, 5, 70

In this paper, based on samples from 78 patients of the TIME trial, Transgene provides the **first data linking directly the development of a specific cellular immune response with an improved clinical benefit in patients with advanced NSCLC upon vaccination with a viral vector.**

It was shown that the significantly longer overall survival (OS) of patients treated with TG4010 is correlated with the diversity and intensity of CD8+ T cell responses against the MUC1 antigen.

Treatment with TG4010 also led to a broadening of immune response to other tumor-associated antigens that were not targeted by the vaccine. This is the first report of such a mechanism of **epitope spreading** for a virus-based immunotherapeutic product. This spreading might contribute to the enrichment of the diversity of the anti-cancer response.

These results support the causality of T-cell response in improved survival in NSCLC, and strengthen the rationale for combination with ICIs to exploit the broad CD8+ T cell repertoire induced by TG4010 vaccination.

“Sequential administration of MVA-based vaccines and PD-1/PD-L1-blocking antibodies confers measurable benefits on tumor growth and survival: preclinical studies with MVA-βGal and MVA-MUC1 (TG4010) in a murine tumor model.” By Remy-Ziller et al., [Human Vaccines & Immunotherapeutics](#), 2017 Sep (19:0), doi: 10.1080/21645515.2017.1373921. epub ahead of print

Transgene further demonstrates the benefit of administration of MVA-vaccines, and ICIs in a preclinical metastatic model. Treatment with MVA vectors showed increased survival rates, and led to the accumulation of CD3^{dim}CD8^{dim} T cells in the lung and an upregulation of PD-1 was observed on these T cells. Targeting the PD-1/PD-L1 pathway with ICIs in association with TG4010 treatment, at late stage of tumor development, enhanced the therapeutic activity induced by the vaccine, supporting the two ongoing clinical evaluation of TG4010 in combination with nivolumab.

All publications on TG4010 can be accessed via www.transgene.fr, Pipeline>Publications.

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About TG4010

TG4010 is an immunotherapy that has been designed to express the coding sequences of the MUC1 tumor-associated antigen and the cytokine, Interleukin-2 (IL2) in a modified vaccinia virus (MVA).

The combination of TG4010 immunotherapy and chemotherapy has demonstrated significant efficacy in terms of progression-free survival and overall survival in patients with advanced stage NSCLC (Quoix et al. [Lancet Oncol.](#) 2015). TG4010 is currently being investigated in combination with nivolumab (ICI) for the 2nd-line treatment of advanced NSCLC ([NCT02823990](#)). A trial in 1st-line treatment of NSCLC is expected to begin at the end of 2017, evaluating the combination regimen of TG4010 + nivolumab + chemotherapy in patients whose tumors express low or undetectable levels of PD-L1.

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 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. Follow us on Twitter: [@TransgeneSA](https://twitter.com/TransgeneSA)

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