Transgene Announces Publication in *OncoImmunology* of Pre-Clinical Data Demonstrating Delivery of a Fully Functional Immune Checkpoint Inhibitor (ICI) with Anti-Tumor Efficacy by a New Generation of Oncolytic Viral Immunotherapy

In vivo and in vitro data shows oncolytic virus-based immunotherapy can express a fully functional ICI (anti-PD-1) within the tumor micro-environment, at levels that achieve a durable anti-tumor effect

---

Strasbourg, France, October 28, 2016, 6:00 p.m. CET—Transgene (Euronext Paris: TNG), a company focused on designing and developing targeted immunotherapies for the treatment of cancer and infectious diseases, today announced that pre-clinical results of a new generation oncolytic viral immunotherapy, encoding for three different ICIs (anti-PD-1), was published in the peer-reviewed journal *OncoImmunology*.

This new generation of oncolytic virus is armed with cancer-fighting genes (here, genes coding for anti-PD-1 antibody sequences[1]) with the aim of providing enhanced efficacy within the tumor micro-environment while reducing systemic toxicity.
The results showed that oncolytic virus-based immunotherapy can express a fully functional ICI (anti-PD-1) within the tumor micro-environment, at levels that achieve a durable anti-tumor effect.

These results support advancing the development of these next generation oncolytic vaccinia viruses armed with antibodies, which can also be designed with other immune-modulating molecules.
They also demonstrate that **oncolytic viruses can be armed with genes that allow the local production into the tumor of efficacious treatments with minimum release of the drug into the bloodstream**. This favorable bio distribution is particularly attractive for biotherapeutics that cannot be administered systemically as single agents due to their unfavorable safety profile.

The findings in this publication highlight Transgene's industry leading capability to design oncolytic viruses that have the ability to express complex therapeutic proteins, such as ICIs within the tumor micro-environment, at levels that deliver clear anti-tumor effects.

Key elements of the publication

In this experiment, three oncolytic vaccinia viruses were armed with three different anti-murine-PD-1 forms: a full monoclonal antibody (mAb), an antigen-binding fragment (Fab) or a single-chain variable fragment (scFv).

The published results report that the expression products of these three forms of PD-1 blockers vectorized in an oncolytic vaccinia virus all:

- displayed a perfect biochemical integrity and folding,
- were fully functional,
- had equivalent biological activity to the corresponding anti-PD-1 reference monoclonal antibody (mAb).

[1] Immune checkpoint inhibitors (ICIs), such as anti-PD-1 (or PD-1 blockers), targeting PD-1 represent a major advance in treating several forms of cancer. PD-1 molecules can be found at the surface of T cells. It binds with another molecule, PD-L1 that can be found on the surface of certain cancer cells. This interaction prevents T cells from attacking the abnormal cell, and allows the development of the tumor. By inhibiting PD-1 or PD-L1, ICIs help the immune system to eliminate cancer cells again.

Furthermore, in a murine model, the results show that:

- an intratumoral (IT) injection of an anti-PD-1 armed oncolytic virus induced a sustained expression of the ICI into the tumor at a fairly high concentration compared to the level detected in the bloodstream.
- IT injection of an oncolytic vaccinia virus induced a massive increase of TIL (Tumor infiltrating lymphocytes, incl. CD8 and CD4 lymphocytes) which displayed some markers of activation.
- In one model, the IT injections of two armed anti-PD1 oncolytic viruses (mAb and scFv) had an anti-tumor efficacy that is similar to the efficacy of the combination of unarmed oncolytic virus together with systemic administration of anti-PD-1.
- The *in vivo* expression of this anti-PD-1 antibody and scFv into the tumor met at least the minimum quantity, quality and duration required for an anti-tumor activity.

A copy of the article*, Vectorization in an oncolytic vaccinia virus of an antibody, a Fab and a scFv against programed cell death-1 (PD-1) allows their intratumoral delivery and an improved tumor-growth inhibition*, can be downloaded from *OncoImmunology* website (http://dx.doi.org/10.1080/2162402X.2016.1220467) and from Transgene's website "Our pipeline/Publication" (www.transgene.fr). These data were presented in April 2016 at the Annual Meeting of the American Association for Cancer Research (AACR) in New Orleans, USA, and were positively received by the scientific community and the pharmaceutical industry.

Contacts

Transgene:

Lucie Larguier
Director Corporate Communications & IR
+33 (0)3 88 27 91 04
investorrelations@transgene.fr

Media contacts:

Citigate Dewe Rogerson
David Dible/Marine Perrier
+ 44 (0)20 7638 9571
transgene@citigatedr.co.uk

About oncolytic viruses

A breakthrough therapeutic class, oncolytic viruses are active and targeted immunotherapy treatments. They are designed to selectively destroy cancer cells by lysing (breaking down) them through viral replication and to stimulate the body's immune response against cancer cells. They can be armed with a wide variety of therapeutics to enhance the activity and the potency of the treatment. Transgene's lead oncolytic virus, Pexa-Vec, is currently being evaluated in a Phase 3 trial in advanced primary liver cancer. Its mechanism of action and its safety profile make it an appropriate candidate for combinations in solid tumors.
Transgene's research teams are also focused on designing a new generation of oncolytic virus that aims at delivering multiple therapeutics within the tumor micro-environment.

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, a therapeutic vaccine for non-small cell lung cancer and Pexa-Vec, an oncolytic virus for liver cancer. The Company has several other programs, including TG4001, in clinical and preclinical development. 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

Forward-looking statements

This press release contains forward-looking statements, which 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, regulatory authorities' agreement with development phases, 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 manufacturing, 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, available on the AMF website (http://www.amf-france.org) or on Transgene's website (www.transgene.fr). Forward-looking statements speak only as of the date on which they are made and Transgene undertakes no obligation to update these forward-looking statements, even if new information becomes available in the future.

Disclaimer

This announcement does not, and shall not, in any circumstances constitute a public offering nor an invitation to the public in connection with any offer.

The distribution of this document may be restricted by law in certain jurisdictions. Persons into whose possession this document comes are required to inform themselves about and to observe any such restrictions.

*This announcement is an advertisement and not a prospectus within the meaning of Directive 2003/71/EC of the European Parliament and of the Council of 4 November 2003, as amended (the "**Prospectus Directive**").*

With respect to the member States of the European Economic Area which have implemented the Prospectus Directive, no action has been undertaken or will be undertaken to make an offer to the public of the securities referred to herein requiring a publication of a prospectus in the context of a public offering in any relevant member State other than France. As a result, the securities may not and will not be offered in any relevant member State other than France except in accordance with the exemptions set forth in Article 3(2) of the Prospectus Directive, if they have been implemented in that relevant member State, or under any other circumstances which do not require the publication by Transgene of a prospectus in the context of a public offering pursuant to Article 3 of the Prospectus Directive and/or to applicable regulations of that relevant member State.

*This document is not an offer of securities for sale nor the solicitation of an offer to purchase securities in the United States of America or any other jurisdiction where such offer may be restricted. Securities may not be offered or sold in the United States of America absent registration under the U.S. Securities Act of 1933, as amended (the "**Securities Act**"), or an exemption from registration. The shares and the preferential subscription rights of Transgene have not been and will not be registered under the Securities Act, and Transgene does not intend to make a public offer of its securities in the United States of America.*

*This document is only being distributed to, and is only directed at, persons in the United Kingdom that (i) are "investment professionals" falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the "**Order**"), (ii) are persons falling within Article 49(2)(a) to (d) ("high net worth companies, unincorporated associations, etc.") of the Order, or (iii) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Article 21 of the Financial Services and Markets Act 2000) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as "**Relevant Persons**"). This document is directed only at Relevant Persons and must not be acted on or relied on by persons who are not Relevant Persons. Any investment or investment activity to which this document relates is available only to Relevant Persons and will be engaged in only with Relevant Persons. Any person other than a relevant person should not act or rely on this document or any of its contents.*

Any investment decision to buy shares or preferential subscription rights in Transgene must be made solely on the basis of publicly available information regarding Transgene.