Transgene's Lead Oncolytic Virus Pexa-Vec Triggers Strong Anti-Tumor Immunity after Intravenous Administration

- *Pexa-Vec selectively targets tumor tissue after intravenous (i. v.) administration and stimulates the adaptive and innate anti-tumor immune response*
- *Pexa-Vec induces expression of PD-L1 and PD-1 pathways reinforcing the rationale for combination with immune checkpoint inhibitors*
- *Of the four evaluable patients with liver metastases, one showed complete tumor pathological response at the time of surgery*
- *Data support ongoing development of Transgene's Vaccinia virus-based oncolytics (Pexa-Vec, TG6002 drug candidates and Invir.IO™ preclinical candidates)*

Strasbourg, France, and Leeds, United Kingdom, June 4, 2018, 5:45 p.m. CET
Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies against cancers and infectious diseases, and University of Leeds, announce that new clinical data[1] obtained with Pexa-Vec further demonstrate anti-tumor activity after intravenous (i. v.) infusion. These data were presented by Dr. Alan Anthoney (University of Leeds) in a poster presentation at the American Society for Clinical Oncology (ASCO) Annual Meeting, June 4, in Chicago.

These first clinical results confirm Pexa-Vec's activation of anti-tumor immunity and targeted oncolytic activity. The key findings of the trial show:

- **selective expression and replication of Pexa-Vec in the tumor tissues**;
- induction of a **robust anti-tumor immune response**:
  - with the stimulation of an adaptive response (T cells) targeted to tumor specific antigens,
  - the activation of innate immune response (NK cells), and
  - an elevation of cytokines associated with immune stimulation;
- **one partial and one complete necrosis of tumors** among the patients with colorectal cancer and liver metastases (pathological responses);
- **upregulation of PD-L1 and PD-1 signaling molecules**, a finding that strongly supports the rationale for combining Pexa-Vec with anti-PD-1 inhibitors.

Dr Alan Anthoney, Consultant in Medical Oncology at Leeds Teaching Hospitals, Senior Lecturer in the Institute of Cancer & Pathology at the University of Leeds and principal investigator of the trial, said: "*We are very encouraged to report that a single IV administration of Pexa-Vec displayed cytolytic activity at tumor sites, where it elicited a robust activation of tumor-antigen specific immune cells. In one patient with colorectal cancer liver metastasis a complete pathological response has been observed. These data clearly support the anti-tumor activity of Pexa-Vec. The final data from this trial will be published in an upcoming paper. Our decision to lead this clinical trial, investigating the potential of new weapons against cancers, testifies to our commitment at Leeds University and Leeds Teaching Hospitals NHS Trust to evaluate new innovative options that might improve the lives of our patients with cancer.*"

Maud Brandely, Chief Medical Officer of Transgene, added: "*These very positive translational data confirm the targeted oncolytic activity and the potential of Pexa-Vec in advanced stages cancers. The observed upregulation of PD-1 and PD-L1 positive pathways strongly supports the rationale for combining Pexa-Vec*

[1] *n = 8; 3 patients with metastatic melanoma and 5 with colorectal cancer metastases to the liver*

with anti-PD-1 immunotherapies, which is the focus of an ongoing Phase 1/2 trial in the first-line treatment of liver cancer (HCC). These data are also crucial for our next generation of multifunctional oncolytic viruses based on our Invir.IO™ platform: this trial clearly shows that Vaccinia virus based immunotherapeutics can reach the tumor sites after i. v. administration, and selectively replicate within cancer cells. This neoadjuvant trial is the first clinical trial led by Transgene to readout this year. We look forward to announcing additional clinical results this year, not only with Pexa-Vec, but also on our four other clinical-stage immunotherapeutics."

About the Pexa-Vec "neo-adjuvant" trial:
This clinical study is aimed at evaluating the biological effects of pre-operative intravenous administration of Pexa-Vec prior to planned surgical resection of locally advanced/poor prognosis or metastatic cancers. This single center, open label, non-randomized trial recruited 9 patients including 8 evaluable patients (3 with metastatic melanoma and 5 with colorectal cancer metastases to the liver). They received a single intravenous dose of $1x10^9$ pfu of Pexa-Vec, 14 days prior to planned surgery. Up to 6 blood samples were collected pre- and post- injection for each patient. Imaging was performed prior at baseline and within 7 days prior to surgery. Tumor tissue was collected at surgery for histologic and translational assessments.
University of Leeds is the sponsor of the trial that was supported by Transgene and run through the NIHR Clinical Research Facility at St James' Hospital, Leeds.

The poster is available on Transgene's website.

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Notes to editors

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About Pexa-Vec

Pexa-Vec (JX594) is an oncolytic immunotherapeutic based on an oncolytic vaccinia virus armed with a GM-CSF gene that promotes an anti-tumor immune response. Pexa-Vec is designed to selectively target and destroy cancer cells through three different mechanisms of action: selectively destroy cancer cells through the direct lysis (breakdown) of cancer cells through viral replication, reduce the blood supply to tumors through vascular disruption, and stimulate the body's immune response against cancer cells.
Pexa-Vec is currently being evaluated in a Phase 3 trial in hepatocellular carcinoma (HCC, liver cancer) in combination with sorafenib (current standard of care). Other trials evaluating the oncolytic virus in solid tumors are underway and expected to readout in 2018, including a Phase 2 trial in combination with nivolumab (HCC).
Transgene has exclusive rights to develop and commercialize Pexa-Vec for the treatment of solid tumors in Europe. Its partner SillaJen, Inc. is focused on developing Pexa-Vec for the North American market and has also granted exclusive development and commercial rights to Pexa-Vec in Hong Kong and The People's Republic of China to Lee's Pharmaceutical.

About University of Leeds

The University of Leeds is one of the largest higher education institutions in the UK, with more than 33,000 students from more than 150 different countries, and a member of the Russell Group of research-intensive universities.

We are a top ten university for research and impact power in the UK, according to the 2014 Research Excellence Framework, and are in the top 100 for academic reputation in the QS World University Rankings 2018. Additionally, the University was awarded a Gold rating by the Government's Teaching Excellence Framework in 2017, recognising its 'consistently outstanding' teaching and learning provision. Twenty-six of our academics have been awarded National Teaching Fellowships – more than any other institution in England, Northern Ireland and Wales – reflecting the excellence of our teaching. www.leeds.ac.uk

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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).
With its proprietary Invir.IO™, Transgene builds on its expertise in viral vectors engineering to design a new generation of multifunctional oncolytic viruses.
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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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 Risques") 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.