Transgene Launches Invir.IO™, its Integrated Platform for the Next Generation of Multifunctional Oncolytic Viruses

Strasbourg (France), September 21, 2017- 5:45 pm CET - Transgene (Euronext Paris: TNG), a biotech company that designs and develops viral-based immunotherapies announces the launch of Invir.IO™, its new technology platform dedicated to the design of the next generation of oncolytic viruses. The platform is based on a proprietary technology. Invir.IO™ will allow Transgene to generate a variety of multifunctional immunotherapies aimed at modulating the tumor micro-environment.

A platform to build a portfolio of immunotherapies with complimentary modes of action

The uncontrolled proliferation of cancer cells is made possible via a number of immunosuppressive mechanisms, which allow the tumor to escape the immune system. These complex cellular and metabolic mechanisms occur in the tumor microenvironment. Transgene's oncolytic viruses are designed to directly and selectively destroy cancer cells by the intracellular replication of the virus in the cancer cell (oncolysis). Oncolysis is important as it induces an immune response against tumors (immunogenic lysis) that it is targeting. In addition, the replication of the virus allows the expression of the genes carried by the oncolytic viral genome including therapeutic "weapons" that have been specifically designed to attack the tumor.

Optimized oncolytic viruses to attack the tumor on several fronts and improve cancer treatments

Most immune effector molecules are very effective locally, but can be toxic when administered systemically. The local expression of such therapeutic payloads can significantly augment the anti-cancer effects of viral oncolysis. This is believed to be the result of them efficiently modulating the tumor micro-environment, increasing the immunocompetency of the tumor and at the same time reducing the systemic exposure to these molecules.

Transgene has already demonstrated that its oncolytic viruses derived from its new proprietary Invir.IO™ platform attack tumors on several fronts and can:

- induce an immunogenic cancer cell death[1];
- and express several "anti-cancer weapons" in the tumor, such as cytokines, chemokines, enzymes and/or monoclonal antibodies[2] or minibodies.

Transgene's unique know-how will enable the Invir.IO™ platform to design, produce and develop, in a very efficient way, multiple product candidates either alone or through partnerships.

Eric Quéméneur, PharmD, PhD, Executive VP, Chief Scientific Officer of Transgene, said: "With Invir.IO™, we are reinforcing our pioneering vision and ambition in the field of oncolytic viruses. The launch of our new generation of multifunctional immunotherapies is an important milestone for Transgene. The large therapeutic payload capacity of our viruses is a major competitive advantage for us that will allow us to design and vectorize several weapons that address different pathways in the tumor microenvironment. The product candidates that we intend to generate will combine the intrinsic merits of oncolytic viruses in terms of tumor cell lysis and immune-genesis, with the properties of the vectorized immuno-modulatory molecules. This

[1] Fend et al., *Immune checkpoint blockade, immunogenic chemotherapy or IFN-α blockade boost the local and abscopal effects of oncolytic virotherapy*, Cancer Research, 2017, 77(15); 4146–57

[2] Kleinpeter et al., *Vectorization in an oncolytic vaccinia virus of an antibody, a Fab and a scFv against programmed cell death -1 (PD-1) allows their intratumoral delivery and an improved tumor-growth inhibition*, OncoImmunology, 2016, 5(10)

approach is highly customizable, and we look forward to generating the new generation of oncolytic viruses that we believe will significantly improve the treatment of multiple aggressive cancers."

Transgene's Invir.IO™ platform is based the Company's years of world-leading expertise in molecular virology. Its most advanced research candidates are based on the Company's proprietary, *Vaccinia* virus strain (VV^{COP} TK-RR-) which displays the ideal features of an oncolytic virus such as better tumor selectivity, a strong ability to induce immunogenic tumor cell death and to trigger a specific immune response. In addition, its high genome capacity makes Invir.IO™ the ideal platform for the development of a pipeline of multifunctional oncolytics.

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Notes to editors

About Invir.IO™

Transgene's proprietary oncolytic virus (OV) platform Invir.IO™ allows it to design innovative multifunctional oncolytic viruses. The platform is among others based on the Company's engineered *Vaccinia* virus strain (VV^{COP} TK-RR-) which can integrate a variety of functional transgenes. The Invir.IO™ platform has already shown that it can generate products that benefit from multifunctional arming (enzyme, antibody, cytokine, etc.), that are currently being evaluated in preclinical.

About Transgene

Transgene S.A. (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.

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