

Transgene presents data on improved cytotoxic activity of oncolytic viruses expressing intrabodies in resistant tumor cell lines

Presented at 10th International Meeting on Replicating Oncolytic Virus Therapeutics
(Vancouver, Canada)

Strasbourg, France, October 5, 2016, 6:00 p.m. CET—Transgene (Euronext Paris: TNG), a company focused on designing and developing viral vector-based immunotherapies for cancer and infectious diseases, presented an original approach to improve the cytotoxic activity of oncolytic viruses at the 10th International Meeting on Replicating Oncolytic Virus Therapeutics, Vancouver, Canada October 1–4, 2016. This approach is based on the use of intrabodies, fragments of recombinant monoclonal antibodies designed to act intracellularly and to bypass a mechanism which prevents viral-induced cytolysis that is seen in some resistant tumor cell lines. These results open new possibilities for engineering the next generation of oncolytic viruses. The poster is available on www.transgene.fr or by clicking on this [link](#).

Dr. Johann Foloppe, Senior Scientist, Oncolytic Virus Research, Transgene, said: *“Despite recent progress in the field of oncolytic virotherapy, there is still a need to design products that could also work in cancer cells resistant to cytolysis. We identified important targets that control cytolytic activity, and have developed an original approach to block these intracellular targets. We believe this approach will allow us to generate the next generation of viral vectors with the ability to lyse cancer cells more effectively and more selectively.”*

The research was conducted with an oncolytic virus candidate, based on the Copenhagen strain of the *vaccinia virus* (VACV), displaying two key mutations that confer tumor selectivity (TK- and RR-).

In the poster, scientists from Transgene and collaborating academic institutions describe the potential of a new approach in designing an oncolytic virus. The research identifies 16 key tumor cell components produced in response to VACV infection, which are implicated in resistance. It also outlines the ability of the construct to express a monoclonal antibody called an “intrabody” in tumor cells, that is able to selectively neutralize one of these tumor cell components by binding to it and re-localizing it into the cell nucleus where it cannot be activated. This relocalizing aims to achieve the same effect as siRNA knockdowns. The research was undertaken in several tumor cell lines that have low susceptibility to VACV-induced cytolysis. These promising results broaden the scope of possible cancer indications that can be targeted using oncolytic viruses.

Transgene intends to create a new generation of improved oncolytic virus based therapeutics VACVs capable of intrabody-mediated relocalizing of tumor cell proteins and as a result to enhance cancer killing.

Eric Quéméneur, Chief Scientific Officer of Transgene, said: *“These original findings that we have presented at this international meeting demonstrate the potency of the vaccinia platform for expressing intracellular antibodies. With this innovative approach, we open new vistas in the field of armed oncolytic viruses. I am confident that the ongoing research effort at Transgene will contribute positioning us as one of the global leaders in the development of new oncolytic virus therapeutics.”*

Transgene's lead oncolytic viral therapeutic Pexa-Vec is in a Phase 3 trial evaluating its potential as a novel treatment for patients with hepatic cell carcinoma. The Phase 3 trial is being conducted by Transgene's partner SillaJen, Inc. Transgene is planning to conduct further trials with Pexa-Vec in combination with immune checkpoint inhibitors in patients with solid tumors.

The second advanced product is TG6002, a second generation of oncolytic virus, is expected to enter Phase 1 trial in H1 2017 in patients with glioblastoma. This study will be conducted at AP-HP with Pr. Delattre as principal investigator, with the support of InCa (French National Cancer Institute). TG6002 is based on the Copenhagen strain of the vaccinia virus (VACV), which has had the TK and RR genes deleted to prevent it from replicating in normal cells. It has also been designed to express the FCU1 gene allowing it to be used in combination with 5FC to locally produce 5 FU, a commonly used chemotherapeutic agent.

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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 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.

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