Transgene - Positive Results from Phase 1 Clinical Trial of TG1050 in Chronic Hepatitis B Presented at the AASLD Liver Meeting 2018

- ***Primary end-point reached:*** *safety established following single dose and multiple doses administration of TG1050 in chronic hepatitis B patients under antiviral (NUC) therapy*
- ***TG1050 triggers T cell-based immune responses****, specific of all 3 encoded HBV antigens, confirming the mechanism of action of the product*
- *New preclinical data clearly support further investigation of* ***TG1050 in combination with antivirals or immunomodulators***

Strasbourg, France, November 12, 2018, 7:30 a.m. CET - Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies, announced the complete data from the Phase 1 trial evaluating the safety and immunogenicity of TG1050 in patients with chronic hepatitis B. The data have been presented at the American Association for the Study of Liver Diseases (AASLD) by Prof. Fabien Zoulim head of the Hepatology and Gastroenterology service of the Croix-Rousse Hospital (Lyon, France). TG1050 is a virus-based therapeutic vaccine encoding for 3 HBV antigens.

Safety and Immunogenicity of Single and Multiple Injections of the Therapeutic Vaccine TG1050 in NUC-Suppressed Chronic Hepatitis B (CHB) Patients: Unblinded Analysis of a Double-Blind, Placebo-Controlled Phase 1b Study - Abstract number: 426

- **Primary end-point reached**: safety established following single dose (SD) and multiple doses (MD) administration of TG1050 in chronic hepatitis B patients under NUC therapy.
- **TG1050 induced cell-mediated immune responses** in both SD and MD cohorts; they are specifically directed **against the HBV antigens that are vectorized in the vaccine** (Core, Polymerase and Env proteins). These responses were mostly seen at the two highest doses (10^{10} and 10^{11} vp) and in patients with no or lower levels of anti-Adeno 5 pre-immunity. **The intermediate dose (10^{10} vp) is consistently immunogenic (~70% of patients)**.

Transgene also presented new and encouraging preclinical data that show an improved antiviral activity of TG1050 when administered in combination with either antivirals or immunomodulators in HBV-persistent mice.

Investigational treatment combining TG1050, an HBV-specific immunotherapeutic, with direct acting antivirals or immunomodulators, improves sustained antiviral effects and immune responses in HBV-persistent mice - Abstract number: 438

- Combination-based therapeutic regimens involving TG1050 and direct antiviral molecules or immunomodulators result in **durable antiviral effects**.
- In a well-established HBV persistent model, three classes of molecules (ie. siRNA, TLR9 agonist and inhibitor of myeloid dendritic suppressive cells (MDSC)) led to an improvement of the antiviral effects of TG1050, and, in some cases **reached undetectability of circulating HBsAg**.
- These results are in line with the current consensus in the field, which is that a combination of therapies is needed to reach functional cure of chronically infected patients.
- **These data support the rationale for clinical trials assessing TG1050 in combination with other HBV-specific or non-HBV specific molecules**.

"These results confirm the robust safety profile of TG1050," commented **Prof. Fabien Zoulim, MD, PhD, principal investigator of the trial**. *"More importantly, TG1050 also induced HBV-specific cellular immunity in virally-suppressed patients, including a sub-group of patients displaying anti-vector pre-immunity. The detection of Env-specific responses is particularly encouraging in a highly tolerogenic context for this antigen. Chronic hepatitis B remains a significant unmet medical need. The robust preclinical package confirms that TG1050 is an interesting option that deserves further clinical exploration, in particular in novel combination regimens."*

Both abstracts published in *Hepatology* can be downloaded from the AASLD website. The posters are accessible from Transgene's website: www.transgene.fr.

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Notes to editors

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About TG1050

TG1050 is a targeted immunotherapy candidate for the treatment of chronic hepatitis B, based on a viral vector expressing three HBV antigens (POL, CORE, ENV). The first-in-man Phase 1/1b trial met its primary safety endpoint and also showed that TG1050 is able to break immune tolerance in patients chronically infected with HBV.
Preclinical results have demonstrated TG1050's capacity to induce robust, broad, and long-lasting HBV-specific T cells with characteristics similar to those found in patients whose infection has been resolved. Antiviral effects of TG1050 have also been shown[1] [2].
The technology of TG1050 is also being developed in Greater China by Tasly Biopharmaceuticals Co., Ltd.

About the Phase 1b trial evaluating TG1050

This international first-in-man Phase 1/1b trial of TG1050 has recruited patients who were being treated for chronic HBV infection with standard-of-care antiviral therapies. This trial was randomized, multi-center, double-blind, and placebo-controlled. The primary objectives of the Phase 1/1b study were safety and tolerability of TG1050 administered in single and multiple doses and to determine the dose and schedule of TG1050 administration for further development. Secondary objectives corresponded to the exploration of antiviral activity and immune responses to TG1050.
48 patients were enrolled (Europe and North America), randomized 1:1:1 across 3 dose levels of 10^9, 10^{10}, 10^{11} viral particles (vp) and then 3:1 within each dose level to placebo. 12 patients were enrolled in the single dose cohort and received a single subcutaneous (sc) injection while 36 patients enrolled in the multiple dose cohort received 3 weekly sc injections. At inclusion, patients had to be HBV DNA negative after at least 2 years of NUC therapy.

About Chronic Hepatitis B

Hepatitis B is a potentially life-threatening liver disease caused by HBV infection. It puts patients at high risk of death from cirrhosis and liver cancer. Recent figures indicate the number of patients being treated for chronic hepatitis B is 200,000 in total in the United States, Germany, France, Italy, Spain and the United Kingdom and 100,000 patients in Japan. The eligible Chinese market represents 500,000 patients. Those numbers are expected to increase (Sources: ECDC- Incidence of Hepatitis B, Decision Resources: expert opinions). Currently available antiviral treatments can control the disease but not cure it. Patients in the developed world must take these treatments for an average of 15 years and often throughout their lifetime. Therefore, there is an urgent need to develop new therapeutic approaches to improve the cure rate.
The latest publications on TG1050 are available on: www.transgene.fr.

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[1] *Gut. 2015; TG1050, an immunotherapeutic to treat chronic hepatitis B, induces robust T cells and exerts an antiviral effect in HBV-persistent mice. Martin P et al., 2015 Dec, 64(12):1961-71. doi: 10.1136/gutjnl-2014-308041*

[2] *Hum Vaccin Immunother. 2018;* A meta-analysis of the antiviral activity of the HBV-specific immunotherapeutic TG1050 confirms its value over a wide range of HBsAg levels in a persistent HBV pre-clinical model, Kratzer R. et al., 2018 Jun 3;14(6):1417-1422.

About Transgene

Transgene (Euronext: TNG) 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 (a therapeutic vaccine for the treatment of chronic hepatitis B) and TG6002 (an oncolytic virus for the treatment of 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.

myvac™, an individualized MVA-based immunotherapy platform designed to integrate neoantigens, completes this innovative research portfolio.

Additional information about Transgene is available at www.transgene.fr.

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