

## **Transgene Announces Important Update on its HCVac Study with its Therapeutic Vaccine TG4040 in Chronic Hepatitis C**

- **Clinical proof of concept obtained**
- **Adverse events reported led to study design amendment**
- **Findings already warrant further clinical development of TG4040**

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**Parc d'Innovation, Illkirch, France, October 11, 2011** – Transgene S.A. (Euronext Paris: FR0005175080) reports today about the Phase II study HCVac testing the therapeutic vaccine TG4040 in chronic viral hepatitis C in combination with standard of care (“SOC”). The HCVac study has enrolled 154 patients (completion of recruitment in March 2011), and is exploring the combination of TG4040 with SOC (combination of Pegylated-Interferon  $\alpha$ 2a and Ribavarin) in treatment-naïve patients with chronic genotype 1 hepatitis C. Patients were randomly distributed in three arms: one control arm with SOC alone and two experimental arms testing two different combinations of TG4040 with SOC.

The HCVac study has met its primary efficacy endpoint based on improvement of complete early viral response (“cEVR”) rate with the combination of TG4040 and SOC. cEVR is defined as the disappearance of HCV’s viral genome in the blood 12 weeks after the start of the treatment.

Three cases of severe hematological adverse events were recently reported in the experimental arms of the study and are under investigation. Although the safety profile of TG4040 was otherwise good as expected from Phase I findings, the Company has decided to submit an amendment to the study design so as to avoid further exposing patients to possible similar adverse events.

The proposed amendment will enable the patients in the experimental arms to continue to receive the SOC as planned but without TG4040 (all patients treated in the experimental arms have received the majority of doses of TG4040 they were expected to receive under the protocol). It will have no impact on protocol observation of other endpoints, including long term efficacy and tolerance. Notably, long term efficacy, defined by Sustained Viral Response (“SVR”) rate, will be measured. It has been demonstrated that patients who achieve cEVR also achieve a high SVR rate. SVR, measured six months after completion of a treatment, is the reference clinical efficacy endpoint for HCV treatments. The HCVac study will also measure TG4040’s ability to elicit an immune response. An additional expected outcome of the study is to identify molecular biomarkers related to TG4040 efficacy in combination with the standard of care. Final data are expected in the fourth quarter of 2012.

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Detailed primary observations, including rate of cEVR in each arm, will be reported during the upcoming AASLD congress (*American Association for the Study of Liver Diseases*) in San Francisco on November 7, 2011.

*“We are extremely pleased with the first efficacy data observed in the trial, full details of which will be given during the upcoming AASLD. These data definitely warrant further clinical development of TG4040 in HCV and are a first in the field of immunotherapy applied to HCV treatment,”* stated Philippe Archinard, Chairman and CEO of Transgene. He added: *“However, patients’ safety is our first priority and we have decided to modify the treatment regimen in the experimental arms to only maintain the standard of care. Long term efficacy and safety will of course continue to be monitored as planned”.*

*“The proof of efficacy of this therapeutic vaccine in a well-designed trial represents an important step for the field. The findings provide a rationale for future studies combining direct acting antivirals with TG4040 and thus enabling potentially interferon-free treatment regimens”* said Pr. Heiner Wedemeyer, MD, of the Department of Gastroenterology, Hepatology and Endocrinology at Hannover Medical School (Germany) and principal investigator of the HCVac study. He added: *“It will now be important to investigate immunogenicity data and to understand if the combination of the therapeutic vaccine may have altered the risk for haematological side effects of PEG-IFNa and ribavirin therapy”.*

#### **About TG4040:**

Transgene’s TG4040 vaccine candidate is a recombinant vector based on the MVA virus carrying and expressing three of the major non-structural proteins (NS3, NS4 and NS5B) of the hepatitis C virus (“HCV”). The MVA vector is a highly attenuated strain of vaccinia virus, which has been tested extensively in humans as a vaccine against smallpox and is known to strongly stimulate innate and adaptive immune responses to antigens.

#### **About TG4040 clinical development program:**

##### **Phase I**

Phase I clinical results in 39 treatment naïve genotype 1 HCV patients showed that the product is safe and well tolerated at all dose levels tested. Immunological analyses on 15 treatment naïve patients were encouraging and supported the expected mechanism of action of TG4040 which aims at inducing an effective HCV-specific T cell based immune response, able to control viral replication. Phase I data were published in the journal *Gastroenterology* and reported in *Nature Reviews* in 2011.

##### **Phase II**

The 154 patients in the HCVac study were recruited in five countries in Europe, in the United States and in Israel, and were randomized in the three arms of the study (one control arm without TG4040 and two experimental arms). HCVac investigated the efficacy and safety of

two different schedules of administration of TG4040 in subcutaneous injections at the dose of  $10^7$  pfu in combination with the standard of care.

#### **About severe adverse events reported in the HCVac study:**

The severe adverse events reported in the HCVac study were hematological disorders: two cases of thrombocytopenia, one with neutropenia, and one case of aplastic anemia. These severe AEs are possible but rare with SOC alone. In the HCVac study these adverse events occurred only after prolonged IFN treatment, but not during the TG4040 monotherapy treatment phase and no such events were observed in Phase I in with TG4040. A possible relationship with TG4040 cannot be today formally ruled out and is under active investigation.

#### **About chronic hepatitis C:**

Hepatitis C currently represents a major public health concern. The population chronically infected with HCV in the world is estimated at 170 to 200 million and hepatitis-C-related deaths at approximately 470,000 annually. Peak of prevalence of HCV-related diseases is expected to occur in 2025-2030 in developed countries.

HCV infection leads to liver diseases such as fibrosis, cirrhosis and liver carcinoma, which are the prime indications for liver transplants. The current standard of care for patients infected with the HCV genotype 1 (a combination of Pegylated Interferon  $\alpha$  and Ribavirin) is lengthy, often poorly tolerated and effective in only approximately 50% of patients completing therapy. In addition, a substantial number of patients never receive therapy. Therefore, there is a strong medical need for new alternative approaches, including combination therapies. A new class of anti-viral agents, protease inhibitors, have reached the market recently and have shown their ability to increase the efficacy of SOC.

#### **About Transgene:**

Transgene is a biopharmaceutical company focused on the development of therapeutic vaccines and immunotherapeutic products in oncology and infectious diseases. The Company has four compounds in Phase II clinical trials: TG4010 (lung cancer), JX594/TG6006 (liver cancer), TG4001 (pre-cancerous lesions of the cervix) and TG4040 (HCV). Transgene has entered into strategic collaborative agreements for the development of two of its immunotherapy products: (i) an option agreement with Novartis for an exclusive license to develop TG4010 and (ii) an in-licensing agreement with US-based Jennerex Biotherapeutics, Inc., to develop and market JX594/TG6006, an oncolytic virus. Transgene has bio-manufacturing capacities for viral-based vectors. Additional information about Transgene can be found at [www.transgene.fr](http://www.transgene.fr).

**Disclaimer:**

*This press release contains forward-looking statements referring to the clinical testing and development of Transgene's product candidates. Clinical testing and successful product development depend on a variety of factors, including the timing and success of future patient enrolment and the risk of unanticipated adverse patient reactions. Results from future studies with more data may show less favorable outcomes than prior studies, and there is no certainty that product candidates will ever demonstrate adequate therapeutic efficacy or achieve regulatory approval or commercial use. For further information on the risks and uncertainties involved in the testing and development of Transgene's product candidates, see Transgene's Document de Référence on file with the French Autorité des marchés financiers on its website at <http://www.amf-france.org> and Transgene's website at [www.transgene.fr](http://www.transgene.fr).*

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