Promethera Biosciences successfully enrolls twenty patients in its multicentric Phase I/II trial

Promethera Biosciences has conducted the trial in Belgium, France, United Kingdom, Italy and Israel, successfully treating twenty patients affected by very rare liver-based metabolic diseases

Mont-Saint-Guibert, Belgium, November 12, 2013 – Promethera Biosciences, a Belgian biotechnology company developing Promethera(R) HepaStem, a cell-based therapy for the treatment of liver-based metabolic diseases including Crigler-Najjar Syndrome and Urea Cycle Disorders, announces today the completion of patient enrolment for its first clinical trial.

Promethera Biosciences is conducting a first-in-man trial with HepaStem in paediatric patients suffering from orphan diseases.

This trial is a prospective, open label, multicenter Phase I/II clinical study involving Urea Cycle Disorders (UCD) and Crigler-Najjar (CN) syndrome paediatric patients. The trial is a dose escalation study designed to evaluate the safety and the preliminary efficacy of Promethera(R) HepaStem.

Most young patients affected by these very rare diseases have limited therapeutic options and may die at an early age. CN syndrome has an incidence of around one in a million births. It becomes apparent during the neonatal period by early intense jaundice due to unconjugated bilirubin. The UCD are a group of eight inborn errors of metabolism that affect the transfer of nitrogen into urea. Although each specific disorder results in the accumulation of different precursors, hyperammonemia and hyperglutaminemia are common biochemical hallmarks of these disorders. UCD are also considered as rare diseases with an incidence between 1 in 8,000 and 1 in 44,000.

Promethera(R) HepaStem is an innovative cell therapy product based on the use of allogeneic progenitor cells derived from livers obtained from adult (non-embryonic) organ donors. These cells are capable of in-vitro expansion and in-vivo differentiation into hepatocyte-like cells. The cells can be used to treat a wide variety of liver diseases from rare inborn metabolic diseases such as UCD and CN (classified as 'orphan diseases' and mainly affecting children), to acquired deficiencies affecting adults such as fulminant hepatitis or liver fibrosis.

Promethera Biosciences has successfully treated 20 patients with HepaStem in collaboration with 11 clinical centers.

Given the scarcity of patients, Promethera Biosciences has conducted the trial in five countries: Belgium, France, United Kingdom, Italy and Israel. In total, 11 clinical centers actively participate in the study: Cliniques Universitaires Saint-Luc, Belgium, Universitair Ziekenhuis Antwerp, Belgium, Hopital Jeanne de Flandre in Lille, France, Centre Hospitalier Universitaire Bicetre in Paris, France, Centre Hospitalier Universitaire de Toulouse, France, Birmingham Children’s Hospital, UK, Great Ormond Street Hospital, UK, IRCCS Ospedale Pediatrico del Bambino Gesu, Italy, Meyer Children’s Hospital at Rambam Health Care Campus, Israel, Hadassah Ein-Kerem Medical Center, Israel, Schneider Children’s Medical Center of Israel. The study started in March 2012 with the first patient treated in Belgium. As of today, 20 patients aged from six weeks to 16 years have been treated with Promethera(R) HepaStem.
Dr. Beatrice De Vos, chief medical officer of Promethera Biosciences said: "The successful recruitment of 20 patients suffering from very rare diseases in only 18 months was achieved thanks to three important factors: an extensive network of collaborating centers of the founder hospital, strong communication with the treating physicians of the patients and dedicated teams at Promethera Biosciences. Each new country and each new clinical center brought new challenges that our teams have addressed inventively and professionally."

Professor Etienne Sokal, chief scientific officer of Promethera Biosciences, paediatric hepatologist at Cliniques Universitaires Saint Luc, Belgium and director of UCL’s Liver Cell Therapy Program, Belgium, said: "With patients treated at their own center separate from Promethera, we have demonstrated the feasibility of proposing HepaStem treatment to any patient around the world, giving them the opportunity to receive innovative treatment locally."

Eric Halioua, chief executive officer of Promethera Biosciences said: "We are very pleased to have achieved this new milestone in the development of our main product HepaStem. During the trial another innovation took place with the use of a mobile formulation unit operating near the medical site. This mobile production unit was used to both carry the material and to formulate the product. The GMP approval process by the Belgian authorities considered the mobile unit as an extension of the Promethera Biosciences GMP certified manufacturing unit. A sterile and closed formulation system for preparing the final product was installed in this unit, operating so that the cells could be delivered in real time at the bedside of the patient. A patent for the mobile unit has been filed and is being examined before issuance."

The end of the trial is scheduled for October 2014 after a patient follow-up period of 12 months.

About the phase I/II clinical trial
Promethera Biosciences has made considerable scientific advances since the discovery in 2005 by Professor Etienne Sokal and Dr Najimi at the Université Catholique de Louvain laboratories, Brussels, of HHALPC (Heterologous Human Adult Liver Progenitor Cells, forming the basis for Promethera® HepaStem product).

The proof of concept for the therapeutic use of the cells has been demonstrated in different animal models. Between 2009 and 2011, the newly discovered cells have been studied in man by treating three patients suffering respectively from Ornithine Transcarbamylase deficiency (a form of Urea Cycle Disorders), Crigler Najjar syndrome, and type I glycogenosis with HHALPC. This was carried out by Professor Etienne Sokal at Cliniques Universitaires Saint-Luc, Brussels, Belgium, within the framework of the hospital exemption rules and with the approval of the Ethics Committee.

These achievements have enabled Promethera Biosciences to obtain authorizations from the British, Belgian, French, Italian and Israeli regulatory authorities to initiate the phase I/II clinical study with Promethera® HepaStem. In the clinical study, the product is assessed in a paediatric setting involving children suffering from Crigler-Najjar syndrome or urea cycle disorders.

Promethera Biosciences has received funding from the Walloon region by means of conditional loans to perform the phase I/II clinical study with Promethera® HepaStem.

About Promethera Biosciences:
Promethera Biosciences is a pharmaceutical company that develops innovative therapies for the treatment of liver disease. It is currently developing two products based on a recently discovered and patented cell, the Heterologous Human Adult Liver Progenitor Cells (HHALPC):

- **Promethera(R) HepaStem** is a cell therapy product based on the use of allogeneic stem cells isolated from healthy adult human livers (Heterologous Human Adult Liver Progenitor Cells, HHALPC). These cells can be used to treat a wide variety of liver diseases, from rare inborn
metabolic diseases, (which can be classified as ‘orphan diseases’ and mainly affecting children), to acquired deficiencies affecting adults, such as fulminant hepatitis or liver fibrosis. Promethera(R) HepaStem has received orphan drug designations for the treatment of Crigler-Najjar syndrome and the treatment of all deficiencies of the urea cycle from the European Medicines Agency (EMA) and FDA.

- Promethera(R) HepaScreen is a different, non-therapeutic product that uses the same adult human liver-derived stem cells as a biotechnology tool designed for evaluation of new chemical entities. This product meets a real need in the market, which currently lacks sufficiently predictive models to assess the hepatic metabolism of chemical compounds in the body. This unique cell model will be made available to the pharmaceutical industry to evaluate the metabolism and toxicity of new drugs in humans in a more reliable way than animal experimentation, thereby reducing the need and number of animals for such experiments.

Promethera Biosciences is a spin-off of the Universite Catholique de Louvain (UCL) located in Mont-Saint-Guibert (Belgium). Since its creation in 2009, Promethera Biosciences has raised EUR 34 million in two financial rounds, in capital, grants and loans from the Walloon region. The main investors are Vesalius Biocapital, Mitsui Global Investment, BI Venture Fund, Shire and SRIW. Promethera Biosciences has 44 employees led by an experienced management team.

For more information, please visit www.promethera.com
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