

Press release

Paris | November 28, 2013

Clinical trial launched to treat Sanfilippo B syndrome using gene therapy

A phase I/II gene therapy clinical trial for children suffering from Sanfilippo B syndrome, a rare genetic disease, enrolled a first patient in October of this year. The trial is being carried out and coordinated by the Institut Pasteur (the trial's sponsor), Inserm, AFM-Téléthon and Vaincre les Maladies Lysosomales (VML). It is being conducted at Bicêtre Hospital (AP-HP) in Paris. If the treatment is successful it will pave the way towards the development of other gene therapy treatments using the same process.

Sanfilippo syndrome is a rare genetic disease (also referred to as an orphan disease) that affects approximately 1 in 100,000 children. It is caused by a gene mutation that affects lysosomes – organelles that play essential roles in cell functions – including digestion and protein recycling mechanisms. The first symptoms of the disease – hyperactivity, speech disorders - arise at roughly 2 years of age and lead to neurodegeneration, progressive hearing loss, gradual loss of autonomy and premature death, in most cases before the age of 20. There is currently no cure or treatments available to address either the symptoms or the progression of the disease.

This clinical trial is the result of 10 years of collaborative research* carried out by Professor Jean-Michel Heard and his team at the Institut Pasteur (Biotherapies for Neurodegenerative Diseases Unit, Institut Pasteur/Inserm U1115) in partnership with AFM-Téléthon and Vaincre les Maladies Lysosomales (VML). It is based on the development of a viral vector capable of delivering one of the four potentially mutated genes in Sanfilippo patients (corresponding to four essential lysosomal enzymes) to the patient's brain cells. This trial focuses on the B form of the disease. Cells incorporate the missing gene, provided by the viral vector, into their DNA thus enabling them to produce the missing enzyme.

The treatment consists of several intracerebral vector deposits in several areas of the brain. It was administered to the first patient in October 2013 by Professors Marc Tardieu, from the pediatric neurology department at Bicêtre Hospital (AP-HP), and Michel Zerah, from the pediatric neurosurgery center at Necker Hospital (AP-HP). Scientists and medical professionals consider that the patient's very young age – two and a half years old –increases the chances of the therapy's success. Three other children will be enrolled into the trial over the coming months thanks to the cooperation and support of Vaincre les Maladies Lysosomales (VML).

The original construction of the viral vector, produced by the company uniQure, uses innovative technology which enables batches to be manufactured with a high level of purity. Because of this, the process is already compatible for large-scale use. uniQure was chosen as a partner because it is the first company to receive market approval in Europe for a gene therapy treatment, Glybera®.

Due to the slow progression of Sanfilippo syndrome, benefits of the treatment on the natural progression of the disease will not be appreciated before several years. This trial, if successful, could also open the door to future applications of the viral vector in gene therapy treatments, particularly in the treatment of neurodegenerative diseases.

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Institut Pasteur, sponsor

Louis Pasteur created the Institut Pasteur in 1887 as a private non-profit foundation that rapidly became world-renowned for its biomedical research. The main aim of the Institut Pasteur is understanding and preventing diseases throughout the world through excellent scientific and public health research, teaching and other activities. Together with its major contribution to a deeper understanding of fundamental aspects of life, the Institut Pasteur continues to devote a large part of its efforts to infectious diseases, inherited disorders, neurodegenerative diseases and certain cancers. Close to 2,600 people work on its main campus in Paris, which is at the heart of an international network of 32 research institutes on 5 continents. Over the years, 10 Institut Pasteur researchers have received the Nobel Prize.

Inserm

Founded in 1964, the French National Institute of Health and Medical Research (Inserm) is a **public scientific and technological institute** which operates under the joint authority of the French Ministry of Health and French Ministry of Research. **The mission of its scientists is to study all diseases, from the most common to the most rare, through their work in biological, medical and public health research.** Inserm supports more than 300 laboratories across France. In total, the teams include nearly 13,000 researchers, engineers, technicians and administrative staff, etc. Inserm is a member of the National Alliance for Life and Health Sciences, founded in April 2009 with CNRS, Inserm, the CEA, INRA, INRIA, the IRD, the Pasteur Institute, the Conference of University Presidents (CPU) and the Conference of Chairmen of The Regional and University Hospital Centres.

AFM-Téléthon is an association for patients and parents of patients committed to fighting disease. Funds raised during the Telethon (€88.1 million in 2012) have enabled the association to become a major player in biomedical research on rare diseases in France and around the world. It currently supports clinical trials focusing on genetic disorders affecting the eyes, the blood, the brain, the immune system, the muscular system, etc. In addition, this association has the unique advantage of being able to develop, produce and test innovative therapeutic medicines via its laboratory, Généthron. Thanks to telethon donations, AFM-Téléthon has pledged nearly €7 million to clinical and pre-clinical work for this trial since 2003.

Vaincre les Maladies Lysosomales (VML) is a state-approved charitable organization created by parents of sick children in 1990. It aims to find cures for patients suffering from lysosomal diseases. The organization has three main focus areas: supporting patients and their families, encouraging scientific and medical research and raising public awareness on the subject of rare diseases. Since 1992, VML has financed the fundamental and pre-clinical research for the gene therapy trial and since 2012 has helped finance the clinical trial.

The Paris Public Hospital Network (AP-HP)

AP-HP, which serves the Greater Paris area, is the number one teaching hospital in Europe. Its 92,000-strong staff is committed to giving round-the-clock, top quality healthcare to all patients. Each year 7 million people benefit from state-of-the-art treatments available in all fields of medicine.

uniQure B.V. (Amsterdam, The Netherlands)

uniQure is delivering on the promise of gene therapy, single treatments with potentially curative results. We have developed a modular platform to rapidly bring new disease modifying therapies to patients with severe disorders. Our approach is validated by multiple partnerships and the regulatory approval of our lead product Glybera.

Iowa State University, College of Veterinary Medicine (Ames, IA, USA)

Ecole nationale vétérinaire de Nantes (Nantes veterinary school, France)

Cornell University (New York, NY, USA)

The Conny-Maeva Charitable Foundation

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Find out more

Read the *Sanfilippo Syndrome* fact sheet:

<http://www.pasteur.fr/ip/easysite/pasteur/en/press/factsheets/Sanfilippo/index>

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