Press Release For Immediate Release

Genethon Launches Pivotal Clinical Trial of Gene Therapy for Crigler-Najjar Syndrome, a Rare Liver Disease

The gene therapy would represent a first-of-its kind treatment for this life threatening genetic disease

PARIS, FRANCE (January 9, 2023) – Genethon, a unique non-profit gene therapy R&D organization founded by the French Muscular Dystrophy Association (AFM-Telethon), has launched a pivotal clinical trial in Europe for treatment of Crigler-Najjar syndrome, a life threatening liver disease. The trial of the gene therapy, GNT-003, will be conducted in France, Italy and the Netherlands and will enroll patients aged 10 years and older with the objective of confirming efficacy and safety seen in the previous clinical part..

"We are very pleased with this new step because if the results of the pivotal part confirm the efficacy of GNT-003, we will be able to move forward towards a registration application and the availability of the treatment for patients," said Frederic Revah, CEO of Genethon. "This new step demonstrates once again the excellence of the research conducted at Genethon, which is today one of the major players in gene therapy at the international level."

Crigler-Najjar syndrome is a rare genetic liver disease characterized by abnormally high levels of bilirubin in the blood (hyperbilirubinemia). The accumulation of bilirubin is caused by a deficiency of the UGT1A1 enzyme, responsible for transforming bilirubin into a substance that can be eliminated by the body.

High levels of bilirubin can result in significant neurological damage and death if not treated quickly. Symptoms of the most severe form of the disease become apparent shortly after birth. At present, patients must undergo phototherapy for up to 12 hours a day to keep their bilirubin levels below the toxicity threshold.

GNT-003 combines normal copies of the UGT1A1 gene coding for the bilirubin metabolizing enzyme with an AAV vector. The gene therapy, administered intravenously, was designed by Genethon's Immunology and Gene Therapy of Liver Diseases team, led by Dr. Giuseppe Ronzitti.

The European trial, conducted in collaboration with the European consortium CureCN, started in 2017. The initial portion of theclinical trial, which treated six adult patients, confirmed the safety of the product. After a demonstration of transient efficacy in the patients of the first cohort treated with a low dose of the gene therapy, treatment at the higher dose in patients of the second cohort established efficacy over time**.** The patients had a reduction in bilirubin levels sufficient to discontinue phototherapy for at least one year.

The pivotal portion of the clinical trial will be conducted at four sites in France (Prof. Labrune, Hôpital Béclère, Clamart); Italy (Prof. Brunetti-Peierri, Hôpital Federico II, and Prof. d'Antiga, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo); and the Netherlands (Prof. Beuers, Academic Medical Center, Amsterdam).

About Genethon

A pioneer in the discovery and development of gene therapies for rare diseases, Genethon is a unique non-profit organization created by a patient association, the AFM-Telethon. A first gene therapy drug, to which Genethon contributed, has obtained marketing for spinal muscular atrophy. With 200+ scientists and professionals, Genethon is pursuing its mission to bring life-changing therapies to patients suffering from rare genetic diseases. 13 products resulting from Genethon's research are in clinical trials for eye, liver, blood, immune system and muscle diseases. A further 6 products are in the preparation phase for clinical trials over the next five years. Find out more: genethon.com

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