Press release

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Data from GNT-018-IDES trial supports feasibility of imlifidase as pretreatment in gene therapy treatment for patients with Crigler–Najjar syndrome who are immune to AAV

Results presented today at ESGCT 2025

PARIS, France, LUND, Sweden (October 10, 2025) - Genethon, a worldwide pioneer and leader in research and development of gene therapy for rare genetic diseases, and Hansa Biopharma, a Sweden-based leader in IgG cleaving enzyme technology announced today that a patient with a rare liver disease and immunity to the AAV vector has been successfully treated with Genethon's AAV-based GNT0003 gene therapy for Crigler-Najjar syndrome, following prior administration of imlifidase, an enzyme capable of temporarily inhibiting the immune response. This encouraging result, achieved in a clinical trial, is a significant advance in the treatment of patients with immunity to AAVs who were previously ineligible for clinical trials and existing gene therapy treatments.

Gene therapy involves injecting a gene drug into an organism using a vector, a "means of transport" usually derived from viruses, such as AAVs (adeno-associated viruses), which are commonly used for gene therapy in for example neuromuscular, liver, and eye diseases. Initial contact with the natural virus can cause the body to develop immunoglobulin G (IgG) antibodies that neutralize AAVs. It is estimated that one in three people is naturally immune to AAVs, thereby excluding a large number of patients from the possibility of benefiting from gene therapy using an AAV vector. To evaluate potential options for treating patients with natural immunity to AAVs, researchers at Genethon tested imlifidase, an enzyme developed by Hansa Biopharma, as a pre-treatment. This enzyme is capable of cleaving IgG, thereby rapidly and significantly reducing the level of anti-AAV antibodies and allowing the administration of a gene therapy drug candidate**.**

Dr. Jérémy Do Cao (Béclère Hospital, AP-HP, France) presented at the 2025 congress of the *European Society of Gene & Cell Therapy (*ESGCT), the results of using imlifidase as a pre-treatment for GNT0003 gene therapy in a patient with a severe form of Crigler–Najjar syndrome who is naturally immune to the AAV8 vector, as part of the clinical trial (GNT-018-IDES) conducted by Genethon in collaboration with Hansa Biopharma.

In this first patient treated, the study demonstrated**:**

- **the feasibility and safety of this approach**: imlifidase administered prior to GNT0003 gene therapy successfully cleaved and inactivated the patient's antibodies and enabled treatment with GNT0003. No severe side effects related to GNT0003 or imlifidase were reported.

- **initial efficacy data**: GNT0003, Genethon's gene therapy drug candidate significantly lowered the patient's bilirubin levels, enabling her to stop hours of daily phototherapy, which had been essential to her survival until then. The phototherapy has been interrupted sixteen weeks after the injection, as planned in the protocol. Additional data will be needed to confirm this efficacy in the longer term.

This is the first time that gene therapy has been successfully administered to a patient with Crigler–Najjar syndrome who has antibodies against AAV8. If the results are confirmed in the next stages of the trial, this approach could become a promising option for patients with antibodies to AAVs, who are currently ineligible for clinical trials and existing gene therapy treatments.

"It's incredible to have had the chance to witness the clinical translation of this project, which I saw come to life in our laboratory," said Giuseppe Ronzitti, Head of the Immunology and Liver Disease Laboratory and Director of Scientific Forecasting at Genethon. "It's a project that involved a significant portion of Genethon working toward a common goal. The preliminary data we've obtained indicate that we still have a lot to learn about the immune response to AAV vectors, but the solution is potentially there."

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Notes to editors

About imlifidase

Imlifidase is a unique antibody-cleaving enzyme, originating from Streptococcus pyogenes, that specifically targets IgG and inhibits the IgG-mediated immune response. [6] It has a rapid onset of action, cleaving IgG antibodies and inhibiting their activity within hours of administration. Imlifidase has conditional marketing approval in EU, Norway, Iceland, Lichtenstein and the UK and is marketed under the trade name IDEFIRIX® for the desensitization treatment of highly sensitized adult kidney transplant patients with a positive crossmatch against an available deceased donor. [6] Is also approved in Switzerland and Australia.

About GNT003

The drug candidate GNT-0003, developed by Genethon to treat Crigler-Najjar syndrome, is currently being evaluated in a trial (GNT-012-CRIG) conducted in France, the Netherlands, and Italy in patients with no pre-existing immunity to AAV, with encouraging results.[5]

About Crigler-Najjar syndrome

Crigler-Najjar syndrome is a rare genetic liver disease characterized by abnormally high levels of bilirubin in the blood (hyperbilirubinemia), which leads to irreversible neurological damage manifested as muscle weakness, lethargy, deafness, mental retardation, and eye movement paralysis. This accumulation of bilirubin is caused by a deficiency of the UGT1A1enzyme, responsible for transforming bilirubin into a substance that can be eliminated by the body. It can result in significant neurological damage and death if not treated quickly. At present, patients must undergo prolonged daily phototherapy (often more than 10 hours a day, sometimes up to 15 hours a day) to keep their bilirubin levels below the toxicity threshold. Crigler-Najjar syndrome is an ultra-rare disease affecting less than one in one million people per year. Liver transplantation remains the only definitive cure to date, but is associated with significant morbidity and mortality, as well as graft shortage. [7]

About Hansa Biopharma

Hansa Biopharma AB is a pioneering commercial-stage biopharmaceutical company on a mission to develop and commercialize innovative, lifesaving and life-altering treatments for patients with rare immunological conditions. The company has a rich and expanding research and development program based on proprietary IgG-cleaving enzyme technology platform, to address serious unmet medical needs in autoimmune diseases, gene therapy and transplantation. The company's portfolio includes imlifidase, a first-in-class immunoglobulin G (IgG) antibody-cleaving enzyme therapy, which has been shown to enable kidney transplantation in highly sensitized patients and HNSA-5487, a next-generation IgG cleaving molecule with redosing potential. Hansa Biopharma is based in Lund, Sweden, and has operations in Europe and the United States. The company is listed on Nasdaq Stockholm under the ticker HNSA. Find out more at https://www.hansabiopharma.com/ and on LinkedIn.

About Genethon

A pioneer in the discovery and development of gene therapies for rare diseases, Genethon is a nonprofit laboratory created by the AFM-Telethon. A first gene therapy drug, to which Genethon contributed, has been approved for marketing for spinal muscular atrophy. With more than 240 scientists and experts, Genethon's goal is to develop innovative therapies that change the lives of patients suffering from rare genetic diseases. Thirteen gene therapy products developed by Genethon or to which Genethon has contributed are currently undergoing clinical trials for diseases of the liver, blood, immune system, muscles, and eyes. Seven other products are in preparation for clinical trials over the next five years. Find out more on visit http://www.genethon.com

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