NEWSLETTER

GENETHON
CURE THROUGH INNOVATION

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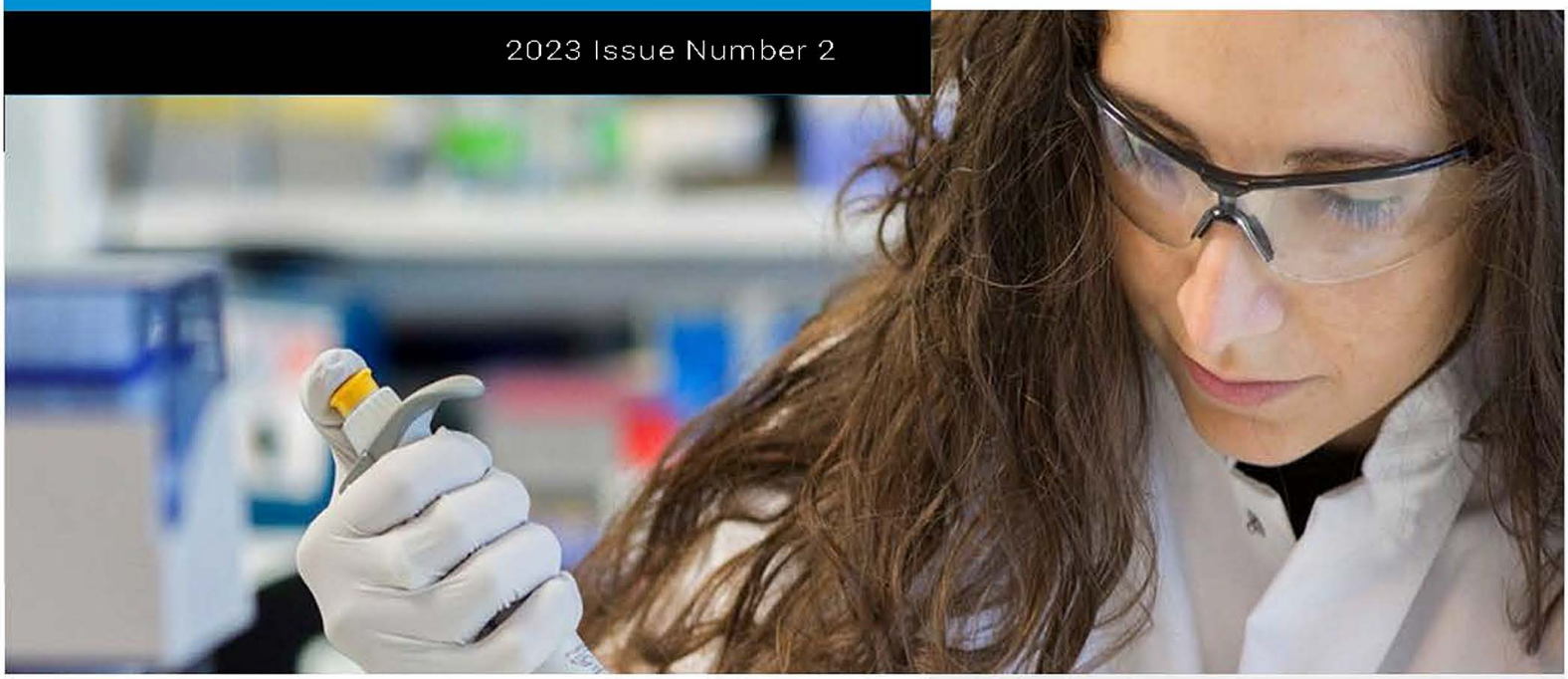

CEO COMMENTARY

A MILESTONE IN GENE THERAPY: PROOF OF LONG-TERM EFFICACY

"In each of these cases, Genethon significantly contributed to the therapeutic innovation"

Recent data presented at the Muscular Dystrophy Association Clinical and Scientific Conference, in March, have detailed long-term benefit of gene therapy in infants affected with Spinal Muscular Atrophy type 1 **(Mendell at al.; Connolly et al.)**.

Virtually all patients affected with this deadly disease die before the age of two if untreated. Strikingly, more than seven years after treatment with Zolgensma® all patients treated at therapeutic dose were alive and had maintained clinical benefits observed in initial reports.

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INSIDE

Genother Co-Founders Celebrate Biocluster Designation as a Center of Excellence in Gene Therapy

Genethon and co-founders of the Genother biomedical community celebrated the Biocluster designation in May 2023 from the French National Research Agency as a major step forward in advancing gene therapies to treat both rare and common diseases.

Genother, in Evry-Courcouronnes, is one of four new designated Bioclusters, which are part of the France 2030 health innovation plan aimed at bolstering France's competitiveness in developing innovative medicines and securing the country's healthcare independence and economic development.

The Biocluster label recognizes the efforts of Genother's founders and partners in joining together to form a center of excellence for gene therapy research and product development. In addition to Genethon, the other founders are Genopole, Assistance Public Hospital of Paris, Inserm, Université d'Évry, Université Paris-Saclay, Spark Therapeutics, and Yposkesi.

"This indicates that gene therapy is a national priority and is seen as a strategic asset for research and industrial development," said Genethon CEO Frederic Revah. "It establishes France's leadership in advancing new gene therapies as a standard of care for a broad range of diseases. This recognition also validates the signficance of the many research and development successes of Genother participants in the field of gene therapy and medical innovation. "

The Biocluster designation will enable the formation of dozens of companies, from research to industrialization, with a goal of developing 15 gene therapies for rare and frequent diseases.

Twenty-four gene therapy drugs are currently approved by health authorities worldwide, 3,000 products are under development, and by 2025, 20% of new products filed are set to be underpinned by gene therapy technologies.

Also, a study focusing on patients treated presymptomatically showed that, in that group, all patients reached and maintained 3.5 years post dosing all assessed motor milestones, including walking alone.

Long-term efficacy of gene therapy is also confirmed in other pathologies with very different pathophysiological mechanisms such as immune deficiencies.

In January 2022, the publication in Nature Medicine of the results of the Phase 1/2 clinical trial in patients with Wiskott-Aldrich syndrome, conducted by Genethon, confirmed the long-term efficacy and safety of this gene therapy approach for this rare and severe immune deficiency (Magnani et al.).

In patients followed up to nine years after dosing, treatment stably corrected the main symptoms of the disease such as recurrent severe infections, and improved or resolved bleeding and signs of autoimmunity in patients.

In each of these cases, Genethon is significantly contributed to the therapeutic innovation. The demonstration of a long-term benefit, which will have to be confirmed for other products currently in development or on the market, is an important positive signal for patients with these incurable diseases, for physicians and researchers.

VIDEO:
"The Spirit of Genethon"

Learn about the people and mission behind Genethon

PRODUCT DEVELOPMENT

Collaboration, Licensing, EMA Status Upgrade

Genethon Given PRIME Status by EMA for Gene Therapy to Treat Crigler-Najjar Syndrome

The European Medicines Agency (EMA) has granted PRIME (Priority Medicines) status to Genethon's gene therapy GNT-0003 currently in clinical trials for Crigler-Najjar syndrome, a rare liver disease.

This status, granted only to drug candidates with major therapeutic potential, follows the successful completion of the first phases of the clinical trials. . If successful, GNT-0003 would be the first gene therapy for Crigler-Najjar syndrome.

The PRIME status is similar to the U.S. FDA's fast track and breakthrough designations. The EMA's program was started in 2016 and in the first five years, only 25% of eligible drug candidates received the PRIME designation.

PRIME status was granted to GNT-0003 following promising results from early phases of the European trial currently underway in collaboration with the CureCN consortium, and sponsored by Genethon. The trial is taking place in three countries: France, Italy and the Netherlands. **Read more**

MIROCALS Signs License Agreement with ILTOO Pharma for ALS Treatment

The European MIROCALS Consortium and ILTOO Pharma SAS signed a Worldwide Exclusive License Agreement granting ILTOO Pharma use of clinical trial data from the H2020 funded MIROCALS project to develop low dose interleukin-2 (IL-2LD) as a treatment for Amyotrophic Lateral Sclerosis (ALS).

The clinical trial found that IL-2LD significantly improves survival compared to placebo over the follow-up period, with no major safety issues. The randomized, double-blind, placebo-controlled study involved 17 ALS clinical research centers across France and the UK, and enrolled 220 patients who were treated for 18 months and followed-up for 21 months.

Genethon is a member of the MIROCALS (Modifying Immune Response and Outcomes in ALS) consortium which also includes research laboratories and organizations in the UK, Italy, Sweden, and Ireland. **Read more**

Hansa Biopharma, Genethon collaborate on development of imlifidase as pre-treatment to gene therapy in Crigler-Najjar syndrome patients with anti-AAV antibodies.

Hansa Biopharma AB and Genethon are collaborating on a strategy to treat gene therapy patients with pre-existing neutralizing antibodies to AAVs. Presence of the antibodies prevents patients from benefiting from gene therapies.

In a clinical trial, Hansa and Genethon will evaluate the safety and efficacy of Hansa's antibody cleaving enzyme imlifidase as a pre-treatment to administration of Genethon's gene therapy product candidate GNT 0003 in

Crigler-Najjar syndrome in patients with pre-existing neutralizing antibodies (NAbs) to adeno-associated virus serotype 8 (AAV8).

The presence of circulating NAbs excludes patients from entering clinical studies with potentially curative gene therapy treatments and from future access to approved gene therapies.

Up to 40% of the population is naturally immune to AAVs, which are the most widely used vectors.

If the results of the Hansa-Genethon clinical trial are conclusive, the strategy could significantly broaden the impact of gene therapies for other diseases. **Read more**

SCIENTIFIC PUBLICATIONS

Muscular Dystrophy Research

Guiseppe Ronzitti

Scientific Review of Gene Therapy Techniques for Duchenne Muscular Dystrophy

Genethon's Giuseppe Ronzitti, Head of the Liver Gene Transfer and Immune Tolerance Laboratory, was a co-author of an article in Revue Neurologique, titled "Gene therapy review: Duchenne muscular dystrophy case study."

The review examined all gene therapy methods applied to DMD and discussed the advantages, limitations and risks associated with each approach.

"We discuss the mechanisms of gene transfer techniques with or without viral vectors, DNA editing with or without matrix repair and those acting at the RNA level (RNA editing, exon skipping and STOP-codon readthrough)," the authors said. "For each method, we present the results obtained in DMD with a particular focus on clinical data." **Read more**

ASGCT Presentations & Awards

Genethon's R&D Featured at the 2023 American Society of Gene & Cell Therapy Annual Meeting

Genethon scientists made four oral presentations and 10 poster presentations at the 26th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), May 16-20, 2023, at the Los Angeles Convention Center in Los Angeles, CA.

The research covers recent progress in the advancement of novel gene therapy candidates for multiple rare genetic diseases and the design of novel vectors and tools.

Ana Buj Bello

Ana Buj Bello, M.D., Ph.D., MBA, leader of the Neuromuscular Diseases and Gene Therapy Team, co-chaired the oral abstract session on AAV Vectors – Clinical/Nonhuman primate studies, and presented a poster titled, **AAV-mediated gene therapy corrects the severe phenotype of acid ceramidase deficient mice.**

Ai Vu Hong, Ph.D., a member of Genethon's Progressive Muscular Dystrophies Team, received two ASGCT awards one for Excellence in Research, which recognizes the top 10 posters submitted by students and fellows; and the other a Meritorious Abstract Travel Award given to associate members based on their high abstract scores.

Read the press release for a full list of presentations and links to the abstracts on the ASGCT website.

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visit our website - Genethon.com