Press release
Paris, May 17, 2025

Genethon Presents Two Year Consolidated Results of Its Gene Therapy Trial for Duchenne Muscular Dystrophy: Maintenance of Motor Functions and Significant, Sustained Reduction in CPK Levels in Patients Treated at the Effective Dose at ASGCT 2025

- ***GNT0004 product confirms its clinical efficacy with stabilization of motor functions in patients treated at the effective dose for up to 2 years.***
- ***Sustained significant reduction in levels of creatine phosphokinase (CPK), a biomarker of muscle damage, with an average decrease of over 75% at 18 months in the 3 patients treated at the effective dose.***
- ***Pivotal phase planned for mid-2025 in Europe and the United States.***

Paris, France (May 17, 2025) - Genethon unveiled the 2-year follow-up data from its GNT0004 gene therapy clinical trial for Duchenne Muscular Dystrophy (GNT-016-MDYF) at the annual meeting of the American Society of Gene & Cell Therapy (ASGCT) in New Orleans, May 13 – 17, 2025. Five patients, aged 6 to 10 years, were treated, 2 at the first dose level and 3 at the second dose level ($3x10^{13}$ vg/kg). The initial part of the clinical trial aimed at selecting the optimal dose (dose escalation phase), evaluating the tolerance and preliminary efficacy of the treatment and **determined the effective dose for the pivotal phase of the GNT-016-MDYF trial, which is expected to start in mid-2025 ($3x10^{13}$ vg/kg).**

Genethon CEO Frederic Revah observed, "The results of our gene therapy GNT0004 are very positive in patients treated at the dose of $3x10^{13}$ vg/kg, both in terms of microdystrophin expression and clinical efficacy criteria. Besides these results, the advantage of our product lies in the selected dose for the pivotal phase, which is lower than those used in other gene therapy trials for Duchenne Muscular Dystrophy. We are currently preparing the pivotal phase that we will conduct in Europe and the US.

Safety, efficacy, and pharmacodynamic results show good tolerance of GNT0004 associated with transient immunological prophylactic treatment, as well as efficacy

data in terms of microdystrophin expression, CPK reduction, and clinical criteria (NSAA, timed tests). Patients treated at the effective dose show prolonged improvement or stabilization of motor functions and significant persistent reduction in creatine kinase (CPK) levels, a key marker of muscle damage.

<u>One-year post-treatment</u>, the comparison of the three patients treated at the effective dose with a group of 34 untreated patients, matched by age and followed in the same centers and by the same practitioners, shows a difference of +4.7 points in the score obtained using the internationally recognized clinical evaluation scale NSAA between treated and untreated patients.

<u>At 24 months post-treatment, key observations include:</u>

- For the 2 patients who reached 2 years post-treatment out of the 3 treated at the effective dose, the trial shows **stabilization of motor functions** measured by the NSAA scale , **while untreated patients from the parallel natural history study showed a continuous and significant average decline in NSAA. For one treated patient, the observed improvement allowed reaching the maximum score of 34 at 12 months, confirmed at 24 months post-treatment.**
- **Stabilization of CPK reduction** between 50% and 87% on average: >75% at 18 months post-treatment (data from the 3 patients treated at the effective dose), and persistent (up to 24 months follow-up for the first two patients treated at this dose).
- **The reassuring safety profile** of the gene therapy drug is confirmed two years after injection, without the occurrence of serious adverse effects at the selected dose, which is notably lower than that used for other gene therapy products under development for Duchenne Muscular Dystrophy.

About GNT0004 and the trial

The GNT0004 gene therapy is composed of an AAV8 (adeno-associated virus) vector and the optimized hMD1 transgene, a shortened but functional version of the gene encoding dystrophin, the protein deficient in people with DMD. This vector is designed to be expressed in muscle tissue and also in the heart, thanks to a tissue-specific Spc5-12 promoter sequence. GNT0004 is administered by a single intravenous injection. It was developed by Genethon, in partnership with the teams of Prof. Dickson (University of London, Royal Holloway) and the Institut de Myologie (Paris). The trial, sponsored by Genethon, combines Phases 1/2/3, a dose-escalation phase followed by a pivotal phase at the dose finally chosen. The trial is being carried out in France and the UK and includes boys aged 6 to 10 with DMD who have retained their ability to walk.

About Duchenne muscular dystrophy

DMD is a rare, progressive genetic disease affecting all the body's muscles, and mainly boys (1 in 5000). It is due to abnormalities in the gene responsible for producing dystrophin, a structural protein essential for the stability of muscle fiber membranes and their metabolism. The absence

of dystrophin leads to progressive degeneration of skeletal and cardiac muscles, loss of walking and respiratory capacity, cardiomyopathy and death between the ages of 20 and 40.

About Genethon

A pioneer in the discovery and development of gene therapies for rare diseases, Genethon is a nonprofit organization created by the AFM-Téléthon. The first gene therapy to treat spinal muscular atrophy, incorporating technologies developed at Genethon, is marketed worldwide. With over 240 scientists and professionals, Genethon pursues its goal of developing innovative therapies that change the lives of patients suffering from rare genetic diseases. Thirteen products from Genethon's R&D or collaborations are in clinical trials for diseases of the liver, blood, immune system, muscles and eyes. A further seven products could enter clinical trials in the next five years. To find out more visit: http://www.genethon.com/.

Genethon made five oral presentations and seven poster presentations by 12 researchers, scientists, engineers and medical experts at ASGCT 2025. Learn more https://urlr.me/kTPBtW

Press contact:

Stephanie Bardon

communication@genethon.fr

06.45.15.95.87