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Genethon Confirms 2-year Efficacy in Duchenne Muscular Dystrophy Patients Treated with Its Low Dose Micro-Dystrophin Gene Therapy (GNT0004) at the ESGCT 32nd Annual Congress

- The Duchenne muscular dystrophy (DMD) patients experiencing long-term efficacy were treated with the therapeutic $3x10^{13}$ vg/kg dose of GNT0004 in the Phase 1/2 dose escalation portion of Genethon's all-in-one Phase 1/2/3 European trial.
- The Phase 3 trial using the $3x10^{13}$ vg/kg dose, which is lower than doses used in other DMD gene therapy clinical trials and treatments, is under way with the first patients included in France.

PARIS, France (October 9, 2025) - Genethon, a worldwide pioneer and leader in research and development in gene therapy for rare genetic diseases, released positive long-term efficacy data revealing three Duchene muscular dystrophy patients showed significant motor function gain as compared to untreated patients, and experienced significant and sustained reductions in creatine phosphokinase (CPK), a biomarker of muscle damage, two years after receiving an injection of Genethon's low dose micro-dystrophin gene therapy (GNT0004). The results were presented at the European Society of Gene and Cell Therapy (ESGCT) 32nd Annual Congress October 7 – 10, 2025, in Seville, Spain.

"These patients were treated in the dose escalation portion of our Phase 1/2/3 European trial and we are excited to present these positive long-term efficacy findings as we begin the Phase 3 pivotal trial, which is under way with the first patients included in France," said Genethon CEO Frederic Revah. "The therapeutic $3x10^{13}$ vg/kg dose administered to the three patients is lower than other DMD gene therapies and is the dose being used the Phase 3 trial, which will enroll 64 boys, ages 6 to 10, who have retained their ability to walk."

Dr. Arnaud Valent, M.D., Genethon's Head of Medical Activities and Pharmacovigilance, presented the findings at the ESGCT conference from the Phase 1/2 dose escalation trial, in which five patients were enrolled, two at the first dose and three at the second dose of $3x10^{13}$ vg/kg, which was selected as the therapeutic dose for the Phase 3 trial. The findings from the patients receiving the therapeutic dose confirm the maintenance of clinical efficacy over two years across various parameters; the persistence of pharmacodynamic effects; and the safety of the treatment in combination with transient prophylactic immunosuppression.

At the micro-dystrophin dose of $3x10^{13}$ vg/kg the following was observed two years after injection:

- **A significant gain in motor function** as measured by a 34-point clinical assessment scale (NSAA): +5.8 points at 18 months compared to a cohort of untreated patients from the natural history study conducted in parallel (matched by propensity score). A gain significantly greater than the minimum difference is considered clinically relevant (>2.5 points).
- **Clinical benefit at 18 months, maintained at 2 years,** on functional parameters via timed tests, key indicators for ambulatory patients: -6.98s to get up from the floor and walking speed over 10 meters of +0.67 m/s (comparison similar to that of the NSAA score).

- **A significant and sustained reduction in CPK levels** by an average of 75% at 18 months and 61% at 2 years (compared to the patients' baseline condition before treatment), reflecting a lasting effect on cell membrane stability.
- **A slowdown in disease progression** with a difference of more than 7% in muscle fat fraction (a marker of disease progression), observed by quantitative MRI, compared to a cohort of untreated patients from the natural history study.
- **No serious side effects,** confirming the safety of the product.

These results also were presented at the World Muscular Society's WMS2025 October 7 – 11 in Vienna, Austria.

About Duchenne muscular dystrophy
Duchenne muscular dystrophy is a rare progressive genetic disease that affects all the muscles in the body and mainly boys (1 in 5,000). It is caused by abnormalities in the gene responsible for the production of dystrophin, a structural protein essential for the stability of muscle fiber membranes and their metabolism. The absence of dystrophin leads to progressive degeneration of the skeletal and cardiac muscles, loss of walking and respiratory abilities, cardiomyopathy, and death, usually between the ages of 20 and 40.

About GNT0004 and the trial
The gene therapy product GNT0004 consists of an AAV8 (adeno-associated virus) vector and the optimized hMD1 transgene, a shortened but functional version of the gene encoding dystrophin, the protein that is deficient in people with Duchenne muscular dystrophy. This vector is designed to express itself in muscle tissue and also in the heart, thanks to a Spc5-12 promoter sequence specific to these tissues. GNT0004 is administered by a single intravenous injection. It was developed by Genethon, in partnership with Prof. Dickson's teams (University of London, Royal Holloway) and the Institut de Myologie (Paris).

About Genethon
A pioneer in the discovery and development of gene therapies for rare diseases, Genethon is a non-profit laboratory created by the AFM-Telethon. The first gene therapy drug, to which Genethon contributed, has been approved for marketing for spinal muscular atrophy. With more than 240 scientists and professionals, 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. Others are in preparation for clinical trials over the next five years. Visit **www.genethon.fr**

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