Press release

Genethon to Launch Pivotal Trial in Europe of GNT0004 a Low-Dose Microdystrophin Gene Therapy for Duchenne Muscular Dystrophy

- *Phase 3 trial clearance is based on the Phase 1/2 results demonstrating safety and efficacy of the $3x10^{13}$ vg/kg dose of microdystrophin, which is lower than doses used in other gene therapies for Duchenne muscular dystrophy (DMD).*
- *The double blind trial will initiated in the UK and France beginning in August and September, and will enroll 64 boys aged 6 to 10 with DMD who have retained their walking ability.*

PARIS, France (July 28, 2025) – Genethon, a worldwide pioneer and leader in research and development in gene therapy for rare genetic diseases, has received approvals from regulatory authorities, MHRA and EMA*, to begin pivotal Phase 3 clinical trials in France and the UK of its gene therapy, GNT0004, for Duchenne muscular dystrophy (DMD).

Genethon CEO Frederic Revah observed, "We are delighted to be able to continue these trials and are determined to bring GNT0004 to market for young patients and their families who are waiting for a therapeutic solution. This marks a decisive step forward for our gene therapy program for DMD, which began in 2021 and has demonstrated extremely promising results in the first children treated in the Phase1/2 portion of our Phase1/2/3 study."

Dr. Revah added, "In addition to the very positive results in patients treated in the early phases, one of the strengths of our product is the dose selected for the pivotal phase, which is lower than those used in other gene therapy trials for DMD. Approvals of our Phase 3 trials reflect the regulatory authorities' confidence in GNT0004 as well as the work accomplished by our teams."

The Phase 3 authorizations in Europe are based on the results of Phase 1/2 studies showing good tolerance of GNT0004 as well as efficacy in terms of microdystrophin expression, creatine phosphokinase (CPK) reduction, and motor function. Patients showed prolonged improvement or stabilization of motor functions and significant persistent reduction in CPK, a key marker of muscle damage.

The Phase 3 double blind trials will begin in August and September in the UK and France using a single intravenous injection of GNT0004, which contains an optimized hMD1 transgene, a shortened ($3x10^{13}$ vg/kg microdystrophin) but functional version of the gene encoding dystrophin in an AAV8 vector associated with transient immunological prophylactic treatment. The vector is designed to express itself in muscle tissue and the heart thanks to a Spc5-12 promoter sequence specific to these tissues. A total of 64 boys aged 6 to 10 with DMD who have retained their walking ability will be enrolled.

** French ANSM as reporting member state for the EMA*

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 capacity, progressive heart failure, 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 non-profit 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. **www.genethon.fr**

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