

First Clinical Trial Results of Gene Therapy (GNT0004) for Duchenne Muscular Dystrophy presented at International Myology 2024 Congress

Today, Professor Francesco Muntoni, principal investigator of the international multicenter gene therapy trial for Duchenne Muscular Dystrophy with GNT0004 product, sponsored by Genethon, presented the innovative trial design and its initial results at the Myology 2024 international scientific congress, currently taking place in Paris.

The trial combines phases I/II/III with a dose escalation phase, followed by a pivotal phase at the selected dose. The trial has been approved by French and UK health authorities and includes ambulant boys aged 6 to 10 suffering from Duchenne Muscular Dystrophy. It began in 2021 and resumed at the end of 2022 after resolution of a serious adverse event experienced by the first patient, similar to those observed in other trials, and discussed within a collaborative group between sponsors of different gene therapy trials for the same disease.

5 patients aged between 6 and 10 have been treated to date with GNT0004, 4 in France and 1 in the UK. 2 patients received the first dose and three received the second dose.

Safety and pharmacodynamic results presented at Myology 2024 demonstrate good tolerability of GNT0004 in combination with transient immunological prophylactic treatment, as well as efficacy data in terms of both microdystrophin expression and functional improvement. Using a dose of 3×10^{13} vg/kg (second dose level), patients showed:

- 8 weeks after injection, up to 85% of muscle fibers expressing microdystrophin (mean 54%; 15%-85%) measured by immunohistochemistry, and reconstitution of the dystrophin-associated protein complex. This expression coincides with a significant number of vector genome copies/muscle fiber nuclei, up to 2.4 (mean 1.2; 0.4-2.4).
- a decrease in CPK levels (a biomarker of muscular distress) comprised between 50% and 87% (mean: 74%) 12 weeks after treatment, and persistent (up to 18 months of follow-up for the first patient treated at this dose).

One-year efficacy results for the first patient in cohort 2 showed a positive clinical evolution, with a clear inflection of clinical score North Star Ambulatory Assessment (NSAA). Other functions assessed (10 Meter Walk Test and ability to stand up) also showed a positive trend.

Note that the dose chosen is lower than those used in other gene therapy trials for Duchenne muscular dystrophy.

Following the positive opinion of the DMC (Data Monitoring Committee), Genethon is preparing the pivotal European phase of the trial with the European Medicines Agency (EMA).

About GNT0004

The GNT0004 product is an AAV8 (adeno-associated virus) vector-based gene therapy containing a shortened, but functional version of DMD gene (hMD1) encoding dystrophin, the protein deficient in people suffering from Duchenne muscular dystrophy. The hMD1 transgene is driven by a Spc5.11 promotor, which leads to express in key tissues such as skeletal and cardiac muscle. 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 Institute of Myology (Paris).

About Duchenne muscular dystrophy

Duchenne muscular dystrophy is a rare, progressive, genetic neuromuscular disease affecting all muscles in the body, affecting 1 in 5,000 boys. It is due to abnormalities in the gene responsible for producing dystrophin, an essential protein 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

As a pioneer in the discovery and development of gene therapies for rare diseases, Genethon is a non-profit laboratory that was established by AFM-Telethon. A first gene therapy for spinal muscular atrophy to which Généthon contributed has obtained a product license. With more than 200 scientists and professional staff, Genethon is pursuing its aim to develop innovative therapies which change the lives of patients suffering from rare genetic diseases. Thirteen products stemming from by Genethon's R&D or from collaborations are in clinical trial for diseases of the liver, blood, immune system, muscles, and eyes. Seven other products could enter clinical trials over the next five years.

To know more www.genethon.com

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