Press Release
Evry, February 5, 2013

Gene Therapy

Genethon receives approval from the UK medicine regulatory agency to start a new clinical trial for an inherited immune deficiency: chronic granulomatous disease.

On January 10th, the British Medicine and Healthcare Regulatory Agency (MHRA) approved Genethon's Phase I / II gene therapy clinical trial application in X-linked chronic granulomatous disease (XCGD) to start at Great Ormond Street Hospital in London. Genethon is also seeking approval for this multicenter trial in Germany, Switzerland and France. In total the trial will include 20 patients (5 per site) to be treated and followed up for 2 years. Genethon also obtained Orphan Drug designation for this treatment from the European Medicines Agency (EMA).

XCGD, a rare genetic disease that selectively affects males, is characterized by an inability of cells of the immune system to produce oxidants necessary for the destruction of micro-organisms entering the body. This deficiency is caused by a defect in the gene coding for an enzyme, NADPH-oxidase, which is normally present in white blood cells such as neutrophils, and which is essential for antimicrobial defenses.

Because of this deficiency XCGD patients are prone to infections caused by fungi and bacteria. XCGD affected children suffer repeated infections, internal abscesses, pneumonia and chronic inflammation. The disease is severe and debilitating, requiring constant treatment to limit infections with sometimes long term hospitalizations. Life expectancy without treatment is 30 to 40 years. Treatment by bone marrow transplantation has made progress, but this approach is not possible for all patients. Gene therapy, which has already been used successfully in other immune deficiencies, represents a hope of cure for patients not eligible for bone marrow transplantation.

The gene therapy approach consists in restoring the activity of NAPDH oxidase which is deficient in phagocytic cells of XCGD patients (neutrophils, monocytes / macrophages) by gene transfer using a lentiviral vector. The lentiviral vector was developed at Genethon by Dr. Anne Galy (Inserm/UMR951/Genethon, UEVE, EPHE), in collaboration with Dr Adrian Thrasher (Great Ormond Hospital, London) and Professor Manuel Grez (Georg Speyer Haus, Frankfurt). Clinical vector batches that will be used to treat patients are produced under GMP (Good Manufacturing Practices) conditions at Genethon.

This clinical study is sponsored by Genethon and will be conducted in parallel in England by Professor Adrian Thrasher and Bobby Gaspar at Great Ormond Street Hospital in London, in Germany by Professor Hubert Serve at the University Hospital in Frankfurt, in Switzerland by Professors Reinhard Seger and Janine Reichenbach at

Children's Hospital of Zurich and in France by Professors Alain Fischer, Marina Cavazzana-Calvo, Stéphane Blanche and Salima Hacein-Bey-Abina at the Necker Hospital for Sick Children in Paris. This multicenter international effort, called Net4CGD, is supported by the European Commission through funding from the FP7 **HEALTH-2012-INNOVATION-1.** for which Genethon is the coordinator.

"This new approval confirms the excellence of our laboratory Genethon thanks to the support of the donors of Telethon. Innovative therapies are not only a real hope of cure for patients with genetic immunodeficiencies but, more broadly, a therapeutic strategy capable of revolutionizing medicine for rare diseases and also for more prevalent disorders " asserts Laurence Tiennot-Herment, President AFM-Telethon.

For Fulvio Mavilio, Scientific Director of Genethon: *"This new gene therapy trial for a rare and severe immune system disorder led by Genethon, in collaboration with the best European clinical experts in the field, once again demonstrates the unique ability of our laboratory to develop therapeutic projects, from proof of concept to clinical trials including the manufacturing of the drug. "*

Genethon, which was created and funded by the AFM Telethon, is the promoter of two international gene therapy trials in immunodeficiencies (Wiskott Aldrich syndrome, XCGD) and has several projects at the preclinical stage for neuromuscular diseases, certain genetic forms of blindness, as well as for nervous system and liver disorders.

About the AFM-Telethon
The French Muscular Dystrophy Association (AFM) federates patients with neuromuscular diseases (genetic diseases that causing progressive irreversible muscle atrophy lead to death) and their parents. Thanks in great part to donations from France's annual Telethon (€94.1 million in 2011), the AFM-Telethon has become a major player in biomedical research for rare diseases in France and worldwide. It currently funds 36 clinical trials for about 30 different genetic diseases affecting the eye, the blood, the brain, the immune system, and muscles... Thanks to its Genethon research lab, the AFM-Telethon stands out through its unique ability to produce and test its own gene-based medicines.
More information can be found at www.afm-telethon.fr

About Genethon
Created by the French Muscular Dystrophy Association (AFM), Genethon is funded almost exclusively by donations from France's annual Telethon. Its goal is to deliver innovative gene therapies to patients affected with orphan genetic disorders. After having played a pioneering role in deciphering the human genome, with over 220 scientists, physicians, engineers and regulatory affairs specialists, Genethon now is one of the world's leading centers for preclinical and clinical research and development in the field of gene therapy for rare diseases. Genethon received the 2012 Prix Galien France for its Innovative Treatments in Gene Therapy. Genethon also has a biomanufacturing platform for clinical-grade vectors, which is the world's largest facility for pre-industrial pilot production (Genethon BioProd). www.genethon.fr

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