Press release

FONDAZIONE TELETHON IS THE FIRST NON-PROFIT ORGANIZATION TO TAKE ON THE COMMERCIALIZATION OF A GENE THERAPY TO CONTINUE ENSURING ACCESS TO ALL ELIGIBLE PATIENTS IN EUROPE

Fondazione Telethon is also working to make a new gene therapy for the Wiskott-Aldrich syndrome available for early access

Milan, January 18th, 2024 – Fondazione Telethon is the first non-profit organization to take on the commercialization of Strimvelis, a gene therapy for the treatment of **adenosine deaminase severe combined immunodeficiency (ADA-SCID),** to continue ensuring access to all eligible patients in Europe.

Strimvelis was the first ex-vivo gene therapy approved worldwide by a Regulatory Agency and the marketing authorization transfer from Orchard Therapeutics, a global gene therapy leader, was approved on July 17th by the European Commission[1] following a positive opinion from the European Medicines Agency (EMA).

Strimvelis originated from research carried out by the San Raffaele-Telethon Institute for Gene Therapy (SR-TIGET) and a commitment by Fondazione Telethon to make these scientific achievements widely available to patients who may potentially benefit. It was approved for reimbursement in Italy by the Agenzia Italiana del Farmaco (AIFA) in 2016 and has been administered exclusively at the San Raffaele Hospital in Milan, Italy. **A total of 45 patients from over 20 countries worldwide have been treated** with Strimvelis in clinical trials and commercially, to date. Fondazione Telethon will continue to make Strimvelis available to eligible patients through the San Raffaele Hospital in Milan, Italy.

Fondazione Telethon is also working on **a new gene therapy for the Wiskott-Aldrich syndrome (WAS)** that has been developed by a dedicated team of researchers at the SR-TIGET and has recently received early access approval in Italy.

The new therapy allows the defect to be corrected in the patient's haematopoietic stem cells by introducing a healthy copy of the defective gene using viral vector technology. This therapy has shown to be effective and safe in pre-clinical studies and is now expected to move to clinical application for patients affected by the most severe forms of the disease.

The progress made by science in the field of advanced therapies for rare diseases has allowed an increase in patient survival and improvement in quality of life. In the future, Fondazione Telethon is committed to working with the regulatory authorities to make these therapeutic innovations available for early access programs to patients in Europe and the US.

[1] https://ec.europa.eu/health/documents/community-register/2023/20230717159799/dec_159799_en.pdf

About Fondazione Telethon ETS

Fondazione Telethon is one of the main Italian biomedical charities, founded in 1990 on the initiative of a group of patients suffering from muscular dystrophy. Its mission is to achieve the cure of rare genetic diseases through scientific research of excellence, selected according to the best practices shared internationally. Through a unique method in the Italian panorama, it follows the entire "research chain" dealing with fundraising, selection and funding of projects and the research activity itself carried out in the centers and laboratories of the Foundation. Telethon also develops collaborations with public health institutions and pharmaceutical industries to translate the results of research into therapies accessible to patients. Since its foundation, Telethon has invested **660,3 million euros** in research, has funded **2,960 projects** with **1,720 researchers** involved and **630 diseases studied**. To date, thanks to Fondazione Telethon, the first gene therapy with stem cells in the world has been made available, thanks to the collaboration with the pharmaceutical industry: since 2023 Fondazione Telethon has gained the marketing authorization. *Strimvelis*, this is the commercial name of the therapy, is intended for the treatment of ADA-SCID, a severe immunodeficiency that compromises the body's defenses from birth. Another gene therapy resulting from Telethon research made available is the one for a serious neurodegenerative disease, metachromatic leukodystrophy, with the commercial name of *Libmeldy*. Another therapeutic approach is in an advanced stage of clinical trials for Wiskott-Aldrich syndrome, another immunodeficiency. Other diseases on which the gene therapy developed by Telethon researchers has been evaluated in patients include beta thalassemia and two metabolic diseases of childhood, mucopolysaccharidosis type 6 and type 1. In addition, within the Telethon institutes a targeted therapeutic strategy is being studied or developed for other genetic diseases, such as haemophilia or various hereditary vision defects. In parallel, the study of basic mechanisms and potential therapeutic approaches for diseases still unanswered continues in all laboratories funded by Telethon.

About Strimvelis

Strimvelis was authorised by the EMA on 26 May 2016 for the treatment of patients with severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), for whom no suitable human leukocyte antigen (HLA)-matched related stem cell donor is available. Strimvelis gene therapy for ADA-SCID is a one-time administration. It consists of a viral-derived vector containing a corrected version of the defective gene in the patient (ADA). When brought into contact with haematopoietic stem cells taken from the patient, this vector aims to restore the production of the missing protein. Reinfused into the bloodstream, the corrected cells are also able to differentiate into the previously missing elements (lymphocytes), thus capable of defending the body against infections.

About ADA-SCID

ADA-SCID (adenosine deaminase deficiency severe combined immunodeficiency) is a very rare, potentially life-threatening genetic disorder in which a defective gene blocks the production of an essential enzyme called adenosine deaminase (ADA), which is necessary for the differentiation and functioning of lymphocytes (a particular type of white blood cell). Children born with ADA-SCID do not develop a healthy immune system, so they cannot fight the most common infections and are forced to live in a sterile and isolated environment. Considering that the incidence of the disease in Europe is estimated to be between 1:375,000 to 1:660,000 live births[2] and that, according to Statista[3] the number of live births in 2021 in EU 27 countries was close to 4 million, the estimated number of new patients per year affected by ADA-deficiency are between 6 and 11.

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[2] A. M. Flinn and A. R. Gennery, “Adenosine deaminase deficiency: A review,” *Orphanet Journal of Rare Diseases*, vol. 13, no. 1. BioMed Central Ltd., p. 65, 24-Apr-2018, doi: 10.1186/s13023-018-0807-5.
[3]https://www.statista.com/statistics/253401/number-of-live-births-in-the-eu/.

Today, there are different treatment options for ADA-SCID. The first is the transplantation of haematopoietic stem cells from a compatible family donor, which can cure the disease but is available in less than 20% of cases[4]. The second, represented by gene therapy, is based on a single administration of stem cells with the correct gene, which are taken from the patient's own bone marrow, thus eliminating possible transplant reactions against the host. In the absence of these options, transplantation from a registry-matched or partially matched donor can be opted for, with a potentially risk of incurring the graft versus host disease (GvHD), infections and other complications, even fatal in certain cases. Finally, enzyme replacement therapy (ERT) is available, *i.e.*, the periodic intramuscular administration of the missing, artificially produced enzyme; ERT is usually administered for short periods of time, waiting for a long-term treatment such as HSC transplantation or gene therapy[5].

About Wiskott-Aldrich syndrome (WAS)[6]

Wiskott-Aldrich syndrome (WAS) is a rare X-linked disorder which classically includes the characteristic triad of immunodeficiency, thrombocytopenia, and eczema. It results from a genetic mutation in the gene encoding Wiskott-Aldrich syndrome protein (WASp). The disease has variable presentation ranging from the severe phenotype (classic WAS) to milder ones (X-linked thrombocytopenia and X-linked neutropenia). This activity describes the pathophysiology, etiology, presentation, and evaluation of Wiskott-Aldrich syndrome, and highlights the role of the interprofessional team in the management of affected patients.

For more information:

Fondazione Telethon Press Office - HAVAS PR Milan
Thomas Balanzoni – thomas.balanzoni@havaspr.com – tel. 02 8545704, 346 3204520
Milva Naguib – milva.naguib-ext@havaspr.com – tel. 355 6267644

IRCCS Ospedale San Raffaele Press Office
Marta Ammoni Tel. 0226436 4466 – 339 6374216 - email ufficio.stampa@hsr.it

[4] J. Heimalla & M. Cowan, “Long term outcomes of severe combined immunodeficiency: therapy implications”. *Expert Rev Clin Immunol*. 2017 November ; 13(11): 1029–1040. doi:10.1080/1744666X.2017.1381558
[5] E. Grunenbaum et al, “Updated Management Guidelines for Adenosine Deaminase Deficiency”. J Allergy Clin Immunol Pract Vol 11, NUMBER 6. June 2023
[6] Wiskott-Aldrich Syndrome - StatPearls - NCBI Bookshelf (nih.gov)