FONDAZIONE TELETHON: WE NEED CONCRETE ACTIONS, ALSO AT EUROPEAN LEVEL, TO COUNTER THE WITHDRAWAL FROM THE MARKET OF LIFE-SAVING GENE THERAPIES FOR CHILDREN SUFFERING FROM RARE DISEASES

After the plea in Nature Medicine on the risk of lack of access to life-saving gene therapies for rare diseases, Fondazione Telethon participates in the meeting in London marking the birth of the European AGORA Consortium (Access to Gene therapies fOr RAre disease)

Milan, 23th September 2022 – Efforts continue to counter the increasing tendency of pharmaceutical and biotechnology companies to disinvest in the field of rare diseases for reasons of insufficient economic return, seeking alternative solutions to make life-saving gene therapies available for children born with rare genetic diseases. Recently, Fondazione Telethon launched an important appeal to avert the withdrawal from the market of life-saving gene therapies for rare diseases, followed by the publication in Nature Medicine of the article 'Ensuring a future for gene therapy for rare diseases'*, signed by Prof. **Luigi Naldini**, Director of the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), Prof. **Alessandro Aiuti**, Deputy Director of the same institute, and **Francesca Pasinelli**, General Manager of Fondazione Telethon.

At the same time, the **AGORA Consortium (Access to Gene therapies fOr RAre disease)**, whose first meeting was held at London's Great Ormond Street Hospital for Children (GOSH) and in which scientists from six European countries participate, was founded today. This initiative is further evidence of the urgency felt by the academic world and advanced scientific research to intervene on the negative path taken in the last year by therapies that very often represent the only chance for many children not only to survive, but also to live a normal and healthy life. Consortium members include Prof. **Luigi Naldini**, Prof. **Alessandro Aiuti** and Prof. **Maria Ester Bernardo**, Clinical Coordinator of the Paediatric Clinical Research Unit at SR-TIGET.

"*It is necessary to analyse the current context of gene therapies for rare diseases, identifying the areas on which to intervene in order to develop strategies that will enable us to make them available to all children who need them - explains Prof. Luigi Naldini. There are problems of a different nature, which we have addressed in the study published in Nature Medicine and solving them requires the intervention of different players: scientists, patient associations, public and private funding agencies, pharmaceutical companies, regulatory and payer bodies, and health technology assessment agencies. Participating in AGORA is a further step, which will allow us to involve these players at European level so that we can implement joint actions at different levels to simplify the development of these complex drugs, while also reducing production costs and making therapies more sustainable".*

Advanced therapies are customized drugs that, with a single administration, correct a disease at its root; in the case of gene therapy, for example, by providing a healthy version of a defective gene. Gene therapy originated in the field of rare diseases: the study and validation of these therapies used rare diseases as pilot cases to develop the necessary technological platforms that are now being applied to commonly used drugs, such as cancer drugs and vaccines used to fight the Covid-19 pandemic. However, the cost of producing these therapies and keeping them on the market is very high and, except for highly profitable therapies, pharmaceutical companies do not find it profitable to commercialize them. The main stumbling block is encountered after the research phase, typically supported by public funds and donations, when industry should take over the project and proceed with the development, production, authorization and marketing phases of the therapy.

"The production and commercialization of gene therapies is expensive, as highly specialized factories, complex processes for handling patient cells and viral vectors, and a very precise final testing phase are required. Added to this are the costs of maintaining them on the market", explains Prof. Alessandro Aiuti. "A possible solution, which we have proposed in the commentary published

in *Nature Medicine* and which we will also study in the AGORA Consortium, could be the creation of a non-profit, sustainable and independent body that would take charge of the authorization, supply and access processes for gene therapies that the industry chooses to no longer make available to patients. Taking action is a clear responsibility not only of us doctors and scientists, but of everyone, starting with the national and European institutions, which represent and must guarantee equal rights to all citizens".

An emblematic case of withdrawal from the market, for purely economic reasons, is represented by **BlueBird Bio**, which has made its gene therapy for **beta thalassaemia (Zynteglo)** and that for **cerebral adrenoleukodystrophy (Skysona)** unavailable on the European market, due to the lack of agreement with the paying agencies of various countries on the price and reimbursement methods; these products are instead marketed in the United States, where in 2022 Zynteglo was priced at $2.8 million, making it one of the most expensive drugs in the world. Another representative case is the announcement in March 2022 by **Orchard Therapeutics** of its decision to withdraw from the market **Strimvelis**, a gene therapy for the treatment of ADA-SCID, a disease that can otherwise lead to death in childhood. Created in the laboratories of the SR-TIGET, this therapy has to date cured more than 40 children from all over the world.

"*Participating in AGORA is a further step, which will allow us to involve these figures at a European level so that we can implement joint actions at different levels to simplify the development of these complex drugs, also reducing production costs, making the therapies more sustainable"* says Francesca Pasinelli*. "What we are doing with Strimvelis is the concrete implementation. Fondazione Telethon has in fact decided to take over the commercialization of the gene therapy for ADA-SCID from Orchard Therapeutics, creating an ad hoc non-profit organization and thus bearing all the costs of management and maintenance on the market. Not only that, with a non-profit organization we will be able to 'donate' the therapy to less affluent patients who are not eligible for reimbursement by the National Health Service as non-European citizens or who do not have medical insurance. However, with six gene therapies abandoned by the industry from the market in the last two years alone, it will be necessary to mobilize a very broad commitment to reverse this trend: Fondazione Telethon and AGORA will work towards this goal on several fronts."*

* Alessandro Aiuti, Francesca Pasinelli and Luigi Naldini, Ensuring a future for gene therapy for rare diseases, Nat. Med. 2022 Aug 15, doi: 10.1038/s41591-022-01934-9.