PRESS RELEASE

Genespire Presents Positive Preclinical Proof of Concept Data at the ASGCT Annual Meeting

- *Data provides preclinical validation for Genespire's liver-directed lentiviral gene therapy in a mouse model of methylmalonic acidemia*
- *Abstract received the ASGCT Excellence In Research Award*

Milan, Italy, 9 May 2024 – Genespire, a biotechnology company developing off-the-shelf gene therapies for pediatric patients affected by genetic diseases, today presented positive preclinical data at the 27th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT) currently taking place in Baltimore, MD, USA. These data demonstrated long-term preclinical efficacy of the Company's liver-directed integrative immune shielded lentiviral vector (ISLV) based gene therapy in a mouse model of methylmalonic acidemia (MMA).

MMA is a rare, genetic metabolic disorder most frequently caused by a faulty gene coding for the mitochondrial enzyme methylmalonyl-coA mutase (MUT). People with this condition are unable to break down and use certain proteins and fats found in food and, as a result, circulating methylmalonic acid accumulates in the body, causing damage to the brain, liver, kidneys, and other organs. At present there are no disease-targeted drugs approved for MMA, and affected patients suffer high levels of morbidity and have a heavily reduced life expectancy.

In the study presented at ASGCT, intravenous administration of an ISLV encoding a human MUT transgene was evaluated in a mouse model of MMA. Treated mice showed a rapid, substantial, and long-lasting (>1 year) reduction in circulating methylmalonic acid, normalization of weight and complete survival. Additionally, ISLV administration led to a systemic effect, resulting in a significant reduction of methylmalonic acid levels not only in the liver but also in the brain and kidney, suggesting an extrahepatic benefit achieved through liver-mediated detoxification.

This work was performed by Dr. Elena Barbon, post-doctoral fellow, and Dr. Alessio Cantore, Group Leader, at the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), in collaboration with Genespire. Dr. Elena Barbon received the ASGCT *Excellence In Research Award* for this abstract. This award is granted by the ASGCT to the top 15 abstracts received from ASGCT members or associate members.

Alessio Cantore, Group Leader at SR-TIGET and co-founder of Genespire added: "These compelling data provide evidence for the efficacy, safety, and extrahepatic benefit of our integrative immune shielded lentiviral vector (LV)-based gene therapy and important preclinical validation."

Julia Berretta, CEO at Genespire, commented: "Receiving the ASGCT Excellence In Research Award provides further external validation on the quality of our research and promise of our technology". She added, "We believe that our unique ISLV gene therapy approach, allowing for stable gene transfer and long-lasting expression of the therapeutic gene, may be optimally positioned to treat MMA patients."

For further information, please reach out to the Company.

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About Genespire
Genespire is a biotechnology company, developing off-the-shelf gene therapies based on immune shielded lentiviral vectors (ISLVs) for pediatric patients affected by genetic diseases. ISLVs are designed to be used intravenously and allow the life-long production of the therapy directly from the patient's liver. Genespire is initially advancing therapeutic programs in inherited metabolic diseases with high unmet medical need. Based in Milan, Italy, Genespire was founded in March 2020 by the gene therapy pioneer Prof. Luigi Naldini and Dr. Alessio Cantore, Fondazione Telethon and Ospedale San Raffaele. Genespire is a spin-out of SR-Tiget, a world leading cell and gene therapy research institute. Find out more about us at www.genespire.com.