Genespire and SR-TIGET Show Durable Preclinical Efficacy of Liver-Directed Gene Therapy for Methylmalonic Acidemia

- **The study shows that ISLV-directed delivery of the MMUT gene produced durable therapeutic benefits in mouse models.**
- **Gene transfer efficiency exceeded 80% of the liver.**
- **Genespire is progressing its lead asset for MMA, GENE202, towards the clinic.**

Milan, Italy, 08 July, 2026 -- Genespire, in collaboration with researchers at the San Raffaele Telethon Institute for Gene Therapy (SR-TIGET), has today announced the publication of preclinical data supporting the potential of its liver-directed immune-shielded lentiviral gene therapy approach to treat methylmalonic acidemia (MMA), a severe inherited metabolic disorder.

The findings, published in the Journal of Hepatology, show that a single systemic administration of a lentiviral vector encoding the MMUT gene led to sustained improvements in disease features in a validated mouse model of MMA, with effects lasting for the average lifespan of laboratory mice. Since the mice were treated when young, the study supports the durability of the gene therapy through postnatal growth and maturation of the liver.

MMA is caused by a deficiency of methylmalonyl-CoA mutase, an enzyme that plays a critical role in the body's metabolism of food. Its absence results in the accumulation of toxic metabolites that lead to recurrent metabolic crises, growth failure, neurological impairment, and multi-organ damage.

In the study, researchers also treated mice with a dose containing an optimized MMUT transgene, thereby improving therapeutic efficacy. In the same mouse model of MMA, this version exhibited a dose-dependent improvement of metabolomic biomarkers, with gene transfer efficiency exceeding 80% of the liver.

The study also highlights that genetically corrected cells in the liver may, over time, replace the diseased ones, suggesting that therapeutic efficacy may progressively improve even when starting at lower initial doses.

“Together, these findings indicate that Genespire is on a clear path towards the long-term correction of metabolic diseases which impact the liver and other organs,” said Lucia Faccio, CEO of Genespire. “We believe our approach has the potential to translate into human health in the form of a single-administration treatment for patients with MMA, and are committed to continuing our efforts in bringing our lead asset for MMA, GENE202, to the clinic. We would like to extend our gratitude to everyone involved in the research project, especially those at the SR-TIGET.”

“We are confident that this study, together with other previous studies from our group at SR-TIGET, provides a comprehensive pre-clinical data package enabling the initiation of clinical testing in pediatric patients affected by MMA” concludes Dr Alessio Cantore, group leader at SR-TIGET and Associate Professor at Vita-Salute San Raffaele University, who supervised and coordinated the study and signed it as senior author.

Click here to access the full paper: https://doi.org/10.1016/j.jhep.2026.05.011

About Genespire

Genespire is a biotechnology company developing off-the-shelf immune shielded lentiviral vector-based gene therapies 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. Initially advancing therapeutic programs in inherited metabolic diseases with high unmet medical need, 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.

About 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). Persons 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.

About San Raffaele Telethon Institute for Gene Therapy (SR-TIGET)

The San Raffaele Telethon Institute for Gene Therapy (SR-TIGET), based in Milan, Italy, is a joint venture between Fondazione Telethon and Ospedale San Raffaele, established in 1996 and currently directed by Luigi Naldini. The Institute is internationally recognized as a center of excellence for research and clinical translation in gene and cell therapy.