Genespire announces that GENE202 has been granted Orphan Drug Designation by the FDA and EC for the treatment of methylmalonic acidemia

- **Methylmalonic acidemia is a pediatric metabolic disease with no approved treatments.**

- **GENE202 utilizes the company's proprietary shielding technology for lentiviral vectors so that the therapy avoids detection by the body's immune system, making it potentially safer and more effective.**
- **If successful, GENE202 will be a proof point for Genespire's wider lentiviral platform.**

Milan, ITALY – 20 January 2026 – Genespire, a biotechnology company developing off-the-shelf gene therapies for pediatric patients affected by genetic diseases, has today announced that orphan drug designation has been granted by both the U.S. Food and Drug Administration (FDA) and the European Commission (EC) for GENE202, its lentiviral vector containing the human methylmalonyl-coA mutase (*MMUT*) transgene.

GENE202, developed by Genespire's scientific founders at the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), is a pioneering *in vivo* off-the-shelf gene therapy which harnesses the Company's Immune Shielded Lentiviral Vector (ISLV) platform to address pediatric patients affected by genetic diseases who currently face the most pressing unmet medical needs.

Genespire is developing a novel proprietary class of lentiviral vectors, ISLVs, with lead candidate GENE202 nearing clinical development for the treatment of methylmalonic acidemia (MMA), a devastating genetic disorder impairing the metabolism of certain amino acids and fats.

The *MMUT* gene provides instructions for producing the mitochondrial enzyme methylmalonyl-CoA mutase. This enzyme is crucial for metabolism, catalyzing the isomerization of methylmalonyl-CoA to succinyl-CoA, a key step in the breakdown of certain amino acids and fatty acids. Mutations in the *MMUT* gene are the most common cause of MMA, a severe, potentially lethal autosomal recessive metabolic disorder. MMA leads to the accumulation of toxic metabolites, such as methylmalonic acid, causing multisystemic problems and neurological damage.

Dr Lucia Faccio, Genespire's CEO added: "This important news highlights the huge unmet need of MMA patients and their families as there are currently no approved treatments for this highly debilitating and life-shortening disease. Gene therapy is starting to deliver results with several recent clinical successes and product approvals, and we believe that Genespire's approach offers huge opportunities."

Orphan drug designation recognizes that a medicine is intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating rare disease, with fewer than 200,000 people

in the US and fewer than 5 in 10,000 people in the EU having the condition. To encourage the development of drugs for rare diseases, the designation in the US confers several incentives including a seven-year period of marketing exclusivity if the drug is approved, tax credits for qualified clinical trials, and a waiver of FDA user fees. In Europe the designation conveys several benefits, including ten years of market exclusivity in the EU after approval, reduced or waived European Medicines Agency fees and access to protocol assistance.

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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, the 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.

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). 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.