PRESS RELEASE

Genespire and the San Raffaele Telethon Institute for Gene Therapy announce publication in Nature Biotechnology on enhanced gene editing technique in hematopoietic stem cells

Italy, Milan, 30 June 2020: Genespire, a gene therapy company developing transformative therapies for genetic diseases, and the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) announce today the publication of data demonstrating an improved targeted gene replacement technology in hematopoietic stem cells (HSCs) in *Nature Biotechnology*.

The paper, entitled *Efficient gene editing of human long-term hematopoietic stem cells validated by clonal tracking*, outlines technology which is included in the strategic alliance between Genespire and SR-Tiget and was developed at the laboratory of Pr. Luigi Naldini at SR-Tiget. It shows increased homology directed recombination (HDR) efficiency in hematopoietic stem cells (HSC) by forcing cell-cycle progression and transiently upregulating components of the HDR machinery.

People with genetic diseases touching the hematopoietic lineage may benefit from corrective targeted gene therapy through gene editing, consisting of replacing the defective gene with a corrected version, in HSCs. These cells are self renewing and can differentiate in all the cell types of the hematopoietic lineage, therefore providing the potential for a one-time therapy. Use of the improved gene editing technology developed by SR-Tiget has shown to yield a greater percentage of gene-edited HSC's and increased clonality, or the number of modified cells passed on. In a clinical setting this should lead to increased hematopoietic cells chimerism in the patient receiving the corrective HSC therapy, and could accelerate the hematopoietic recovery after conditioning and increase the size, long-term stability, and safety of the engineered cell graft.

This approach can be applied to genetic diseases originating in the hematopoietic lineage, including primary immune deficiencies (PIDs), a key area of focus for Genespire. Genespire will continue to work with SR-Tiget and apply this technology to its future pipeline of gene therapies.

The technology, developed by SR-Tiget, is part of the strategic alliance announced in May 2020, under which the organisations will study and further develop novel gene therapies which have the unique potential to address severe unmet medical need and exploit gene editing and lentiviral vector technologies developed by SR-Tiget.

Julia Berretta, Chief Executive Officer of Genespire, commented: ""The focus of Genespire's alliance with SR-Tiget is to research and develop novel gene therapies, addressing severe diseases with high unmet medical need. We are pleased with the publication of these data in Nature Biotechnology, which provides valuable insight into this pioneering technology developed by SR-Tiget, and we look forward to our future work with SR-Tiget translating their cutting edge science into transformational therapies"

Professor Luigi Naldini, Director of SR-Tiget and scientific co-founder of Genespire, said "We are excited that this body of work has been recognized in Nature Biotechnology Our findings elucidate

and overcome two main biological barriers to efficient HDR-mediated gene editing in HSCs, and show by clonal tracking that our enhanced editing protocol preserves their multilineage and self-renewal capacity long term after serial transplant. We look forward our future work with Genespire to explore its potential in primary immunodeficiencies."

The full publication details are below and can be accesed online here.

Efficient gene editing of human long-term hematopoietic stem cells validated by clonal tracking

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About Genespire

Genespire is a biotechnology company focused on the development of transformative gene therapies for patients affected by genetic diseases, particularly primary immunodeficiencies and inherited metabolic diseases. 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. It is a spin-off of SR-Tiget, a world leading cell and gene therapy research institute and is backed by Sofinnova Partners. www.genespire.com

About SR-Tiget

Based in Milan, Italy, the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) is a joint venture between the Ospedale San Raffaele and Fondazione Telethon. SR-Tiget was established in 1995 to perform research on gene transfer and cell transplantation and translate its results into clinical applications of gene and cell therapies for different genetic diseases. Over the years, the Institute has given a pioneering contribution to the field with relevant discoveries in vector design, gene transfer strategies, stem cell biology, identity and mechanism of action of innate immune cells. SR-Tiget has also established the resources and framework for translating these advances into novel experimental therapies and has implemented several successful gene therapy clinical trials for inherited immunodeficiencies, blood and storage disorders, which have already treated >115 patients and have led through collaboration with industrial partners to the filing and approval of novel advanced gene therapy medicines.