PRESS RELEASE

Genespire and SR-Tiget announce strategic alliance for the development of transformative gene therapies for genetic diseases and disclose collaboration focus

Pre-clinical data from SR-Tiget, included in the alliance with Genespire, to be presented at ASGCT 23rd Annual Meeting

Italy, Milan, 13 May 2020: The San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), one of the world's leading gene therapy research institutes jointly managed by Fondazione Telethon and Ospedale San Raffaele and Genespire, a gene therapy company developing transformative therapies for genetic diseases, and spin-out of SR-Tiget, announced today their alliance on the research and development of candidate therapeutic products for people affected by primary immunodeficiencies and metabolic diseases based on novel gene editing and lentiviral vector technologies developed by SR-Tiget.

Genespire was co-founded in March 2020 by SR-Tiget director and gene therapy pioneer Prof. Luigi Naldini and Dr. Alessio Cantore, Fondazione Telethon and Ospedale San Raffaele. Genespire recently raised €16 million in a Series A financing round from Sofinnova Partners.

Under the terms of the alliance, Genespire and SR-Tiget 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.

Genespire was granted an exclusive global license for the research, development and commercialization of gene therapies for metabolic diseases based on SR-Tiget's alloantigen free, microRNA-regulated lentiviral vectors, which allow for stable liver gene therapy even for diseases with early onset, requiring administration at a young age.

Genespire was also granted exclusive licenses and options to the results of a joint research and development program with SR-Tiget in the T-cell and Hematopoietic Stem Cells field to address genetic diseases, in particular primary immunodeficiencies, exploiting the ex vivo gene editing technology. SR-Tiget and Genespire will first collaborate to bring an ex-vivo autologous edited T-cell gene therapy for X-linked Hyper IgM syndrome (HIGM1) to the clinic, which becomes Genespire's lead candidate product. HIGM1 is caused by inherited mutations of the CD40 ligand gene (*CD40L*), resulting in impaired antibody response and innate immunity, meaning that people find it difficult to fight off infections and eventually succumb to them. The treatment objective is to correct the defective gene through targeted editing of the endogenous locus, thereby maintaining physiological regulation of the CD40L gene, with the aim of improving the immune response of the patients.

Preclinical results of SR-Tiget on HIGM1 will be disclosed in an oral presentation at the American Society for Cell and Gene Therapy (ASGCT) 23rd Annual Meeting, taking place virtually from 12-15 May 2020 by SR-Tiget (details of Presentation 1 below). The presentation will outline the technology and

its preclinical validation in the disease model and patient derived cells and discuss the potential of the gene edited T-cell treatment approach for patients with Hyper IgM.

Dr. Alessio Cantore will also present novel data related to the potential of the lentiviral vector platform for liver gene therapy in an oral presentation at ASGCT (details of Presentation 2 below). The presentation will focus on investigating the stability of lentiviral vector genetically modified liver cells following post-natal liver growth in mice, in view of its potential application to pediatric patients.

Luigi Naldini, Director of SR-Tiget and scientific co-founder of Genespire said: "We are excited to have secured a path for bringing forward some of the gene therapy work pioneered at SR-Tiget to eventually help individuals affected by severe metabolic and immunodeficiency disorders. SR-Tiget's alliance with Genespire will provide the means to progress effectively to clinical trials, with a strong view to develop efficacious and safe medicines ready for market access."

Julia Berretta, Chief Executive Officer of Genespire commented: "SR-Tiget brings outstanding expertise and significant experience in developing gene therapies from bench to bedside. We believe that our strong partnership with SR-Tiget, led by internationally recognized experts Prof. Luigi Naldini and Dr. Alessio Cantore will be fundamental for Genespire to carry out its goal of translating pioneering science into transformative therapeutic solutions for patients."

-ENDS-

Oral presentation 1 details:

Title:

Modeling, Optimization and Comparative Efficacy of HSC- and T-cell Based Editing Strategies for Treating Hyper IgM Syndrome

Authors:

Valentina Vavassori, Elisabetta Mercuri, Genni Marcovecchio, Maria Carmina Castiello, Giulia Schiroli , Luisa Albano, Elena Fontana, Andrea Annoni, Valentina Capo, Carrie Margulies, Frank Buquicchio, Joseph Kovacs, Eugenio Scanziani, Cecilia Cotta-Ramusino, Anna Villa, Luigi Naldini, Pietro Genovese

Date and time: May 14th 2020, 3:45 PM EDT

Session: 354 Gene Therapies for Hemophilia and Immune Disorders

Abstract #937

Oral Presentation 2 Details

Title:

Investigating the stability of lentiviral vector targeted liver cells during post-natal growth for in vivo gene therapy applications

Authors:

Michela Milani, Francesco Starinieri, Cesare Canepari, Tongyao Liu, Federica Moalli, Gioia Ambrosi, Tiziana Plati, Mauro Biffi, Cesare Covino, Timothy Nichols, Matteo Iannacone, Robert Peters, Luigi Naldini, Alessio Cantore

Date and time: May 14th 2020, 4:15 pm EDT

Session: 350 RNA Virus Vectors

Abstract #911

Notes to Editors

About Hyper IgM Syndrome ("HIGM")

Hyper IgM is a Primary Immune Deficiency affecting 1:250,000-500,000 patients. The disease is linked to mutations in the CD40L gene, which is expressed in activated CD4 T cells, and results in impaired

antibody production and innate immunity. The current standard of care is constituted by continuous Ig replacement, and antibiotic-antifungal prophylaxis, but the disease is still linked to high morbidity and reduced life expectancy. Allogeneic hematopoietic stem cell transplant (HSCT) is potentially curative, but is limited by matched donor availability and is associated with high risk of graft versus host disease, infections and death. Thus, improved therapeutic alternatives are strongly needed.

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.

About Fondazione Telethon

Fondazione Telethon is a non-profit organisation created in 1990 as a response to the appeals of a patient association group of stakeholders, who saw scientific research as the only real opportunity to effectively fight genetic diseases. Thanks to the funds raised through the television marathon, along with other initiatives and a network of partners and volunteers, Telethon finances the best scientific research on rare genetic diseases, evaluated and selected by independent internationally renowned experts, with the ultimate objective of making the treatments developed available to everyone who needs them. Throughout its 30 years of activity, Fondazione Telethon has invested more than € 528 million in funding more than 2.630 projects to study more than 570 diseases, involving over 1.600 scientists. Fondazione Telethon has made a significant contribution to the worldwide advancement of knowledge regarding rare genetic diseases and of academic research and drug development with a view to developing treatments. For more information, please visit: www.telethon.it

About Ospedale San Raffaele

Ospedale San Raffaele (OSR) is a clinical-research-university hospital established in 1971 to provide international-level specialised care for the most complex and difficult health conditions. OSR is part of Gruppo San Donato, the leading hospital group in Italy. The hospital is a multi-specialty center with over 60 clinical specialties; it is accredited by the Italian National Health System to provide care to both public and private, national and international patients. Research at OSR focuses on integrating basic, translational and clinical activities to provide the most advanced care to our patients. The institute is recognized as a global authority in molecular medicine and gene therapy, and is at the forefront of research in many other fields. Ospedale San Raffaele is a first-class institute which treats many diseases and stands out for the deep interaction between clinical and scientific area. This makes the transfer of scientific results from the laboratories to the patient's bed easier. Its mission is to improve knowledge

of diseases, identify new therapies and encourage young scientists and doctor to grow professionally. For more information, please visit: www.hsr.it

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