# PRESS RELEASE

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# GSK, Fondazione Telethon and Fondazione San Raffaele to collaborate on gene therapy for rare diseases

GlaxoSmithKline PLC (GSK), Fondazione Telethon and Fondazione San Raffaele today announced a new strategic alliance to research and develop novel treatments to address rare genetic disorders, using gene therapy carried out on stem cells taken from the patient's bone marrow (*ex vivo*). The alliance capitalises on research performed at the San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET), a joint venture between Fondazione Telethon and Fondazione San Raffaele established since 1995.

Under the terms of the agreement, GSK will gain an exclusive licence to develop and commercialise an investigational gene therapy, currently in Phase III, for ADA Severe Combined Immune Deficiency (ADA-SCID) - a rare and life-threatening immune deficiency, which affects approximately 350 children worldwide. Phase I/II studies have demonstrated the potential of this treatment option to restore long-term immune function and protect against severe infections in children with ADA deficiency.[i]

In addition, GSK will co-develop with Fondazione Telethon and Fondazione San Raffaele, six further applications of *ex vivo* stem cell therapy, using a new gene transfer technology developed by HSR-TIGET scientists, with the potential to treat a range of rare disorders. This first of these will be metachromatic leukodystrophy (MLD) and Wiskott-Aldrich Syndrome (WAS). Others include; beta-thalassemia, mucopolysaccharoidosis type I (MPS); globoid leukodystrophy (GLD); and chronic granulomatous disorder (CGD). Clinical trials for WAS and MLD were initiated at HSR-TIGET last spring and are currently recruiting patients.

All of these disorders have a molecular mechanism that is well understood and are caused by faults in a single gene, making it possible for this ex vivo gene technology to correct the patient's own bone marrow stem cells. When the treated stem cells are returned to the patient they express the corrected protein, providing an opportunity to treat the disease and side step much of the risk associated with immune-incompatibility that comes from stem cells supplied by a donor.

Fondazione Telethon will receive an upfront 10 million euro payment from GSK and is eligible to receive further payments upon successful completion of a number of predetermined development milestones.

"This alliance is an important addition to GSK's growing portfolio in rare diseases and advances the work our stem cell researchers have been doing to deliver transformative regenerative therapies," said Dr Philippe Monteyne, Head of Development and Chief Medical Officer for GSK Rare Diseases. "Not only does the lead programme for ADA-SCID represent an opportunity to provide a treatment option for an under-served patient population, by combining our experience in manufacturing complex biological products with the pioneering research of world-leaders in gene and stem cell therapies, we have the chance to dramatically advance this field."

"This collaboration is a breakthrough for gene therapy in rare diseases," said Professor Luigi Naldini, Director of HSR-TIGET. "We have spent years researching these promising new technologies, but

without GSK's experience in developing medicines, we would not be able to take all the steps towards making a potential therapy available to patients."

"This day is one of extraordinary importance for us," said Francesca Pasinelli, General Manager of Fondazione Telethon. "Through the years we have been raising donations with the promise of advancing towards the cure of rare genetic diseases. With this alliance we can show that the excellent scientific research we have funded could actually lead to viable therapies available to all patients."

"San Raffaele and Telethon have a shared ambition to translate basic discoveries in the field of molecular medicine into treatments for patients," said Maria Grazia Roncarolo, Scientific Director of the San Raffaele Scientific Institute. "We are really excited by the alliance with GSK, because we can now progress our research and know-how into potential treatments."

**About ADA-SCID**
ADA-SCID is one form of Severe Combined Immune Deficiency (SCID), commonly referred to as the 'bubble boy disease'. It is caused by a mutation in a single gene, and this defect prevents the body from producing the enzyme adenosine deaminase (ADA), which is involved in the creation of disease-fighting immune cells. Patients with this condition are unable to mount their own defence against foreign organisms like bacteria and viruses so without specialist intervention are at risk from life threatening infections.

ADA-SCID is an autosomal recessive inherited disorder. Around 14 children in EU and 12 children in the US are born each year with the condition. A bone marrow transplant from a matched donor is currently the best treatment option available to patients. Unfortunately suitable bone marrow donors cannot always be found for all patients. In some cases, patients are treated with enzyme replacement therapy (ERT) but this requires frequent injections and is not a cure.

**About the *ex vivo* gene therapy**
Replacing faults in stem cells has been practised for more than 40 years, in the form of donor haematopoetic stem cell (HSC) transplants (bone marrow transplants). However such transplants rely on stem cells taken from an immune matched, or closely related, donor, which is not always available. There is always a risk of graft rejection but this is particularly high when matched donors cannot be found.

This *ex vivo* gene therapy transfers the corrected gene to the patient's own stem cells. The patient's HSCs are harvested from the body, 'healthy' copies of the gene are inserted into the cell using a modified viral vector and the cells are re-introduced to the patient. Because the technique uses the patient's own cells there is much less risk of immune rejection compared to a bone marrow transplant.

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**Fondazione Telethon and Fondazione San Raffaele Collaboration**
**Fondazione Telethon** is one of the biggest biomedical charities in Italy, whose mission is to advance biomedical research towards diagnosis, cure and prevention of genetic diseases.

Settled in Milan, the **San Raffaele Scientific Institute**, belonging to the San Raffaele del Monte Tabor Foundation and recognised by the Italian Ministry of Health as a University Hospital (IRCCS), is the largest private Italian Institute, carrying out cutting edge biomedical research and clinical activities in the field of molecular medicine.

**The San Raffaele Telethon Institute for Gene Therapy** (HSR-TIGET) stems from a collaboration initiated in 1995 between Telethon and the Fondazione San Raffaele del Monte Tabor. The laboratories are located within the DiBiT, San Raffaele Hospital in Milan. HSR-TIGET focuses on

basic research and on experimental protocols for gene therapy of inherited diseases, in particular congenital immunodeficiencies, lysosomal diseases and blood disorders. For further information, please visit www.telethon.it/english/ and www.sanraffaele.org/EN_Home/

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[i] Aiuti et al. N Engl J Med 2009; 360:447-458. http://www.nejm.org/doi/full/10.1056/NEJMoa0805817