Sirolimus has been granted Orphan Drug Designation for the treatment of sickle cell disease also in USA

Milan (Italy) April 20th 2018 – Rare Partners Srl Impresa Sociale announces today that the American Agency Food and Drug Administration has granted Orphan Drug Designation (ODD) to sirolimus (Rapamycin) for the treatment of sickle cell disease.

The ODD granting by FDA follows the previous similar decision recently adopted by the European Agency EMA on January 17th 2018.
As a consequence of this last official act by FDA, to date sirolimus has been designated as orphan drug for the treatment of beta-thalassemia as well as for the treatment of sickle cell disease in both territories, Europe and USA.

Marco Prosdocimi, Managing Director of Rare Partners, said that "*This important achievement is the outcome of the very fruitful collaboration that we established since 2011 with professor Roberto Gambari and his research group at the Ferrara University. The results of the experimental work performed in these past years has allowed not only the obtaining of the orphan drug designation for beta-thalassemia, where we will start very soon the first trial in man, but also the further widening of the potential use of sirolimus in another very important rare indication, such as sickle cell disease. The granting in USA as well as in EU of the ODD for both therapeutic indications underlines the huge clinical potential of this new use of sirolimus".*

Roberto Gambari, professor of Biochemistry at the Department of Life Sciences and Biotechnology, Ferrara University, said that: "*The research results that convinced us to propose the use of sirolimus for the treatment of patients with sickle cell disease are based on the study of the effect in vitro of sirolimus on erythroid cells isolated from patients. The effect we tried to verify is the induction of fetal hemoglobin. This particular type of*

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hemoglobin, if produced, has the effect of reducing the "sickle" phenotype of red blood cells, responsible for their rigidity and very serious clinical phenomena, starting from the pediatric age. Therefore, if the effect of sirolimus will be confirmed through a clinical trial, we could think of addressing the clinical application in the future also towards pediatric patients. At present, the activity of our laboratory is focused on the analysis of the effects on SCD erythroid cells of several molecules found to be HbF inducers in beta-thalassemia. With this in mind, patient stratification is being considered for determining possible links between genomic polymorphism and response to the inducers, including sirolimus. This would greatly help in the process of patient recruitment in pilot clinical trials. With respect to the activity of our group in this field, we would like to mention the participation to the THALAMOSS Project (THALAssaemia MOdular Stratification System for personalized therapy of beta-thalassemia; Health-2012-INNOVATION-1) and the continuous support of Fondazione Cassa di Risparmio di Padova and Rovigo, which was the major national sponsor of our research activity on hemoglobinopathies".

Orphan Drug Designation is granted to novel drugs or biologics that treat a rare disease or condition affecting fewer than 200,000 patients in the U.S. The designation provides developers with a seven-year period of U.S. marketing exclusivity upon marketing approval for the designated indication, as well as with tax credits for clinical research costs, the ability to apply annually for grant funding, clinical research trial design assistance and the waiver of Prescription Drug User Fee Act (PDUFA) filing fees.

About Sickle Cell Disease

The term sickle cell disease (SCD) describes a group of inherited red blood cell disorders. People with SCD have abnormal hemoglobin, called hemoglobin S (HSS) or sickle hemoglobin, in their red blood cells. The disease affects the red blood cells, causing episodes of sickling, which produce episodes of pain and other symptoms. In between episodes of sickling, people with SCD are normally well. Long-term complications can

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occur. Certain conditions, such as infection, lack of fluid in the body (dehydration) or low oxygen, can trigger sickling.

About sirolimus application in Sickle Cell Disease

It is known that an elevated level of fetal haemoglobin in SCD patients may result in a relevant clinical improvement. Sirolimus, already used as an immunosuppressant in transplanted patients, should act in SCD patients by inducing erythroid differentiation and expression of fetal haemoglobin, thus reducing the need of frequent blood transfusions. This new use of the drug has been patented by professor Gambari and co-workers. Rare Partners finalized an agreement with the assignees (University of Ferrara and Associazione Veneta per la Lotta alla Talassemia), aimed at completing the preclinical studies and proceeding with Orphan Drug Designation and clinical development in patients with haemoglobin pathologies.

About Rare Partners

Rare Partners Srl, founded in Milan in March 2010 and registered as a Social Enterprise, brings a new approach to finding diagnostic and therapeutic solutions in the field of rare diseases, thanks to the creation of a network of collaborations with research institutes, charities and service organizations.

Rare Partners works as a virtual company that combines the use of non-profit financial resources (public and private) with its expertise in the industrial field, in order to create new opportunities for collaborations between the world of not for profit organizations, the scientific community, and biopharmaceutical companies.

For more information: www.rarepartners.org

About University of Ferrara

The University of Ferrara, established in 1391 is one of the oldest universities in Italy, counting more than 18,000 students and with an outstanding track-record of excellence in scientific research, including life sciences. Professor Roberto Gambari is the founder and

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Director of the Laboratory for the development of genetic and pharmacogenomic therapy of thalassemia, ThalLab at the University of Ferrara.

For more information: www.unife.it

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