Orchard Therapeutics announces extension of its collaboration with Manchester University to include Sanfilippo Syndrome type B

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Orchard Therapeutics Limited, announces today that it has acquired an exclusive license to develop lentivirus-based autologous *ex-vivo* gene therapy for Sanfilippo syndrome type B (or MPS-IIIB) from The University of Manchester, UK.

The technology, developed in Professor Brian Bigger's laboratory, and recently published in the journal Brain, involves the use of a high-titre lentiviral vector to drive the expression of a codon-optimized *α-N-acetylglucosaminidase* (*NAGLU*) gene under the control of the myeloid-specific CD11b promoter (LV.CD11b.NAGLU).

MPS-IIIB is a rare neurodegenerative inherited lysosomal storage disease caused by mutations in the *NAGLU* gene. The disease, which affects children as early as 2 years of age, results in severe and rapidly progressive brain disease and neurological symptoms. There is currently no effective treatment option for MPS-IIIB.

This programme in MPS-IIIB complements the existing collaboration program between Orchard, The University of Manchester and Manchester University NHS Foundation Trust in MPS-IIIA. Autologous *ex-vivo* lentiviral haematopoietic stem cell gene therapy is anticipated to correct neurological manifestations through the engraftment of subpopulations of haematopoietic stem cells in the central nervous system, thereby providing supranormal and widespread enzyme expression throughout the brain. In both MPS-IIIA and MPS-IIIB, preclinical studies have produced encouraging results showing a normalization of heparan sulphate levels in the brain and peripheral organs, as well as neurological disease correction.

Dr Jesus Garcia-Segovia, Orchard's VP Clinical Development, CNS and Metabolic Disorders stated: " *The incorporation of MPS-IIIB into our development pipeline is a significant milestone in the consolidation of our neurometabolic franchise, which is currently focused on the development of autologous ex-vivohaematopoietic stem-cell gene therapy for children suffering from MPS-IIIA. We are very excited at the possibility of bringing effective treatments capable of addressing the high unmet medical need in children suffering from these devastating conditions*".

Prof Brian Bigger, Professor of Cell and Gene Therapy in the Faculty of Biology, Medicine and Health, The University of Manchester commented: "*It's incredibly exciting for us to work with our trusted partner Orchard Therapeutics to translate another autologous ex-vivo gene therapy that has demonstrated efficacy in a preclinical mouse model of MPS-IIIB into clinical development and scale-up*".

Dr. Andrea Spezzi, Orchard's Chief Medical Officer added: " *MPS-IIIA and MPS-IIIB are devastating diseases. Orchard and its collaborators are highly motivated to develop gene therapies to address the root cause of these disorders and will work tirelessly to make treatments available to patients as soon as possible. We are now focusing all our efforts on completing the preclinical activities required to enable the start of clinical studies in MPS-IIIA towards the end of 2018 and thereafter in MPS-IIIB*".

Orchard's development pipeline of autologous *ex-vivo* gene therapies includes novel treatments for primary immune deficiencies, and inherited metabolic disorders including other undisclosed early and late-stage programmes.

About MPS-IIIA (Mucopolysaccharidosis type IIIA or Sanfilippo syndrome type A)
MPS-IIIA is a rare neurodegenerative lysosomal storage disease caused by mutations in the *sulfoglycosamine sulfohydrolase* (*SGSH*) gene. There are no effective treatments for MPS-IIIA to date. The disease affects children in early life causing a progressive decline in cognitive and behavioural function and a subsequent decline in motor function. It results in severe dementia and early death, usually in the teens or early twenties. Orchard's autologous *ex-vivo* gene therapy for MPS-IIIA, OTL-201, was awarded orphan drugs designations by the European Medicines Agency (EMA) and FDA.

About MPS-IIIB (Mucopolysaccharidosis type IIIB or Sanfilippo syndrome type B)
MPS-IIIB is a severe inherited autosomal recessive disorder caused by mutations in the *NAGLU* gene. Affected children exhibit the first signs of development delay between 2 or 3 years of age, and suffer from severe central nervous system degeneration, with progressive cognitive impairment and behavioural problems, alongside more attenuated somatic symptoms. Life expectancy is 15–20 years. There are currently no treatments approved for MPS-IIIB.

Professor Bigger's publication on autologous *ex-vivo* lentiviral gene therapy utilizing myeloid-specific CD11b promoter (LV.CD11b.NAGLU) in the journal Brain can be found under the DOI 10.1093/brain/awx311; https://academic.oup.com/brain/advance-article-abstract/doi/10.1093/brain/awx311/4657148

About The University of Manchester
The University of Manchester, a member of the prestigious Russell Group, is the UK's largest single-site university with 38,600 students and is

consistently ranked among the world's elite for graduate employability.
The University is also one of the country's major research institutions, rated fifth in the UK in terms of 'research power' (REF 2014). World class research is carried out across a diverse range of fields including cancer, advanced materials, addressing global inequalities, energy and industrial biotechnology.
No fewer than 25 Nobel laureates have either worked or studied here.
It is the only UK university to have social responsibility among its core strategic objectives, with staff and students alike dedicated to making a positive difference in communities around the world.
Manchester is ranked 35th in the world in the Academic Ranking of World Universities 2016 and 5th in the UK. The University had an annual income of almost £1 billion in 2015/16.

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