Khondrion announces first patients dosed in 6-month paediatric Phase II study of sonlicromanol for mitochondrial diseases

Study will examine the pharmacokinetics, safety and efficacy of sonlicromanol, one of the most advanced disease-modifying drug candidates in development for mitochondrial disease

NIJMEGEN, the Netherlands – 21 April 2021: Khondrion, a clinical-stage biopharmaceutical company discovering and developing therapies targeting mitochondrial disease, today announces that the first patients have been successfully dosed in its KHENERGYC paediatric Phase II study (NCT04846036) to explore the pharmacokinetics, safety and efficacy of sonlicromanol in children with a genetically confirmed primary mitochondrial disease and suffering from motor symptoms.

Sonlicromanol, Khondrion's wholly-owned, investigational lead asset, is currently being tested in a Phase IIb study as a potentially disease-modifying treatment for adults with mitochondrial disease. The compound is a first-in-class, oral small molecule targeting key underlying mechanisms of mitochondrial disease based on the drug's unique triple mode of action: redox modulation to help restore the cell's metabolism, radical trapping preventing ferroptotic cell death, and mPGES-1 inhibition resulting in anti-inflammatory effects.

The placebo-controlled, double blind KHENERGYC study is underway at internationally recognised mitochondrial disease centres in Europe. First patients are being dosed at the Radboud Centre for Mitochondrial Medicine, Nijmegen, The Netherlands. The 6-month study, supported by Dutch Patient Foundations and an EFRO Grant (PROJ-00582) will investigate the effect of sonlicromanol in 24 children (from birth to 17 years) with genetically confirmed mitochondrial disease of which the gene defect is known to hamper the functioning of one or more oxidative phosphorylation system enzymes and who are suffering from motor symptoms. The study's primary objective is to evaluate the effect of sonlicromanol on motor function using a range of validated, quantitative assessments including the Gross Motor Function Measure-88 and the Nine Hole Peg Test.

Prof. Dr. Jan Smeitink, Chief Executive Officer at Khondrion, said: *"Mitochondrial diseases present a serious unmet medical need in children, with those diagnosed experiencing a rapid progression of symptoms that can have a significant impact on their quality of life and having a substantially reduced life expectancy. Despite advances in the understanding of mitochondrial disorders, treatment options are extremely limited and, to date, largely consist of supportive care. There is an urgent need for treatments."*

"At Khondrion we don't want to leave any mitochondrial disease patient behind, that's why this paediatric study is important so that, together with our ongoing phase IIb study in adult patients, we can truly understand the disease-modifying potential of sonlicromanol across all age groups."

Sonlicromanol is one of the most advanced disease-modifying drug candidates for mitochondrial disease in development. A Phase IIb clinical trial in adult patients with MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) spectrum disorders is ongoing, investigating the effect of sonlicromanol on cognitive functioning. Sonlicromanol has been granted Orphan Drug Designations for the treatment of MELAS, Leigh disease and patients with maternally inherited diabetes and deafness (MIDD) in Europe, and for all inherited mitochondrial respiratory chain

disorders in the US. It has also been granted a Rare Pediatric Disease (RPD) designation in the US for the treatment of MELAS.

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About Khondrion

Khondrion is a privately-held clinical-stage biopharmaceutical company discovering and developing therapies targeting mitochondrial disease. Founded by Prof. Jan Smeitink, a world-leader in mitochondrial medicine, the company is advancing its proprietary science through a wholly-owned clinical and preclinical small molecule pipeline of potential medicines.

The company's in-house discovery engine is using unique live-cell imaging technologies, patient-derived cell lines and predictive cell-based disease models to build a portfolio of promising compounds. Active discovery programmes are underway developing new therapies, biomarkers and new read-out technologies in the field of mitochondrial diseases.

To accelerate the discovery and development of its potential medicines for mitochondrial diseases, Khondrion collaborates with a global clinical and academic network and patient organisations internationally. Khondrion is headquartered in Nijmegen, The Netherlands. For more information visit www.khondrion.com.

About mitochondrial disease

Mitochondrial disease occurs when mitochondria, found within all cells of the human body and responsible for producing the energy necessary for cells to function, are defective. This can result in a wide range of serious and debilitating illnesses occurring shortly after birth or later in life. Signs and symptoms of these can include: cognitive problems, learning disabilities, blindness, deafness, heart failure, diabetes, fatigue, intolerance to exercise, muscle weakness and gait problems, and stunted growth. Orphan diseases of the oxidative phosphorylation system like Leigh disease, MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) spectrum disorders including MIDD (maternally inherited diabetes and deafness), LHON (Leber's hereditary optic neuropathy) and other respiratory chain/ oxidative phosphorylation disorders, are all examples of mitochondrial disease.