Khondrion announces first patients dosed in Phase IIb study of Sonlicromanol for mitochondrial diseases

Study will examine impact on cognitive function from one of the most advanced disease-modifying drug treatments for mitochondrial disease in development

NIJMEGEN, the Netherlands – Monday January 27, 2020: Khondrion, a clinical-stage pharmaceutical company discovering and developing therapies targeting mitochondrial disease, today announces that the first patients have been successfully dosed in its phase IIb KHENERGYZE study of Sonlicromanol (previously known as KH176), its wholly-owned lead asset in development to treat a range of mitochondrial diseases.

KHENERGYZE is being initiated at three internationally recognised mitochondrial disease centres in Europe – Radboud University Medical Center, Nijmegen, Netherlands; Newcastle University, United Kingdom and Ludwig-Maximilians-University of Munich, Germany. The double-blind, randomised, placebo-controlled three-way cross-over study examining cognitive function will recruit patients with a specific genetically confirmed DNA mutation in the mitochondrial transfer $RNA^{Leu(UUR)}$ (MT-TL1m.3243A>G). This mutation is responsible for MELAS spectrum disorders, including MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) and MIDD (maternally inherited diabetes and deafness) syndromes, and mixed phenotypes.

The study's primary objective is to evaluate the dose-effect of Sonlicromanol on the attention domain score of cognitive functioning, as assessed by a computerized Cogstate visual identification test. Results are expected in the second half of 2020.

Sonlicromanol is a potentially first-in-class oral small molecule and one of the most advanced disease-modifying drug treatments for mitochondrial disease in development, having shown clinical proof of concept and efficacy, and a well-tolerated safety profile in phase I and IIa studies. It has been granted Orphan Drug Designation for MELAS spectrum disorders, Leigh disease and patients with MIDD in Europe and for all inherited mitochondrial respiratory chain disorders in the USA.

Prof. Dr. Jan Smeitink, Chief Executive Officer at Khondrion, said: *"The start of our phase IIb trial is another significant milestone for Khondrion as we aim to bring this important treatment to patients suffering from these devastating mitochondrial diseases. This study is targeting the most frequently encountered group of mitochondrial disorders, estimated to affect around 50,000 people in Europe, US and Japan. Their impact on everyday life can be significant, particularly from cognitive impairment which affects everything we do involving thought or memory – whether that's getting ready for work, chatting with friends or planning for the future.*

"We believe Sonlicromanol has the potential to be an important disease-modifying treatment option and could address a significant unmet medical need and improve the lives of patients with mitochondrial diseases."

Further details of the KHENERGYZE study are available here through ClinicalTrials.gov.

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About Khondrion

Khondrion is a clinical-stage pharmaceutical 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.

Khondrion's lead asset, Sonlicromanol, is a potentially first-in-class oral small molecule in phase IIb clinical development to treat a range of mitochondrial diseases including m.3243A>G spectrum disorders including MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes), maternally inherited diabetes and deafness (MIDD) and mixed phenotypes. It has been granted Orphan Drug Designation for MELAS spectrum disorders, Leigh disease and patients with MIDD in Europe and for all inherited mitochondrial respiratory chain disorders in the USA.

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 life, are defective. This can result in a wide range of serious and debilitating illnesses, signs and symptoms of which 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, 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.

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