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Khondrion Announces First Patient Dosed in Pivotal Phase 3 KHENERFIN Study of Sonlicromanol in Mitochondrial DNA 3243A>G Primary Mitochondrial Disease

- *52-week Phase 3 trial evaluating the efficacy and safety of sonlicromanol, a novel brain-penetrant redox-modulator with anti-ferroptotic and anti-inflammatory properties, in adult patients with the most common genetic defect causing primary mitochondrial disease, m.3243A>G*
- *Primary endpoints focus on most bothersome and frequently occurring effects of disease – chronic fatigue and muscle weakness – supported by consistent signals observed in Phase 2b program*

NIJMEGEN, The Netherlands – April 16, 2026 – Khondrion today announced that the first patient has been dosed in the pivotal, randomized, placebo-controlled Phase 3 *KHENERFIN* study (NCT 06451757) evaluating the efficacy and safety of sonlicromanol, its investigational small molecule for m.3243A>G-related Primary Mitochondrial Disease.

"The initiation of patient dosing in our Phase 3 KHENERFIN study marks an important milestone in the development of a potential treatment for patients with m.3243A>G primary mitochondrial disease," said Jasper Levink, CEO of Khondrion. "This trial is designed to rigorously evaluate the safety and efficacy of sonlicromanol in a larger, randomized setting, with endpoints reflecting key aspects of disease burden, building on the signals observed in our earlier clinical program."

Dr. Mirian Jansen, head of the clinical metabolic department of the Radboudumc and PI in the KHENERFIN study noted: "m.3243A>G mitochondrial disease is a progressive and debilitating condition with significant unmet medical need, affecting patients across multiple organ systems and often leading to increasing disability over time. As investigators, we are committed to advancing this Phase 3 study and working closely with patients to ensure high-quality data collection on outcomes that matter in daily life. This trial is designed to determine whether this investigational therapy can meaningfully impact patient function and fatigue."

"The most burdensome symptoms m.3243A>G patients experience are fatigue and muscle weakness. These symptoms are often debilitating and impact every area of life. The initiation of the Phase 3 *KHENERFIN* study by Khondrion is a significant achievement and provides hope to the international mitochondrial disease community. As the Chair of International Mito Patients (IMP), which represents 25 mitochondrial disease patient advocacy groups across five continents, we are encouraged by the progress being made in research and drug development for those living with Primary Mitochondrial Diseases. We optimistically await the outcome of the trial." stated Paula Morandi, Chair of IMP.

Jan Smeitink, Khondrion's founder and CMO continued: "The KHENERFIN study will enroll up to 220 adult patients from 18 years and older across Europe, the United Kingdom and the US with genetically confirmed m.3243A>G Primary Mitochondrial Disease. Participants will be randomized 1:1 to receive sonlicromanol or placebo over a 52-week treatment period. Participants will receive 90 mg sonlicromanol or matching placebo as dispersible tablets twice daily. The study's two independent primary endpoints are change in NeuroQoL Fatigue Short Form score and performance on the 5-times sit-to-stand test, reflecting key aspects of disease burden."

NOTES TO EDITORS

About Khondrion
Khondrion is a late-stage clinical biopharmaceutical company focused on developing therapies for patients with primary mitochondrial disease (PMD). Its lead asset, sonlicromanol, is a brain-penetrant redox modulator with anti-inflammatory properties designed to target key pathways underlying mitochondrial dysfunction. Sonlicromanol is being developed as a potential disease-modifying therapy targeting core disease mechanisms across multiple organ systems.

Sonlicromanol has been evaluated in multiple clinical trials in patients with m.3243A>G PMD, including a randomized Phase 2b program and long-term extension studies. Named patients have received sonlicromanol for over three years, providing long-term safety and treatment experience.

Sonlicromanol has received orphan drug designation in Europe for inherited mitochondrial oxidative phosphorylation defects, and in the United States for inherited mitochondrial respiratory chain disorders. It has also been granted Rare Pediatric Disease Designation in the United States for MELAS.

Khondrion is also exploring additional applications of its redox-modulating compounds in other diseases characterized by mitochondrial dysfunction.

About Primary Mitochondrial Disease
Primary mitochondrial diseases are a group of genetic disorders caused by defects in mitochondrial function, leading to impaired cellular energy production and progressive cellular dysfunction and loss. These conditions can affect multiple organ systems and are associated with a wide range of symptoms that worsen over time, including fatigue, muscle weakness, neurological impairment, diabetes, and cardiac involvement.

The m.3243A>G variant in mitochondrial DNA is one of the most common genetic causes of primary mitochondrial disease and is associated with a spectrum of clinical phenotypes, including MELAS, maternally inherited diabetes and deafness (MIDD), and mixed multi-system presentations.

Learn more: https://www.khondrion.com/melas-syndrome/.

Forward-looking statements
This press release contains forward-looking statements regarding, among other things, the expected conduct, progress and timing of the company's clinical trials. These statements are based on current expectations and assumptions and are subject to risks and uncertainties beyond the company's control that could cause actual results to differ materially. Forward-looking statements may be identified by words such as "aim," "believe," "expect," "anticipate," "plan," "may," "will," "could," and similar expressions. Except as required by law, the company undertakes no obligation to update these statements.

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