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## Khondrion BV receives positive opinion from COMP on Orphan Drug Designation for treatment of Leigh syndrome

NIJMEGEN – Khondrion, the Dutch biopharmaceutical company focusing on small molecule therapeutics for mitochondrial diseases, announces today that it has received a positive opinion from the Committee on Medicinal Products (COMP) of the European Medicines Agency (EMA) for Orphan Drug Designation of its frontrunner compound KH176 to treat Leigh syndrome. An orphan designation allows a pharmaceutical company to benefit from incentives from the European Union to develop a medicine for a rare disease, such as reduced fees in protocol assistance and protection from competition once the medicine is placed on the market. Applications for orphan designation are examined by the COMP, which adopts an opinion that is forwarded to the European Commission. The European Commission finally decides whether to grant an orphan designation for the medicine in question. This decision follows a few weeks after the COMP opinion is issued.

Leigh syndrome is a progressive, early fatal disease caused by a defect in the cell's powerhouses, the mitochondria. "The positive COMP opinion on Orphan Drug Designation is a pivotal milestone in the development of KH176 to treat this rare and devastating disease" said Jan Smeitink, Khondrion's CEO and Professor of Mitochondrial Medicine at the Radboud University Medical Centre, Nijmegen, The Netherlands . "The positive opinion will enable resources for continued development, but more importantly the positive opinion provides an additional avenue with the EMA on the best path for bringing KH176 to market".

**About mitochondrial disease**

Mitochondrial diseases are devastating, early fatal, multi-system disorders that affect 1:5000 live births. These rare diseases are caused by mutations in two different genomes: the nuclear DNA and the mitochondrial DNA. Mutations in the latter are maternally transmitted and consequently every child born in the family (100% recurrence risk) can be affected. As mitochondria, the cells powerhouses, are present in virtually every cell of the body all organs and tissues can be affected leading to symptoms like mental retardation, epilepsy, deafness, blindness, heart- and liver failure, and muscle weakness and severe exercise intolerance.

**About Leigh syndrome**

Leigh syndrome belongs to the increasing family of mitochondrial diseases caused by either nuclear or mitochondrial DNA gene defects affecting the so-called oxidative phosphorylation system (OXPHOS). OXPHOS is the final biochemical pathway involved in the cells energy currency, ATP. Disturbances of the OXPHOS system lead to a plethora of cellular consequences disturbing normal cell metabolism. Leigh disease is highly progressive often early fatal disorder affecting organs and tissues with a high-energy demand, like the brain and the skeletal muscle for which there are no approved treatments.

**About small molecules**

For the synthesis, maintenance and functioning of mitochondria, cells need about 1000-1500 genes being 10% of the human genome. Currently, about 250 different gene defects are known of which more than 100 are involved in the process of oxidative phosphorylation, the final pathway in the production of the cell's energy. Common consequences include the increased production of reactive (toxic) oxygen species, an altered cellular redox-state, and disruption of the cellular mitochondrial network. Khondrion's small molecules are able to (partially) correct most, if not all of these cellular alterations, and are currently in development for mitochondrial disease affecting the OXPHOS-system. Khondrion's small molecule pipeline includes compounds in different stages of development and different mode of actions.

**KH176**

KH176 is an orally bio-available small molecule developed by Khondrion for the treatment of Leigh syndrome and other mitochondrial diseases. KH176 is a member of a class of drugs essential for the control of oxidative and redox pathologies. It's expected that KH176 will enter the clinical trial phase mid 2015.

**About Khondrion**

Khondrion is an innovative Dutch biopharmaceutical mitochondrial medicine company focusing on developing small molecule therapeutics for mitochondrial diseases. The potential of several lead compounds to serve as new treatment modalities for mitochondrial disease is currently being explored. Thanks to its strategic partnership with the Nijmegen Centre for Mitochondrial Disorders

(www.ncmd.nl) of the Radboud University Medical Centre, Nijmegen, The Netherlands, Khondrion has access to all mitochondrial tools, technologies and expertise. Besides, Khondrion has established collaborations with university research groups around the world as well as small, medium and large enterprises. Khondrion is a privately held biopharmaceutical company, among others supported by the Dutch Foundations Energy4All, Join4Energy, Tim Foundation, Zeldzame Ziekten Fonds, the Prinses Beatrix Fonds, and National (NWO, ALW, ZonMW) and European Governments (Marie-Curie ITN, Eurostars). For more information, please visit www.khondrion.com .

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