

Santhera Announces Phase 4 LEROS Trial with Raxone® Met Primary Endpoint in Patients with Leber's Hereditary Optic Neuropathy

Pratteln, Switzerland, June 23, 2021 – Santhera Pharmaceuticals (SIX: SANN) announces positive topline results from its long-term Phase 4 LEROS study with Raxone® (idebenone) in the treatment of Leber's hereditary optic neuropathy (LHON). The primary endpoint, proportion of eyes with clinically relevant benefit after 12 months treatment with Raxone versus untreated patients from an external control group, was met with high statistical significance ($p=0.002$). The efficacy data confirm and extend previous findings which demonstrated that Raxone can prevent further vision loss and promote recovery of vision in LHON patients.

"Raxone® represents an indispensable therapy for patients with LHON and still today is the first and only medicine approved for this condition," said **Dario Eklund, CEO of Santhera**. "The strong evidence of efficacy will also support market access in countries where this is not yet the case, allowing patients who have no therapeutic alternative to benefit from treatment with Raxone."

Santhera holds the EU marketing authorization for Raxone (idebenone) and out-licensed rights to the product outside North America and France for the treatment of LHON to Chiesi Group. Subject to the achievement of certain commercial milestones for Raxone, Santhera is entitled to contingent variable near- to mid-term milestone payments from Chiesi Group of up to EUR 49 million.

LEROS, a Phase 4 externally-controlled open-label intervention study, was designed to confirm the efficacy of Raxone in patients with LHON after 12 months of treatment and to further assess the long-term efficacy and safety of Raxone over 24 months (ClinicalTrials.gov Identifier: NCT02774005). The study, which was designed with guidance and approval from the European Medicines Agency (EMA), together with the natural history data collection used as an external control, were part of a post-authorization commitment.

The positive results confirm and extend earlier findings from the double-blind, randomized, placebo-controlled RHODOS trial ([1], ClinicalTrials.gov Identifier: NCT00747487) and data from an Expanded Access Program (also part of the post-authorization commitment), which both showed clinically relevant beneficial responses to Raxone in patients with LHON [2]. Treatment benefit manifests as a clinically relevant stabilization (CRS) or a clinically relevant recovery (CRR) of visual acuity or both [3].

"These results confirm the efficacy of idebenone in the treatment of LHON by significantly increasing the chances for vision recovery and/or for prevention of further vision loss," said **Thomas Klopstock, MD, Professor for Neurology at the University of Munich, LHON researcher and principal LEROS study investigator**. "LHON is a particularly devastating condition because sufferers, who are otherwise healthy and often young, rapidly become bilaterally blind within a few months. Most will remain permanently blind if untreated."

The primary objective of the LEROS study was to assess the efficacy of Raxone (150 mg tablets, daily dose of 900 mg) in the promotion of recovery or stabilization of visual acuity (VA) after 12 months. This was evaluated in patients starting treatment up to one year after the onset of symptoms, compared to an external untreated, matched, natural history (NH) control group. The study, conducted in 199 patients, met its pre-specified and agreed primary endpoint and key secondary objectives, including confirmation of its overall favorable safety profile during long-term treatment. After 12 months of treatment, 43.1% of patients treated with Raxone achieved a clinically relevant benefit (CRB) with high statistical significance compared to 20.7% in the NH group ($p=0.002$; OR [95% CI]: 2.286 [1.352; 3.884]). The clinically relevant beneficial treatment effect was maintained at 24 months compared to the NH group ($p=0.0297$; OR [95% CI]: 2.082 [1.074; 4.099]). Positive results were also seen after 12 months of treatment in patients starting Raxone treatment >1 year after the onset of symptoms, one of the secondary endpoints, compared to the NH population ($p=0.0058$; OR [95% CI]: 1.994 [1.219; 3.296]). Santhera conducted the LEROS trial in 31 study sites across nine European countries and the USA.

References:

- [1] Klopstock T, et al. Brain. 2011 Sep;134(Pt 9):2677-86.
- [2] Raxone Summary of Product Characteristics, available [here](#)
- [3] Catarino CB et al. Real-World Clinical Experience With Idebenone in the Treatment of Leber Hereditary Optic Neuropathy. J Neuroophthalmol. 2020 Dec;40(4):558-565.

About Leber's Hereditary Optic Neuropathy and Raxone

Leber's hereditary optic neuropathy (LHON) is a heritable genetic disease-causing profound vision loss and blindness. The disease presents in young adulthood, more commonly in males, as rapid, painless loss of central vision, usually leading to permanent bilateral blindness within a few months of the onset of symptoms. About 95% of patients harbor one of three pathogenic mutations of the mitochondrial DNA, which cause a defect in the complex I subunit of the mitochondrial respiratory chain. This defect leads to decreased cellular energy (ATP) production, increased reactive oxygen species (ROS) production and retinal ganglion cell dysfunction, which cause progressive loss of visual function.

Raxone® (idebenone), a synthetic short-chain benzoquinone and a cofactor for the enzyme NAD(P)H:quinone oxidoreductase (NQO1), has shown to promote recovery of visual acuity by circumventing the complex I defect, thus reducing and scavenging ROS, as well as restoring cellular energy levels in retinal ganglion cells. The new data confirm previous findings that around 50% of patients may benefit from treatment, either by preventing from progression of visual acuity loss or by experiencing a clinically relevant recovery of visual acuity. In September 2015, Raxone received the marketing authorization from the European Medicines Agency (EMA) for the treatment of patients with Leber's hereditary optic neuropathy (LHON).

About Santhera

Santhera Pharmaceuticals (SIX: SANN) is a Swiss specialty pharmaceutical company focused on the development and commercialization of innovative medicines for rare neuromuscular and pulmonary diseases with high unmet medical need. Santhera has an exclusive license for all indications worldwide to vamorolone, a first-in-class dissociative steroid with novel mode of action, which was investigated in a pivotal study in patients with DMD as an alternative to standard corticosteroids. The clinical stage pipeline also includes lonodelestat (POL6014) to treat cystic fibrosis (CF) and other neutrophilic pulmonary diseases as well as an exploratory gene therapy approach targeting congenital muscular dystrophies. Santhera out-licensed rights to its first approved product, Raxone® (idebenone), outside

North America and France for the treatment of Leber's hereditary optic neuropathy (LHON) to Chiesi Group. For further information, please visit www.santhera.com.

Raxone® is a trademark of Santhera Pharmaceuticals.

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