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Santhera Completes Patient Enrollment in Phase IV Long-term Study with Raxone® for the Treatment of Leber's Hereditary Optic Neuropathy

Pratteln, Switzerland, March 12, 2019 – Santhera Pharmaceuticals (SIX: SANN) announces that it has completed patient enrollment in the ongoing Phase IV study (LEROS) with Raxone® (idebenone) for the treatment of Leber's hereditary optic neuropathy (LHON). Results from the 24-month active treatment study conducted in 31 study centers in Europe and the USA are expected in 2021.

LEROS is a Phase IV, external natural history controlled, open-label intervention study to further assess the efficacy and safety of long-term treatment with Raxone® in patients with LHON (ClinicalTrials.gov Identifier: NCT02774005). Patients were eligible for enrolment up to five years after the initial onset of symptoms of vision loss and were stratified according to their time since onset of vision loss to investigate the influence of disease duration on treatment efficacy.

The primary objective of the trial is to assess the efficacy of Raxone to improve or stabilize visual acuity (VA) in patients starting treatment up to one year after the onset of vision loss, compared to an external natural history control group.

Following a pre-planned sample size recalculation, the study has now completed recruitment with 197 patients enrolled. Study participants are treated with Raxone (150 mg idebenone tablets, daily dose of 900 mg) for 24 months. Santhera is conducting the LEROS trial in 31 study sites across nine European countries and the USA and expects to complete the study by the second quarter 2021.

The LEROS study builds on the results from the double-blind, randomized, placebo-controlled RHODOS trial and data from an Expanded Access Program which demonstrated clinically meaningful outcomes of Raxone treatment for patients with LHON [1]. Treatment benefit manifests as a clinically relevant stabilization (CRS) or a clinically relevant recovery (CRR) of visual acuity or both. [2]

"I am delighted that we have now completed patient enrollment of this long-term post-authorization trial with Raxone in LHON," stated **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development at Santhera**. "We are especially grateful to trial participants and study personnel for their tremendous support in advancing this important study which will provide useful insights to further inform physicians on how to best use Raxone for the treatment of their LHON patients."

In September 2015, the European Commission granted a marketing authorization valid throughout the European Union for Raxone for the treatment of visual impairment in adults and adolescents with LHON. With approval under exceptional circumstances, several specific obligations – including the LEROS study – were agreed with the European Medicines Agency to further assess the efficacy and safety under routine use and longer term treatment.

In addition to the ongoing LEROS trial, Santhera has recently completed an Expanded Access Program with 111 patients receiving Raxone treatment, as well as a retrospective natural history data collection with data from 592 patients. Santhera currently is conducting a multicenter, prospective, non-interventional post-authorization safety study (PASS) for patients with LHON treated with Raxone (ClinicalTrials.gov Identifier: NCT02771379).

Several abstracts with additional data from the development program with Raxone in the treatment of LHON have been accepted for presentation at upcoming leading international ophthalmological conferences including NANOS (March 16-21, 2019 in Las Vegas, USA), ARVO (April 28-May 2, 2019 in Vancouver, Canada) and EUNOS (June 16-19, 2019 in Porto, Portugal).

References:

[1] Raxone Summary of Product Characteristics, available here
[2] Llòria X, et al. Poster Presentation, NANOS, 2018; Hawaii, USA

About Leber's Hereditary Optic Neuropathy and the Therapeutic Use of 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. Current data demonstrate 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.

Raxone for the treatment of LHON has orphan drug status in the EU, US, Switzerland and South Korea.

About Santhera

Santhera Pharmaceuticals (SIX: SANN) is a Swiss specialty pharmaceutical company focused on the development and commercialization of innovative medicines for rare and other diseases with high unmet medical needs. The portfolio comprises clinical stage and marketed treatments for neuro-ophthalmologic, neuromuscular and pulmonary diseases. Santhera's Raxone® (idebenone) is authorized in the European Union, Norway, Iceland, Liechtenstein, Israel and Serbia for the treatment of Leber's hereditary optic neuropathy (LHON) and is currently commercialized in more than 20 countries. For further information, please visit www.santhera.com.

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