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Santhera Submits Marketing Authorization Application to the European Medicines Agency for Puldysa® (Idebenone) in Duchenne Muscular Dystrophy

Pratteln, Switzerland, May 27, 2019 – Santhera Pharmaceuticals (SIX: SANN) announces that it has submitted a marketing authorization application (MAA) for Puldysa® (idebenone) for the treatment of respiratory dysfunction in patients with Duchenne muscular dystrophy (DMD) to the European Medicines Agency (EMA). Santhera is seeking conditional marketing authorization (CMA).

The indication for Puldysa sought under CMA is the treatment of respiratory dysfunction in patients with DMD who are not using glucocorticoids. The MAA is supported by data from Santhera's Phase II (DELPHI) study, the long-term DELPHI-Extension study, the pivotal Phase III (DELOS) study [1-5] and the recently completed SYROS study, a collection of long-term data from patients who completed the DELOS study and continued to be treated with idebenone for up to six years [6].

"The new data included in this regulatory submission confirm clinically relevant patient benefits and long-term therapeutic efficacy with idebenone in patients with DMD. Thereby, we have closed earlier data gaps and respond to requirements from the regulatory authorities," said **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development at Santhera**.

In line with previous communications, Santhera plans to submit a new drug application (NDA) with the US FDA following the completion of the currently ongoing double-blind, placebo-controlled Phase III (SIDEROS) study that investigates the efficacy and safety of idebenone in delaying the loss of respiratory function in patients with DMD taking glucocorticoid steroids over a period of 18 months (ClinicalTrials.gov Identifier: NCT02814019; www.siderosdmd.com). With 266 patients to be enrolled, SIDEROS is the largest actively recruiting clinical trial in DMD. To date, the study has 214 patients enrolled at approximately 60 clinical trial sites in Europe, the US and Israel, with patient recruitment expected to complete in 4Q 2019. Eligible patients who complete SIDEROS are offered to enroll in the open-label SIDEROS-Extension study (ClinicalTrials.gov Identifier: NCT03603288).

Idebenone for the treatment of DMD has been granted orphan drug designation by European, US, Swiss and Australian authorities, and it has fast track designation in the US.

References

[1] Buyse et al. (2015), The Lancet 385:1748-1757
[2] McDonald et al. (2016), Neuromuscular Disorders 26:473-480
[3] Buyse et al. (2017), Pediatric Pulmonology 52:580-515
[4] Mayer et al. (2017), Journal of Neuromuscular Diseases 4:189-198
[5] Buyse et al. (2018), Journal of Neuromuscular Diseases 5: 419-430
[6] Posters presented at the 2019 MDA Clinical & Scientific Conference

About Duchenne Muscular Dystrophy

DMD is one of the most common and devastating types of progressive muscle weakness and degeneration starting at an early age and leading to early morbidity and mortality due to respiratory failure. It is a genetic, degenerative disease that occurs almost exclusively in males with an incidence of up to 1 in 3,500 live male births worldwide. DMD is characterized by a loss of the protein dystrophin, leading to cell damage, impaired calcium homeostasis, elevated oxidative stress and reduced energy production in muscle cells. With age, progressive respiratory muscle weakness affecting thoracic accessory muscles and the diaphragm causes respiratory disease, impaired clearance of airway secretions, recurrent pulmonary infections due to ineffective cough, and eventually respiratory failure. There is currently no treatment approved for slowing loss of respiratory function in patients with DMD.

About Idebenone in Duchenne Muscular Dystrophy

Idebenone is a synthetic short-chain benzoquinone and a cofactor for the enzyme NAD(P)H:quinone oxidoreductase (NQO1) capable of stimulating mitochondrial electron transport, reducing and scavenging reactive oxygen species (ROS) and supplementing cellular energy levels.

DELOS was a Phase III, double-blind, placebo-controlled 52-week study which randomized 64 patients, not taking concomitant steroids, to receive either idebenone (900 mg/day) or matching placebo. The study met its primary endpoint, the change from baseline in peak expiratory flow (PEF) expressed as percent of predicted, which demonstrated that idebenone can slow the loss of respiratory function. Supportive data for idebenone were shown in the Phase II double-blind, placebo-controlled DELPHI study and its 2-year open-label extension study (DELPHI-E).

SYROS was a prospectively planned, retrospective collection of long-term respiratory function data from 18 patients who completed the DELOS study and subsequently received idebenone (900 mg/day) under Expanded Access Programs (EAPs). The SYROS study showed that the previously observed beneficial effect of idebenone in reducing the rate of respiratory function decline was maintained for up to six years during treatment.

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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