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Santhera Completes Enrollment of Phase 3 SIDEROS Study with Puldysa® (Idebenone) in Duchenne Muscular Dystrophy (DMD)

Pratteln, Switzerland, May 20, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces full recruitment of its Phase 3 SIDEROS study with idebenone in Duchenne muscular dystrophy (DMD). The sample-size and variability re-assessment performed according to study protocol demonstrated that with the currently enrolled patients the study has a very high power (>99%). Given the strong powering of SIDEROS, the Company is now assessing the potential of conducting an interim analysis to test for overwhelming efficacy with a view of completing the trial early.

With patient recruitment into the 18-month international SIDEROS trial in its final stages, Santhera performed the planned sample size and variability re-assessment in accordance with the study protocol to confirm adequate study power. This blinded analysis showed that variability is lower than anticipated per protocol and, with the current number of enrolled patients, the SIDEROS study has a very high power of over 99% to detect a treatment difference. On this basis, Santhera has taken the decision to complete enrollment into the SIDEROS trial. At present, approximately half of the recruited patients in SIDEROS have completed 18 months of treatment and about two thirds of patients have completed 12 months of treatment.

Owing to the decision to complete enrollment of this advanced study, its very high power as well as the urgent unmet medical need, Santhera is assessing the potential of conducting an interim analysis to test for overwhelming efficacy with a view of completing the trial early. Such an interim analysis would be performed by the independent Data and Safety Monitoring Board (DSMB) to preserve the integrity of the study. If overwhelming efficacy is not established in the interim analysis, the study could continue as planned with the currently enrolled patients and the corresponding high power. However, if overwhelming efficacy is demonstrated, it would be considered unethical to continue with the blinded study and the Company would decide to end the study later this year. This would result in acceleration of corresponding regulatory filings by approximately one year both in Europe and the US.

”Santhera is the only company that has dedicated its clinical development program towards finding a treatment to preserve respiratory function in DMD. The large Phase 3 SIDEROS study was designed to confirm the efficacy of idebenone in patients with respiratory function decline who are concurrently taking glucocorticoids,” said **Gunnar Buyse, MD, PhD, Professor of Child Neurology** at the University Hospitals Leuven (Belgium), SIDEROS Principal Investigator and Lead Investigator for Europe. “We are truly excited that SIDEROS has completed recruitment and is on track to generate a comprehensive dataset in an area of such high unmet need.”

“There are currently no approved treatments to slow the rate of respiratory function decline leading to respiratory failure, which remains a leading cause of premature death in young men at the advanced stages of DMD,” commented **Oscar Henry Mayer, MD, Medical Director of the Pulmonary Function Testing Laboratory** at the Children’s Hospital of Philadelphia and Lead Investigator for US. “By slowing

the rate of respiratory function decline, we open the possibility to delaying the time to chronic respiratory failure and the need to assisted ventilation and reducing the risk of other life-threatening respiratory complications."

"We are delighted to have reached such an important milestone and wish to express our sincere thanks to patients and families, caregivers, physicians and study personnel for their support and commitment," added **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development of Santhera**.

SIDEROS, the largest currently ongoing clinical trial in DMD, is a double-blind randomized placebo-controlled Phase 3 study evaluating the efficacy of idebenone in delaying the loss of respiratory function in patients with DMD. Patients on any stable glucocorticoid treatment scheme and irrespective of the underlying dystrophin mutation or ambulatory status were randomized to receive oral idebenone (900 mg/day, divided in three doses) or placebo for 18 months. The primary endpoint of the trial estimates the treatment difference in FVC%p (forced vital capacity % predicted). Patients completing the trial are offered the opportunity to enroll in an open label extension study where all patients receive idebenone. The study is currently conducted in 62 sites in the United States, Europe and Israel. Further information is available at ClinicalTrials.gov NCT#02814019.

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 is a Phase 3, double-blind, placebo-controlled 52-week study which randomized 64 patients, not taking concomitant glucocorticoids, 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 and reduces the risk of bronchopulmonary adverse events [1-5]. Supportive data for idebenone were shown in the Phase 2 double-blind, placebo-controlled DELPHI study and its 2-year open-label extension study (DELPHI-E).

SYROS is 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 [6].

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 52:508-515
[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] Servais et al. (2019), Neuromuscular Disorders. DOI: https://doi.org/10.1016/j.nmd.2019.10.008

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 is building a Duchenne muscular dystrophy (DMD) product portfolio to treat patients irrespective of causative mutations, disease stage or age. A marketing authorization application for Puldysa® (idebenone) is currently under review by the European Medicines Agency. Santhera has an option to license vamorolone, a first-in-class anti-inflammatory drug candidate with novel mode of action, currently investigated in a pivotal study in patients with DMD to replace standard corticosteroids. The clinical stage pipeline also includes lonodelestat (POL6014) to treat cystic fibrosis (CF) and other neutrophilic pulmonary diseases, as well as omigapil and an exploratory gene therapy approach targeting congenital muscular dystrophies. Santhera out-licensed ex-North American rights to its first approved product, Raxone® (idebenone), for the treatment of Leber's hereditary optic neuropathy (LHON) to Chiesi Group. For further information, please visit www.santhera.com.

Raxone® and Puldysa® are trademarks of Santhera Pharmaceuticals.

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