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Santhera's SYROS Study Shows Long-term Efficacy with Idebenone in Slowing Respiratory Function Loss in Patients with Duchenne Muscular Dystrophy

Pratteln, Switzerland, February 25, 2019 – Santhera Pharmaceuticals (SIX: SANN) announces results from the SYROS study demonstrating that long-term treatment with idebenone consistently reduced the rate of respiratory function loss in patients with Duchenne muscular dystrophy (DMD) for up to 6 years in a real-world setting. This long-term data further supports the potential for idebenone to modify the course of respiratory function decline and delay the time to clinically relevant milestones.

The SYROS study was a prospectively planned collection of long-term, retrospective real-world data from patients who completed the positive Phase III DELOS trial (18 out of 64) and were subsequently treated with idebenone (900 mg/day) for on average 4.2 years (range 2.4-6.1 years) under Expanded Access Programs (EAPs). The primary objective of this study was to evaluate the long-term evolution of the respiratory function in patients who maintained treatment with idebenone for up to 6 years compared to their preceding off-idebenone period.

The result of this study, which is consistent with outcomes from the pivotal DELOS study, demonstrated that:

- Switching to and maintaining long-term treatment with idebenone reduced the annual rate of decline in forced vital capacity percent of predicted (FVC%p) by 50%.
- The treatment effect was consistently maintained year-on-year for up to 6 years.
- These findings are further supported by consistent reductions in the rate of both inspiratory and expiratory respiratory function loss over the same period.
- Prolonged treatment with idebenone also reduced the risk of important patient-relevant outcomes, including bronchopulmonary adverse events and hospitalizations due to respiratory causes.

"We are very excited to see that the significant treatment effect with idebenone observed in our 52-week Phase III DELOS study is maintained over the long-term," said **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development at Santhera.** "The new findings are highly relevant for DMD patients in respiratory decline who have an urgent need for a therapy to modify the declining course of respiratory function decline and ultimately delay the need for assisted ventilation."

The findings from the SYROS study have been accepted for presentation at the 2019 MDA Clinical & Scientific Conference (April 13-17, 2019, in Orlando) and will be submitted for publication in a peer-reviewed journal.

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. Additional respiratory function and clinical outcomes supported the results of the primary endpoint [1-5].

SYROS was a prospectively planned collection of long-term, retrospective real-world respiratory function data from 18 patients who completed the DELOS study and subsequently received idebenone (900 mg/day) under Expanded Access Programs (EAPs). These long-term data showed that the previously observed beneficial effect of idebenone in reducing the rate of respiratory function decline was maintained over a >4 year average treatment period.

References:

1. Buyse et al., 2015; Lancet 385:1748-57
2. McDonald et al., 2016; Neuromuscular Disorders 26: 473–480
3. Mayer et al. 2017; J Neuromuscular Diseases. 4:189-98
4. Buyse et al., 2017; Pediatric Pulmonology 52:508-515
5. Buyse et al. 2018; J Neuromuscular Diseases 5: 419–430

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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