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Santhera Updates on U.S. Regulatory Filing for Raxone[®] (idebenone) in Duchenne Muscular Dystrophy (DMD)

Liestal, Switzerland, July 14, 2016 – Santhera Pharmaceuticals (SIX: SANN) announces that it has received written correspondence from the U.S. Food and Drug Administration (FDA) on its proposed subpart H approval pathway for Raxone in DMD patients not taking concomitant glucocorticoids. Santhera had proposed that the planned SIDEROS trial would provide confirmatory evidence of efficacy in these patients whilst expanding the label to include the treatment of glucocorticoid-using patients.

From its review of this strategy, the FDA concluded that results from the SIDEROS trial, which is powered to detect a difference in the established surrogate endpoint Forced Vital Capacity percent predicted (FVC%p) in glucocorticoid-using patients, should be provided at the time of filing to support an NDA for the treatment of DMD patients irrespective of their glucocorticoid use status.

The protocol of the SIDEROS trial has previously been reviewed by the FDA which confirmed that this trial has the potential, if positive, to provide the necessary efficacy data, along with data from previous trials to support NDA filing in patients with DMD.

“While we are disappointed that the FDA does not support our plan to file an NDA for Raxone under subpart H for patients not using concomitant glucocorticoids, we now have clarity that successful completion of the SIDEROS trial will provide the necessary data to support NDA filing for Raxone in all DMD patients irrespective of the glucocorticoid use status,” commented **Thomas Meier**, PhD, CEO of Santhera. “Enrolment in the SIDEROS trial will start shortly and we are committed to working closely with the FDA, clinical experts and the DMD patient community to make Raxone available for all DMD patients in the U.S. as quickly as possible.”

About the SIDEROS Trial

SIDEROS is a Phase III double-blind, randomized, placebo-controlled trial of Raxone in Duchenne muscular dystrophy (DMD) patients receiving concomitant glucocorticoids. Patients with declining respiratory function on any stable glucocorticoid treatment scheme irrespective of the underlying dystrophin mutation or ambulatory status will be eligible for participation. Study participants will receive either Raxone (900 mg/day; given as 2 tablets 3 times a day with meals) or placebo for 78 weeks (18 months). The primary endpoint of the trial is change from baseline to week 78 in forced vital capacity % predicted (FVC%p). Secondary endpoints include changes from baseline in % predicted peak expiratory flow (PEF%p), time to first 10% decline in FVC, and change from baseline in inspiratory flow reserve. Patients completing the trial will be offered the opportunity to enroll in an open label extension study where all patients receive Raxone. It is currently expected that the results of the SIDEROS trial will become available in 2H 2019.

About Raxone[®] (Idebenone) in Duchenne Muscular Dystrophy and Regulatory Status

Duchenne muscular dystrophy (DMD) is one of the most common and devastating types of muscle degeneration and results in rapidly progressive muscle weakness. 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. This results in progressive muscle weakness and wasting and early morbidity and mortality due to respiratory failure.

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 trial which randomized 64 patients, not taking concomitant glucocorticoids, to receive either Raxone (900 mg/day) or matching placebo. The trial met its primary endpoint and demonstrated that Raxone can slow the loss of respiratory function and reduces bronchopulmonary complications. The positive outcome of the Phase III DELOS study was published by Buyse et al., *The Lancet* 2015 385(9979):1748-57 and McDonald et al., *Neuromuscular Disorders* <http://dx.doi.org/10.1016/j.nmd.2016.05.008>.

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) is currently assessing a Marketing Authorization Application (MAA) for Raxone in DMD patients with respiratory function decline who are not taking concomitant glucocorticoids. The indication would include patients who previously were treated with glucocorticoids or in whom glucocorticoid treatment is not desired, not tolerated or is contraindicated. The MAA was recently submitted as a Type II variation of the company's existing marketing authorization for Raxone. In September 2015, Raxone was approved for the treatment of visual impairment in adolescent and adult patients with Leber's hereditary optic neuropathy (LHON) in all EU member states, Norway, Iceland and Liechtenstein.

About Santhera

Santhera Pharmaceuticals (SIX: SANN) is a Swiss specialty pharmaceutical company focused on the development and commercialization of innovative pharmaceutical products for the treatment of orphan mitochondrial and neuromuscular diseases. Santhera's lead product Raxone[®] is authorized in the European Union for the treatment of Leber's hereditary optic neuropathy (LHON). For Duchenne muscular dystrophy (DMD), the second indication for Raxone[®], Santhera has filed a Marketing Authorization Application (MAA) in the European Union. Santhera develops Raxone[®] in a third indication, primary progressive multiple sclerosis (PPMS), and omigapil for congenital muscular dystrophy (CMD), all areas of high unmet medical need. For further information, please visit the Company's website www.santhera.com.

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