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# Santhera Starts Phase III Study (SIDEROS) with Raxone in Patients with Duchenne Muscular Dystrophy Using Glucocorticoids

**Liestal, Switzerland, September 28, 2016 – Santhera Pharmaceuticals (SIX: SANN) announces that the first patient has been enrolled at the University of Kansas Medical Center (KUMC), Department of Neurology, Kansas (USA) in Santhera's randomized, double-blind, placebo-controlled phase III (SIDEROS) trial. The trial will assess the efficacy of Raxone in slowing the rate of respiratory function decline in Duchenne muscular dystrophy (DMD) patients receiving concomitant glucocorticoids.**

"We first observed the efficacy of Raxone in slowing the rate of respiratory function decline in DMD patients in both glucocorticoid-using and non-using patients in the phase II DELPHI study," commented **Thomas Meier**, PhD, CEO of Santhera. "The successful Phase III DELOS trial which enrolled glucocorticoid non-using patients then confirmed a clinically relevant and statistically significant benefit of Raxone treatment on pulmonary function. The now initiated Phase III SIDEROS trial is designed to confirm the efficacy of Raxone in patients experiencing respiratory function decline that are currently taking glucocorticoids. If successful, this study will provide data that support use of Raxone in all DMD patients experiencing respiratory decline irrespective of their glucocorticoid use. The high level of interest from investigators and the patient community should allow us to recruit this study quickly."

"We are hopeful that this phase III trial is the final step in the development program with Raxone in DMD," said **Gunnar Buyse**, MD, PhD, Professor of Child Neurology at the University Hospitals Leuven (Belgium) and SIDEROS PI and Lead Investigator for Europe. "Following the exploratory phase II program and the successful phase III DELOS trial, I am grateful that Santhera is committed in exploring the full therapeutic potential of Raxone for patients with DMD."

"Maintaining pulmonary function in patients with DMD has only recently become a prominent therapeutic objective in DMD, particularly in non-ambulatory patients," added **Oscar Henry Mayer**, MD, Medical Director of the Pulmonary Function Testing Laboratory at the Children's Hospital of Philadelphia and Lead Investigator for US. "A patient and caregiver survey conducted by Parent Project Muscular Dystrophy clearly demonstrated that the DMD community highly values treatment options for pulmonary complications."

**About the SIDEROS Trial**
SIDEROS is a phase III, double-blind, randomized, placebo-controlled trial with Raxone in approximately 260 DMD patients receiving concomitant glucocorticoids. Patients with declining respiratory

function on any stable glucocorticoid treatment scheme and irrespective of the underlying dystrophin mutation or ambulatory status will be eligible. 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. The study will be conducted at about 50 centers in the United States and Europe. Patients wishing to enroll in the study should contact their neuromuscular clinic physician. Further information about the study is available under www.clinicaltrials.gov.

**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: Buyse et al., *The Lancet* 2015, 385:1748-1757; McDonald et al., *Neuromuscular Disorders* 2016, 26: 473–480 and Buyse et al., *Pediatric Pulmonology* 2016: http://dx.doi.org/10.1002/ppul.23547.

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 submitted as a Type II variation of the company's existing marketing authorization for Raxone for the treatment of visual impairment in patients with Leber's hereditary optic neuropathy (LHON).

**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, Norway, Iceland and Liechtenstein 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. In collaboration with the US National Institute of Neurological Disorders and Stroke (NINDS) Santhera is developing 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.

*Raxone® is a trademark of Santhera Pharmaceuticals.*

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