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## **Santhera Updates on Regulatory Filings for Raxone<sup>®</sup> (idebenone) in Duchenne Muscular Dystrophy (DMD)**

**Liestal, Switzerland, May 3, 2016 –Santhera Pharmaceuticals (SIX: SANN) announces that it has submitted comprehensive briefing material and a meeting request to the FDA to discuss the filing of a New Drug Application (NDA) for Raxone<sup>®</sup> (idebenone) for the treatment of DMD patients not taking concomitant glucocorticoids. A Marketing Authorization Application for DMD in Europe is also expected to be submitted in coming weeks. The Company also reports that, as part of its strategy to expand the Raxone label, a new phase III study (SIDEROS) in DMD patients using glucocorticoids will start enrolling patients in coming weeks.**

The FDA-meeting request included a very comprehensive data package intended to prepare for discussions with the Agency on an accelerated NDA approval (under Subpart H) for Raxone in patients with DMD not taking concomitant glucocorticoids. The intended indication is for patients in whom respiratory function has started to decline and would include patients who previously were treated with glucocorticoids or in whom glucocorticoid treatment is not desired, not tolerated or is contraindicated.

The data package provided to the FDA summarizes data from Santhera's phase II (DELPHI) program and the successful pivotal phase III (DELOS) study, which demonstrated a clinically relevant and statistically significant benefit of idebenone treatment in slowing the rate of respiratory function decline compared to placebo. Importantly, the package also includes data from the Cooperative International Neuromuscular Research Group's (CINRG) Duchenne natural history study (DNHS), which, in collaboration with CINRG, were used to conduct the first prospectively planned external control group study to compare outcomes for patients participating in DELOS with matched, contemporaneously-observed patients from the CINRG DNHS. The results demonstrate that the respiratory function decline observed in the placebo group of the DELOS study is consistent with the rate of decline observed in matched patients from the CINRG DNHS and therefore with the expected natural history of DMD. However, the slower rate of decline observed in idebenone-treated patients in DELOS was not observed in matched patients from the CINRG DNHS, indicating that the rate of respiratory function decline in idebenone-treated patients in DELOS differs from the expected natural history of DMD.

"We foresaw the FDA requirement for prospective planning of the natural history control group matching process and have been working with CINRG since last year to provide such a study in support of our NDA dossier" commented **Thomas Meier**, PhD, CEO of Santhera. "The successful outcome of this prospectively-planned, matched-patient study is unprecedented in clinical research in DMD and provides additional external validation of the results of our successful DELOS study".

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Submission documents using the same data sets are currently being finalized for a Type II-variation of the existing Marketing Authorization granted for Raxone for Leber's hereditary optic neuropathy in Europe to add the treatment of DMD patients not using glucocorticoids to the label.

The Company also reported that the SIDEROS protocol for a new phase III study in DMD patients using glucocorticoids has successfully completed the FDA review process. The Company will make a further announcement as soon as the study starts enrolling patients. Patients with declining respiratory function on any stable glucocorticoid treatment scheme will be eligible. Study participants will receive either Raxone (900 mg/day) or placebo for 78 weeks. The trial targets to enroll approximately 260 DMD patients and will be conducted in Europe and the US. Patients completing the trial will be offered the opportunity to enroll in an open label extension study. Santhera intends to position this study to provide confirmatory evidence (under Subpart H) of the efficacy of idebenone in patients both taking and not taking concomitant glucocorticoids.

"Following the successful outcome of our DELOS study, a further placebo-controlled study in patients not taking glucocorticoids is not considered feasible. However, patients taking glucocorticoids represent a different but related population that is capable of verifying predicted clinical benefit and in which a successful outcome can be considered confirmation of clinical benefit in DMD patients with respiratory function decline, irrespective of glucocorticoid use", commented **Nicholas Coppard**, PhD, Head of Development at Santhera.

### **About Duchenne Muscular Dystrophy and DELOS**

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, 10-18 years of age, to receive either Raxone tablets or matching placebo. The trial met its primary end-point and demonstrated that Raxone can slow the loss of respiratory function in patients not taking concomitant glucocorticoids. The positive outcome of the phase III DELOS study was published in *The Lancet* ([Buyse et al., The Lancet 2015 385\(9979\):1748-57](#)).

### **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). Santhera develops Raxone® in two additional indications, Duchenne muscular dystrophy (DMD) and primary progressive multiple sclerosis (PPMS), and omigapil for congenital muscular dystrophy (CMD), all

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areas of high unmet medical need. For further information, please visit the Company's website [www.santhera.com](http://www.santhera.com).

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