Santhera Pharmaceuticals Holding AG
Hohenrainstrasse 24, 4133 Pratteln, Switzerland

Phone: +41 61 906 89 50 | Fax: +41 61 906 89 51
www.santhera.com

A conference call will be held today at 13:00 CEST, 12:00 BST, 07:00 EDT. Details are at the end of this statement.

Santhera Provides Update on the Ongoing Regulatory Review of Puldysa® (Idebenone) by the CHMP in Duchenne Muscular Dystrophy (DMD)

Pratteln, Switzerland, May 29, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces that the EMA's CHMP has granted a requested extension of the clock-stop in the regulatory procedure for its conditional marketing authorization (CMA) application for Puldysa® (idebenone) in Duchenne muscular dystrophy (DMD). During this clock-stop, the Company is evaluating the potential of conducting an interim analysis to test for so-called overwhelming efficacy of its SIDEROS study with a view of including the data in the review procedure and potentially completing the trial early. This will result in a CHMP opinion in Q4 2020. A positive early completion of the SIDEROS study would allow acceleration of subsequent regulatory filings in the US and Europe by approximately one year.

During its May meeting the CHMP accepted a requested extended clock-stop to address the list of outstanding issues adopted at Day 180 of the ongoing review procedure of the conditional marketing authorization (CMA) application for Puldysa® (idebenone) in DMD for patients not using concomitant glucocorticoids. This extends the review time into the fourth quarter 2020.

Santhera recently communicated that it has completed enrollment into its SIDEROS study. SIDEROS 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 using concomitant glucocorticoids. As previously announced, and given the strong powering of SIDEROS, Santhera now intends to pursue the conduct of an interim analysis by the independent Data and Safety Monitoring Board (DSMB) to test if the trial can be stopped early due to overwhelming efficacy.

Under the scenario that overwhelming efficacy is demonstrated, the outcome of the interim analysis would be added within the clock-stop to the dossier currently under review by the CHMP to further enhance the CMA data package. Furthermore, the study would be completed with the option for trial participants to transfer into the open label extension of SIDEROS, where all patients are treated with idebenone.

Positive interim data supporting overwhelming efficacy from the SIDEROS study and a potential early completion of the study would also allow acceleration of filings for a label including patients irrespective of their glucocorticoid use status. Such NDA filing with the US FDA could be accelerated by approximately one year. In Europe, subject to approval in the indication currently under CHMP review for patients not using concomitant glucocorticoids, such positive SIDEROS data could also shorten time to a label extension to include glucocorticoid using DMD patients by around one year.

"We are delighted about the completion of enrollment of the SIDEROS study and hope to now be able to proceed with an interim analysis which potentially paves the way for an earlier close of the trial," said **Dario Eklund, Chief Executive Officer of Santhera**. "Despite the delay in our plans to get a CMA approved resulting from the clock-stop, we are convinced that this is the right strategy to both strengthen our current filing dossier and also to accelerate time to market in the US, and in the EU for patients using glucocorticoids."

Conference Call

Santhera will host a conference call today at 13:00 CEST / 12:00 BST / 07:00 EDT. Dario Eklund, CEO of Santhera, will discuss this update. Participants are invited to call one of the following numbers 10-15 minutes before the conference call starts (no dial-in code is required):

Europe: +41 58 310 50 00
UK: +44 207 107 06 13
USA: +1 631 570 56 13

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].

SIDEROS, the largest currently ongoing clinical trial in DMD, is a double-blind randomized placebo-controlled Phase 3 study evaluating the efficacy of idebenone (900 mg/day) in delaying the loss of respiratory function in DMD patients using concomitant glucocorticoids. The trial is fully enrolled and an

assessment of the potential of conducting an interim analysis by the independent Data and Safety Monitoring Board (DSMB) to test for overwhelming efficacy with a view of potentially completing the trial early is ongoing. Further information is available at ClinicalTrials.gov NCT#02814019.

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. (2020), Neuromuscular Disorders 30: 5-16

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.

For further information please contact:

public-relations@santhera.com or
Eva Kalias, Head External Communications
Phone: +41 79 875 27 80
eva.kalias@santhera.com

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