

## **Santhera to Present Novel Data Highlighting the Clinical Relevance of Peak Expiratory Flow as Predictor of Disease Progression in Duchenne Muscular Dystrophy**

**Pratteln, Switzerland, July 5, 2018 – Santhera Pharmaceuticals (SIX: SANN) announces that new data further supporting the clinical relevance of Peak Expiratory Flow (PEF) and providing a link between the treatment effect of idebenone observed in the pivotal phase III DELOS study and measures of disease progression will be presented at the 15th International Congress on Neuromuscular Diseases (ICNMD) from July 6-10, 2018, in Vienna, Austria.**

At Santhera's lunchtime symposium on Sunday, July 8, a panel of clinical experts will present new data from natural history studies that support Peak Expiratory Flow as clinically relevant primary study endpoint. This new data shows that

- Peak Expiratory Flow as percent predicted (PEF%p) is a sensitive and early marker of respiratory function decline in DMD applicable over a wide age range.
- Both PEF and Forced Vital Capacity (FVC) are predictors of time to clinically relevant events including time to hospitalization due to respiratory causes, time to initiation of assisted ventilation and death.
- Comparative analysis of the outcome of the DELOS trial with data from natural history studies allows the extrapolation of the observed treatment benefit of idebenone in PEF%p. This analysis shows that the treatment effect with idebenone observed in the DELOS trial can be linked to a delay in the initiation of assisted ventilation by 3 years, which is of high clinical relevance.

"Peak Expiratory Flow is increasingly being established as a sensitive measure of respiratory function decline over a wider age range in patients with DMD. As our knowledge of the natural history of respiratory function decline in DMD increases, the understanding of the clinical relevance of different respiratory function measures continues to evolve. The most recent work is showing that both PEF and FVC are equally important predictors of time to life-altering events such as assisted ventilation and death," said **Oscar H Mayer**, MD, Professor of Clinical Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Division of Pulmonary Medicine and Medical Director of Pulmonary Function Testing Laboratory, The Children's Hospital of Philadelphia, USA.

**Thomas Voit**, MD, Professor of Pediatrics at the Great Ormond Street Hospital for Children and University College London, and Director of the NIHR Great Ormond Street Hospital Biomedical Research Centre, London, UK, added: "Today glucocorticoid steroids are recommended standard of care, particularly in young patients with DMD, primarily to maintain upper and lower limb strength. With respect to respiratory function, data now becoming available show that steroids delay the time to the onset of respiratory function decline but not the rate of decline. Our priority must be to develop therapeutic options that can reduce the rate of respiratory decline in the hope of delaying the time to subsequent life-altering events, such as starting assisted ventilation."

“We are delighted that the expert panel participating at our symposium will present novel data which demonstrate that decline in PEF is a direct indicator of time to initiation of assisted ventilation and risk of death and can serve as a measure for disease progression,” said **Thomas Meier**, PhD, CEO of Santhera. “These data are highly relevant to complement and strengthen our ongoing analyses of efficacy data with idebenone and for the regulatory dossier in preparation of marketing authorization applications for Europe and the US.”

### Symposium

**Title:** Respiratory function decline in Duchenne muscular dystrophy (DMD) – Insights and evolving treatment strategies. Chair: Thomas Voit, MD

- “New insights into the natural history of respiratory function decline in patients with DMD” – **Craig McDonald**, MD, Professor and Chair, Department of Physical Medicine & Rehabilitation and Director of Neuromuscular Disease Clinics, UC Davis Health, USA
- “Establishing clinically relevant thresholds of respiratory function decline and respiratory complications in DMD” – **Oscar H Mayer**, MD, pediatric pulmonologist and Director of the Pulmonary Function Laboratory at Children's Hospital of Philadelphia, USA
- “Treatment strategies to slow respiratory function decline in DMD and address unmet needs” – **Thomas Voit**, MD and Professor of Pediatrics at the Great Ormond Street Hospital for Children and University College London, London, UK

**When and where:** Sunday, July 8, 2018, 12:15-13:45 | Room Congress Park 2

### Poster Presentations

**Title:** Impact of idebenone on respiratory burden, including risk of bronchopulmonary complications, in Duchenne muscular dystrophy (Poster PS1Group1-057)

**Title:** Evaluating the effects of baseline variables on the respiratory function benefit of idebenone in Duchenne muscular dystrophy (Poster PS1Group1-105)

**When:** Saturday, July 7, 2018, 17:15 - 18:30, Guided Poster Session

**Title:** Comparison of home-based versus hospital-based spirometry measurements in Duchenne muscular dystrophy (Poster PS2Group5-023)

**Title:** Assessing idebenone's impact on respiratory function in Duchenne muscular dystrophy: Meta-analysis of two clinical trials (Poster PS2Group9-003)

**Title:** Alternative analyses of respiratory function in Duchenne muscular dystrophy: Consistent treatment benefit of idebenone (Poster PS2Group9-016)

**When:** Sunday, July 8, 2018, 17:15 - 18:30, Guided Poster Session

### **About Duchenne Muscular Dystrophy**

DMD is one of the most common and devastating types of muscle degeneration and leads to progressive muscle weakness starting at an early age. DMD 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. 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**

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, muscle wasting, 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 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.

Data from the pivotal Phase III DELOS trial are published in peer-reviewed medical journals: Buyse et al., *The Lancet* 2015, 385:1748-1757; McDonald et al., *Neuromuscular Disorders* 2016, 26:473-480; Buyse et al., *Pediatric Pulmonology* 2017, 52:580-515; Mayer et al., *Journal of Neuromuscular Diseases* 2017, 4:189-198; Meier et al., *Neuromuscular Disorders* 2017, 27:307-314.

### **About Santhera**

Santhera Pharmaceuticals (SIX: SANN) is a Swiss specialty pharmaceutical company focused on the development and commercialization of innovative medicines for orphan 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 and Israel for the treatment of Leber's hereditary optic neuropathy (LHON) and currently commercialized in more than 20 countries. For further information, please visit [www.santhera.com](http://www.santhera.com).

*Raxone® is a trademark of Santhera Pharmaceuticals.*

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