Santhera and ReveraGen Start Rolling NDA Submission to the FDA for Vamorolone for the Treatment of Duchenne Muscular Dystrophy

Pratteln, Switzerland, March 29, 2022 – Santhera Pharmaceuticals (SIX: SANN) and ReveraGen BioPharma, Inc (US: private) announce the initiation of a rolling new drug application (NDA) submission to the U.S. Food and Drug Administration (FDA) for vamorolone for the treatment of Duchenne muscular dystrophy (DMD). Vamorolone for DMD has been granted Fast Track Designation by the FDA.

Santhera and ReveraGen have now commenced the NDA filing as a rolling submission following a successful pre-NDA meeting with the FDA in November 2021. In its conclusions from this meeting, the FDA considered the proposed clinical efficacy and safety data sufficient to support an NDA filing of vamorolone for the treatment of DMD. Acceptance of the NDA will be subject to FDA's review of the complete filing.

"The NDA filing for vamorolone marks a tremendous milestone for Santhera and an important next step for the Duchenne community. The potential benefits of vamorolone could address significant unmet needs that represent a burden to DMD patients and their families," said **Dario Eklund, Chief Executive Officer of Santhera**. "We are fully focused on working closely with the FDA and completing the submission as soon as possible."

"We are delighted about the initiation of the filing for approval for vamorolone as it represents a culmination of over a decade of scientific research for the benefit of patients with DMD. In having granted Fast Track Designation, the FDA has acknowledged the significant innovation vamorolone could bring in addressing a high unmet medical need of patients with DMD," said **Eric Hoffman, PhD, President and CEO of ReveraGen BioPharma**. "We thank study participants, their families and caregivers, as well as investigators and study personnel, for their commitment to the vamorolone program."

Santhera and ReveraGen expect to complete the NDA filing in the second quarter of 2022. Based on FDA review timelines, notification from the FDA on the acceptance of the filing for review is expected in August 2022. In its assessment, the FDA will also determine eligibility of vamorolone for priority review which Santhera and ReveraGen will request upon completion of the rolling NDA submission. If granted, this would shorten review time and set an anticipated approval date for as early as the first quarter of 2023. Subject to FDA approval, Santhera plans to launch vamorolone in the U.S., the first country, shortly thereafter with its own organization.

In Europe, Santhera plans to submit a marketing authorization application (MAA) for vamorolone for the treatment of DMD to the European Medicines Agency (EMA) in Q3-2022. Assuming a review time of about one year, this could pave the way for approval and launch in H2-2023. Santhera expects the first European launch country to be Germany.

Vamorolone has been granted Orphan Drug status in the US and in Europe for DMD, and has received Fast Track and Rare Pediatric Disease designations by the US FDA and Promising Innovative Medicine (PIM) status from the UK MHRA for DMD. Vamorolone is an investigational medicine and is currently not approved for use by any health authority.

Vamorolone was discovered by US-based ReveraGen and is being developed in collaboration with Santhera who owns worldwide rights to the drug candidate for all indications. In January 2022, Santhera licensed rights to vamorolone in rare diseases for the Greater China region to Sperogenix Therapeutics.

About Vamorolone and the VISION-DMD study

Vamorolone is a drug candidate with a novel mode of action that binds to the same receptor as corticosteroids but modifies its downstream activity and as such is a dissociative agonist [2-4]. This mechanism has the potential to 'dissociate' efficacy from typical steroid safety concerns.

VISION-DMD was a Phase 2b study comprising a (1) pivotal double-blind 24-week period to demonstrate efficacy and safety of vamorolone (2 and 6 mg/kg/day) versus placebo and prednisone (0.75 mg/kg/day), followed by a (2) 24-week period to evaluate the maintenance of efficacy and collect additional longer-term safety and tolerability data. 121 ambulant boys aged 4 to <7 years with Duchenne muscular dystrophy (DMD) were included in the study. The trial met its primary endpoint of superiority in change of time to stand from supine position (TTSTAND) velocity with vamorolone 6 mg/kg/day versus placebo (p=0.002) at 24 weeks (period 1). Vamorolone 6 mg/kg/day also met its secondary efficacy endpoints and no statistically significant differences were observed between vamorolone and prednisone. During the second 24-week period of this 48-week study, all participants received vamorolone. Participants from the placebo and prednisone arms were randomized to either the 2 or 6 mg/kg/day dose of vamorolone and the vamorolone arms continued on their existing dose. Efficacy observed at 24 weeks for vamorolone 6 mg/kg/day was maintained across multiple endpoints over 48 weeks. In addition to efficacy, the study aimed to confirm the favorable tolerability profile of vamorolone with the potential to offer an alternative to current standard of care.

In clinical studies, vamorolone was generally well tolerated. The most commonly reported adverse events versus placebo from the VISION-DMD study were cushingoid features, vomiting and vitamin D deficiency. Adverse events were generally of mild to moderate severity.

References:
[1] ClinicalTrials.gov Identifier: NCT03439670, link
[2] Heier CR at al. (2013). EMBO Mol Med 5: 1569–1585.
[3] Reeves EKM, et al (2013). Bioorg Med Chem 21(8):2241-2249.
[4] Liu X, et al. (2020). Proc Natl Acad Sci USA 117:24285-24293.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a rare inherited X-chromosome-linked disease, which almost exclusively affects males. DMD is characterized by inflammation which is present at birth or shortly thereafter. Inflammation leads to fibrosis of muscle and is clinically manifested by progressive muscle degeneration and weakness. Major milestones in the disease are the loss of ambulation, the loss of self-feeding, the start of assisted ventilation, and the development of cardiomyopathy. DMD reduces life expectancy to before the fourth decade due to respiratory and/or cardiac failure.

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 has an exclusive license for all indications worldwide to vamorolone, a dissociative steroid with novel mode of action, which was investigated in a pivotal study in patients with DMD as an alternative to standard corticosteroids. The Company plans to complete the rolling submission of its filing for approval for vamorolone with the US FDA in Q2-2022. The clinical stage pipeline also includes lonodelestat to treat cystic fibrosis (CF) and other neutrophilic pulmonary diseases. Santhera out-licensed rights to its first approved product, Raxone® (idebenone), outside North America and France for the treatment of Leber's hereditary optic neuropathy (LHON) to Chiesi Group. For further information, please visit www.santhera.com.

Raxone® is a trademark of Santhera Pharmaceuticals.

About ReveraGen BioPharma

ReveraGen was founded in 2008 to develop first-in-class dissociative steroidal drugs for Duchenne muscular dystrophy and other chronic inflammatory disorders. The development of ReveraGen's lead compound, vamorolone, has been supported through partnerships with foundations worldwide, including Muscular Dystrophy Association USA, Parent Project Muscular Dystrophy, Foundation to Eradicate Duchenne, Save Our Sons, JoiningJack, Action Duchenne, CureDuchenne, Ryan's Quest, Alex's Wish, DuchenneUK, Pietro's Fight, Michael's Cause, Duchenne Research Fund, and Defeat Duchenne Canada. ReveraGen has also received generous support from the US Department of Defense CDMRP, National Institutes of Health (NCATS, NINDS, NIAMS), and European Commission (Horizons 2020). www.reveragen.com

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