Santhera Announces Publication of Long-Term Clinical Data with Vamorolone in Patients with Duchenne Muscular Dystrophy

Pratteln, Switzerland, September 22, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces that partner ReveraGen Biopharma Inc. and their academic collaborators have published new open-label, long-term clinical data on the safety, tolerability and efficacy of vamorolone in patients with Duchenne muscular dystrophy (DMD). These 18-month treatment data extend previously published 24-week treatment data, and show a reduction of corticosteroid-specific side effects and sustained efficacy with vamorolone including clinical improvement through the 18-month follow-up period.

This publication in the journal *PLOS Medicine* [1] provides peer-reviewed and detailed open-label data in patients with DMD treated for 18 months with vamorolone. A multi-center, open-label, 24-week trial (VBP15-003; [2, 3]) with a total 24-month long-term extension (VBP15-LTE; [4]) was conducted by the Cooperative International Neuromuscular Research Group (CINRG) and evaluated drug-related effects of vamorolone on motor outcomes and corticosteroid-associated safety concerns. This publication covers the 24-week Phase 2a trial (VBP15-003) and the first 12 months of the open-label extension trial (VBP15-LTE) adding up to a total treatment period of 18 months.

"This long-term study showed significant continued clinical improvement of all outcomes measured over an 18-month follow-up period," said **Edward C. Smith, MD, Associate Professor of Pediatrics, Duke University**, Durham (North Carolina, USA), clinical investigator and lead-author of the publication. "Treatment-related efficacy responses with vamorolone were similar to those seen in an external control group with corticosteroid-treated patients. Both 4-stair climb and 10-meter run/walk tests were significantly improved when compared to steroid-naïve natural history control subjects."

"Importantly, we also found that vamorolone did not show stunting of growth seen with deflazacort and prednisone, and vamorolone also showed fewer physician-reported adverse events such as mood disturbance, excessive hair growth, and Cushingoid appearance," noted **Eric Hoffman, PhD, Vice President of Research at ReveraGen BioPharma, Inc.** and co-author of the study.

DMD trial participants (4 to <7 years at entry) treated with 2.0 or 6.0 mg/kg/day vamorolone for the full 18-month period (n=23) showed clinical improvement of all motor outcomes from baseline to month 18 (time to stand velocity, $p = 0.012$ [95% CI 0.010, 0.068 event/second]; run/walk 10 meters velocity, $p < 0.001$ [95% CI 0.220, 0.491 meters/second]; climb 4 stairs velocity, $p = 0.001$ [95% CI 0.034, 0.105 event/second]; 6-minute walk test, $p = 0.001$ [95% CI 31.14, 93.38 meters]; North Star Ambulatory Assessment, $p < 0.001$ [95% CI 2.702, 6.662 points]). Outcomes in vamorolone-treated DMD patients (n = 46) were compared to group-matched participants in the CINRG Duchenne Natural History Study (corticosteroid-naïve, n = 19; corticosteroid-treated, n = 68) over a similar 18-month period. Time to stand was not significantly different between vamorolone-treated and corticosteroid-naïve participants ($p = 0.088$; least squares [LS] mean 0.042 [95% CI –0.007, 0.091]), but vamorolone-treated participants showed significant improvement compared to group-matched corticosteroid-naïve participants for run/walk 10 meters velocity ($p = 0.003$; LS mean 0.286 [95% CI 0.104, 0.469]) and climb 4 stairs velocity ($p = 0.027$; LS mean 0.059 [95% CI 0.007, 0.111]). The vamorolone-related improvements were similar in magnitude to corticosteroid-related improvements. Corticosteroid-treated participants showed stunting

of growth, whereas vamorolone-treated trial participants did not ($p < 0.001$; LS mean 15.86 [95% CI 8.51, 23.22]). Physician-reported incidences of adverse events (AEs) for Cushingoid appearance, hirsutism, weight gain, and behavior change were less for vamorolone than published incidences for prednisone and deflazacort.

About Vamorolone

Vamorolone is a first-in-class drug candidate that binds to the same receptor as corticosteroids but modifies its downstream activity and as such is a dissociative partial agonist [5-8]. This mechanism has the potential to 'dissociate' efficacy from typical steroid safety concerns and therefore vamorolone could emerge as a promising alternative to existing corticosteroids, the current standard of care in children and adolescent patients with DMD. There is substantial unmet medical need in this patient group as high-dose corticosteroids have significant systemic side effects that diminish patient quality of life. The fully-enrolled, pivotal Phase 2b VISION-DMD trial (VBP15-004, [10, 11], https://vision-dmd.info/2b-trial-information) is currently being conducted at study sites across North America, Europe, Israel and Australia and topline 6-month data are expected in Q2-2021, paving the way for a US NDA submission in Q4-2021. Vamorolone has been granted Orphan Drug status in the US and in Europe, and has received Fast Track and Rare Pediatric Disease designations by the US FDA and Promising Innovative Medicine (PIM) status from the UK MHRA.

Vamorolone was discovered by US-based ReveraGen BioPharma, Inc. and is being developed in collaboration with Santhera, which owns worldwide rights to the drug candidate in all indications. The vamorolone development program has received funding from several international non-profit foundations and patient organizations, the US National Institutes of Health, the US Department of Defense and the European Commission's Horizon 2020 program.

References:

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[8] Liu X et al. (2020). Disruption of a key ligand-H-bond network drives dissociative properties in vamorolone for Duchenne muscular dystrophy treatment. Proc Natl Acad Sci USA. Link
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[10] Clinicaltrials.gov: A Study to Assess the Efficacy and Safety of Vamorolone in Boys with Duchenne Muscular Dystrophy (DMD), Link
[11] Press release "Santhera Announces Full Enrollment of ReveraGen's Pivotal VISION-DMD Study with Vamorolone in Duchenne Muscular Dystrophy", September 11, 2020, Link

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 from early to late disease stages, irrespective of causative mutations, ambulatory status or age. A marketing authorization application for Puldysa® (idebenone) is currently under review by the European Medicines Agency. Santhera has an exclusive license for all indications worldwide to vamorolone, a first-in-class anti-inflammatory drug candidate with novel mode of action, currently investigated in a pivotal study in patients with DMD as an alternative to 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. Further information at www.santhera.com. For further information, please visit www.santhera.com.

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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 also 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, and Duchenne Research Fund. 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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