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Santhera Announces Completion of ReveraGen's Long-Term Extension Study with Vamorolone in Duchenne Muscular Dystrophy

Pratteln, Switzerland, June 2, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces that partner ReveraGen Biopharma Inc. has completed a long-term, open-label extension study of 24 months duration with vamorolone in patients with Duchenne muscular dystrophy (DMD). Including 6 months treatment in the preceding study, ReveraGen has now obtained safety and efficacy data with vamorolone over a period of 2.5 years in 41 boys with DMD.

Eligible for enrolment into the now completed 24-month long-term, open-label extension study (VBP15-LTE, clinicaltrials.gov ID: NCT03038399) were boys who had previously completed the 6-month dose escalation study VBP15-003 (clinicaltrials.gov ID: NCT02760277). Data from this VBP15-003 study in comparison to natural history study data demonstrated dose-dependent improvement in timed function tests. Vamorolone was reported to be safe and well tolerated up to the highest dose tested (6.0 mg/kg/day) [1].

"With most participants continuing treatment with vamorolone long-term, we have assembled a solid safety database, with 106 patient-years of vamorolone exposure in DMD boys, with no serious adverse events attributable to vamorolone to date," said **Eric Hoffman, PhD**, Vice President of Research at ReveraGen BioPharma. "We will now analyze the efficacy data and plan to report the results in upcoming scientific conferences and publications."

All 46 patients who completed the VBP15-003 study requested to continue vamorolone treatment in the long-term extension, rather than transition to corticosteroids. This VBP15-LTE study enabled dose escalation and de-escalation at the preference of the physician and family (suggested range 2.0 to 6.0 mg/kg/day). Of the 41 participants completing end-of-study visit after 24 months, 27 ended at 6.0 mg/kg/day (66%), 11 at 2.0 mg/kg/day (27%), and 3 at 4.0 mg/kg/day (7%). Thus, the majority of physicians/families chose treatment at the highest tested dose of vamorolone by the end of the VBP15-LTE study. Upon their expressed wish, the large majority of the boys completing the 2-year VBP15-LTE study have transitioned to Expanded Access Programs (USA, Canada, Israel) or compassionate use programs (UK, Sweden, Australia) to receive continued vamorolone treatment.

The currently ongoing Phase 2b VISION-DMD study (VBP15-004; clinicaltrials.gov: NCT03439670) is designed as a pivotal trial to demonstrate efficacy and safety of vamorolone administered orally at doses of 2.0 mg/kg/day and 6.0 mg/kg/day versus prednisone 0.75 mg/kg/day and placebo over a treatment period of 24 weeks. The study is currently being conducted at 33 sites across North America, Europe, Israel and Australia. For more information: https://vision-dmd.info/2b-trial-information.

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. In November 2018, Santhera acquired from Idorsia Pharmaceuticals Ltd (SIX: IDIA), who has an option to an exclusive, worldwide license to vamorolone, the option to an exclusive sub-license to vamorolone in all indications and all countries worldwide, except Japan and South Korea.

About Vamorolone – first-in-class dissociative steroid

Vamorolone is a first-in-class drug candidate that binds to the same receptors as corticosteroids but modifies the downstream activity of the receptors [2, 3]. This has the potential to 'dissociate' efficacy from typical steroid safety concerns and therefore could replace existing corticosteroids, the current standard of care in children and adolescent patients with DMD. There is significant unmet medical need in this patient group as high dose corticosteroids have severe systemic side effects that detract from patient quality of life. Vamorolone is being developed by US-based ReveraGen BioPharma Inc. with participation in funding and design of studies by several international non-profit foundations, the US National Institutes of Health, the US Department of Defense and the European Commission's Horizon 2020 program.

About the clinical development program of Vamorolone in patients with DMD

The clinical development program with vamorolone in patients with DMD was initiated following a clinical pharmacology study (VBP15-001) in healthy volunteers in which biomarker assessments indicated reduced occurrence of side effects typical for traditional corticosteroid drugs like bone fragility, metabolic disturbance, immune suppression [4].

The Phase 2a program with vamorolone consisted of two studies that were conducted back-to-back in 48 boys with DMD aged 4 to <7 years (VBP15-002 and VBP15-003). These studies with a combined duration of 6 months investigated the efficacy, safety and tolerability of oral administration of vamorolone at doses of 0.25, 0.75, 2.0 and 6.0 mg/kg/day (12 boys per treatment group). Data from these studies reported that vamorolone was safe and well tolerated and over a period of 6 months with dose- and time-related improvements in various timed function tests and motor function outcomes [1, 5]. Vamorolone treatment led to increased serum levels of osteocalcin, a biomarker of bone formation, suggesting possible reduction of bone morbidities typically associated with corticosteroids. Biomarker outcomes for adrenal suppression and insulin resistance also indicated better tolerability of vamorolone treatment, relative to published studies of corticosteroid therapy.

Patients completing VBP15-003 study were offered continued treatment with vamorolone under the 24-month long-term open-label extension study (VBP15-LTE) which has now been successfully completed.

References:

[1] Hoffman EP et al. (2019). Vamorolone trial in Duchenne muscular dystrophy shows dose-related improvement of muscle function. Neurology 93: e1312-e1323.

[2] Heier CR at al. (2013). VBP15, a novel anti-inflammatory and membrane-stabilizer, improves muscular dystrophy without side effects. EMBO Mol Med 5: 1569–1585.

[3] Heier CR et al. (2019). Vamorolone targets dual nuclear receptors to treat inflammation and dystrophic cardiomyopathy. Life Science Alliance DOI 10.26508/lsa.201800186.

[4] Hoffman EP et al. (2018). Phase 1 trial of vamorolone, a first-in-class steroid, shows improvements in side effects via biomarkers bridged to clinical outcomes. Steroids 134: 43-52.

[5] Conklin LS et al. (2018). Phase IIa trial in Duchenne muscular dystrophy shows vamorolone is a first in-class dissociative steroidal anti-inflammatory drug. Pharmacological Research 136:140-150.

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, 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

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.

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