



Santhera Pharmaceuticals Holding AG
Hohenrainstrasse 24, 4133 Pratteln, Switzerland

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

Santhera Announces Full Enrollment of ReveraGen's Pivotal VISION-DMD Study with Vamorolone in Duchenne Muscular Dystrophy

Pratteln, Switzerland, September 11, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces that partner ReveraGen Biopharma Inc. has completed enrollment into the pivotal VISION-DMD study with vamorolone in patients with Duchenne muscular dystrophy (DMD). Subject to a positive study outcome, this could allow for a regulatory submission to the US FDA in the fourth quarter of 2021 with the potential to offer an alternative to current standard of care in young boys with DMD.

The 48-week Phase 2b VISION-DMD study (VBP15-004; clinicaltrials.gov: NCT03439670 [1]) 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 in ambulant boys ages 4 to <7 years with DMD. Efficacy outcome measures after the first 24-week treatment period are muscle strength and motor function outcomes with Time to Stand test (TTSTAND) as the primary study endpoint. Additional analyses compare various safety and tolerability markers between the vamorolone dose groups, placebo and prednisone. The second 24-week treatment period where all patients receive one of two vamorolone doses will evaluate the persistence of effect in the longer term. In addition to efficacy, the study aims to confirm the favorable tolerability profile of vamorolone with the potential to offer an alternative to current standard of care. Although glucocorticoids are part of the current care recommendations for DMD, their adverse effect profile limits their use.

With the current number of 121 patients recruited, the VISION-DMD study has reached its pre-planned enrollment target. The last patient is expected to complete the first 24-week treatment period in the first quarter of 2021 with a topline data readout in the second quarter of 2021. Subject to positive results of this first 24-week treatment period, this would pave the way for a regulatory submission to the US FDA in the fourth quarter of 2021.

Vamorolone has been granted Orphan Drug status in the US and in Europe, and has received Fast Track and Rare Pediatric Disease designations from the US FDA and Promising Innovative Medicine (PIM) status from the UK MHRA. On September 2, Santhera signed agreements with ReveraGen and Idorsia that granted Santhera an exclusive license to vamorolone for all indications worldwide [2].

"We are very pleased having achieved full enrollment of our pivotal trial with vamorolone in patients with Duchenne muscular dystrophy," said **Eric Hoffman, PhD, Vice President of Research at ReveraGen BioPharma**. "On behalf of the entire study team we would like to thank patients and their families for their enthusiastic engagement to help advance the clinical development of vamorolone. We also thank investigators and study site personnel for their interest and commitment in completing this study as planned."

"We congratulate ReveraGen on this accomplishment of fully enrolling the VISION-DMD trial, in times where the conduct of any clinical trial is very challenging for patients and families, study sites and study personnel," said **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development at Santhera.** "It is already clear from existing data from previous studies that vamorolone has tremendous therapeutic potential for patients with Duchenne muscular dystrophy and we are looking forward to the outcome of the 6-month randomized, placebo- and prednisone-controlled period of the VISION-DMD trial."

About Vamorolone

Vamorolone is a first-in-class drug candidate that binds to the same receptors as corticosteroids but modifies the downstream activity of the receptors [3, 4]. This has the potential to 'dissociate' efficacy from typical steroid safety concerns and therefore could emerge as a valuable alternative to 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 significant 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 [5].

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 over a period of 6 months with dose- and time-related improvements in various timed function tests and motor function outcomes [6, 7]. 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.

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 24-month long-term open-label extension study (VBP15-LTE) study enabled dose escalation and de-escalation at the preference of the physician and family and the majority of physicians/families chose treatment at the highest tested dose of vamorolone by the end of the VBP15-LTE study.

The now fully enrolled, Phase 2b VISION-DMD trial (VBP15-004) complements previously conducted clinical studies in DMD. The study is currently being conducted at over 30 sites across North America, Europe, Israel and Australia. For more information: <https://vision-dmd.info/2b-trial-information>.

Santhera Announces Full Enrollment of ReveraGen's Pivotal VISION-DMD Study
with Vamorolone in Duchenne Muscular Dystrophy
September 11, 2020 / Page 3 of 4

References:

- [1] <https://www.clinicaltrials.gov/ct2/show/NCT03439670?term=vamorolone&draw=2&rank=3>
- [2] Press release "Santhera Exercises Option to Obtain Worldwide Rights to Vamorolone in Duchenne Muscular Dystrophy and All Other Indications", September 2, 2020, accessible [here](#).
- [3] Heier CR et al. (2013). VBP15, a novel anti-inflammatory and membrane-stabilizer, improves muscular dystrophy without side effects. *EMBO Mol Med* 5: 1569–1585.
- [4] Heier CR et al. (2019). Vamorolone targets dual nuclear receptors to treat inflammation and dystrophic cardiomyopathy. *Life Science Alliance* DOI 10.26508/lsa.201800186.
- [5] 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.
- [6] Conklin LS et al. (2018). Phase IIa trial in Duchenne muscular dystrophy shows vamorolone is a first in-class dissociative steroid anti-inflammatory drug. *Pharmacological Research* 136:140-150.
- [7] Hoffman EP et al. (2019). Vamorolone trial in Duchenne muscular dystrophy shows dose-related improvement of muscle function. *Neurology* 93: e1312-e1323.

About ReveraGen BioPharma

ReveraGen was founded in 2008 to develop first-in-class dissociative steroid 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 (Horizon 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 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.

Puldysa® and Raxone® are trademarks of Santhera Pharmaceuticals.

For further information please contact:

Santhera

public-relations@santhera.com or

Eva Kalias, Head External Communications

Phone: +41 79 875 27 80

eva.kalias@santhera.com

Santhera Announces Full Enrollment of ReveraGen's Pivotal VISION-DMD Study
with Vamorolone in Duchenne Muscular Dystrophy
September 11, 2020 / Page 4 of 4

ReveraGen BioPharma

Eric Hoffman, PhD, Vice President of Research
Phone: + 1 240-672-0295
eric.hoffman@reveragen.com

Disclaimer / Forward-looking statements

This communication does not constitute an offer or invitation to subscribe for or purchase any securities of Santhera Pharmaceuticals Holding AG. This publication may contain certain forward-looking statements concerning the Company and its business. Such statements involve certain risks, uncertainties and other factors which could cause the actual results, financial condition, performance or achievements of the Company to be materially different from those expressed or implied by such statements. Readers should therefore not place undue reliance on these statements, particularly not in connection with any contract or investment decision. The Company disclaims any obligation to update these forward-looking statements.

#