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Santhera Announces Publication on Molecular Distinctions of Vamorolone Compared to Corticosteroids

Pratteln, Switzerland, September 14, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces that Emory University scientists and partner ReveraGen Biopharma Inc. have published new data on the molecular mode of action of vamorolone compared to standard corticosteroids (prednisone and deflazacort) which are thought to explain the unique dissociative properties of vamorolone. Vamorolone is currently in advanced clinical development in patients with Duchenne muscular dystrophy (DMD) to offer an alternative to current standard of care in young boys with DMD.

The publication in the Proceedings of the National Academy of Sciences of the US (PNAS) by scientists at the Emory University (Atlanta), the Binghamton University-State University of New York (New York) and ReveraGen Biopharma Inc. [1] summarizes structural, biophysical, computational and biochemical data that further explain the unique pharmacological properties of vamorolone, clearly setting it apart from standard corticosteroids, including those currently used as treatment for patients with DMD. It extends previous publications which characterized the unique pharmacological properties of vamorolone, a dissociative steroidal drug candidate that decreased muscle inflammation and improved muscle strength in mouse models of DMD [2-4]. Moreover, initial open-label clinical trials with vamorolone showed dose-responsive efficacy in DMD while biomarker measurements indicated reduced safety concerns typically associated with traditional corticosteroid treatments [5-7].

Vamorolone and the active metabolites of prednisone and deflazacort were compared regarding their molecular interactions with the target receptor (glucocorticoid receptor, GR), and required accessory proteins (co-activators, co-repressors). Vamorolone has one less single contact point with the GR compared to prednisone and deflazacort, and this changes conformation of the accessory protein binding sites. The data further show that vamorolone uniformly weakens co-activator associations, which leads to loss of gene transcriptional activities associated with safety concerns of corticosteroids. In contrast, vamorolone retains co-repressor binding necessary for anti-inflammatory activities associated with efficacy of corticosteroids. This suggests that vamorolone is a first-in-class partial agonist of the GR, and explains the dissociative and advantageous pharmacological properties seen in mouse models of inflammatory disease, and DMD patients.

“Our study provides a molecular model for understanding of the unique mode of action of vamorolone, which distinguishes it from standard glucocorticoids such as prednisone and deflazacort”, said **Eric A. Ortlund, PhD, Professor at Emory University** and corresponding author of the publication.

“We now understand the molecular basis of the dissociative properties of vamorolone, which retains the anti-inflammatory capacity but result in a reduced liability for undesirable side effects. Vamorolone is in advanced clinical development with the potential to offer an alternative to current standard of care treatments in young boys with DMD,” said **Eric Hoffman, PhD, Vice President of Research at ReveraGen BioPharma** and co-author of the study.

References:
[1] 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. https://doi.org/10.1073/pnas.2006890117. Link
[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] Reeves EKM, et al (2013) VBP15: preclinical characterization of a novel anti-inflammatory delta 9,11 steroid. Bioorg Med Chem 21(8):2241-2249.
[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 steroidal 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 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

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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