

ReveraGen BioPharma completes 2.5 years vamorolone treatment of 41 Duchenne muscular dystrophy boys.

[Rockville MD – 2 June 2020]

Vamorolone is a first-in-class daily oral drug being developed to improve muscle function in Duchenne muscular dystrophy. Vamorolone has multiple mechanisms of action shown by published pre-clinical studies, including potent anti-inflammatory activities, cardioprotective activity, promotion of membrane repair, and synchronization of cell repair. While a steroidal drug, pre-clinical and clinical data has shown that vamorolone may lack multiple safety concerns of corticosteroidal anti-inflammatories, such as deflazacort and prednisone, while adding novel aspects of potential efficacy such as mineralocorticoid antagonism.

In 2016-2017, 48 DMD boys (age 4 to <7 years) entered a series of pharmacokinetics, safety and dose-finding efficacy studies (VBP15-002; VBP15-003). After 6-months of treatment, the DMD participants and their families were given the option to transition to standard of care (deflazacort or prednisone), or remain on vamorolone via a 2-year long-term extension study (VBP15-LTE). Of the 46 DMD boys completing the 6-month dose-ranging study, all (100%) requested to continue vamorolone treatment in the long-term extension, rather than transition to corticosteroids. The last participant, last visit of VBP15-LTE occurred in April 2020, with 41 of 46 DMD boys completing the full 2-year treatment period. The large majority of the 41 DMD boys completing the 2-year LTE have transitioned to Expanded Access Program (USA, Canada, Israel), or compassionate use programs (UK, Sweden, Australia).

“Parents and their physicians seem to be satisfied with vamorolone, as nearly all wish to continue vamorolone treatment,” said Paula Clemens, MD, Professor at the University of Pittsburgh School of Medicine, and Study Chair. The long-term extension 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 those 41 participants completing the 2-year end-of-study visit, 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 (2/3) of physicians/families chose treatment at the highest tested dose of vamorolone by the end of the LTE study (6.0 mg/kg/day).

“With most participants continuing treatment with vamorolone long-term, we have assembled a strong 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.

A registration trial, VBP15-004, is ongoing with 103 of 128 DMD participants enrolled. Enrollment is expected to complete soon, with 6-month read-out for FDA NDA submission in 4Q2020 or 1Q2021. Information on the VBP15-004 trial can be obtained from Suzanne Gaglianone (Suzanne.gaglianone@reveragen.com) or Andrea D’Alessandro (adalessandro@trinds.com).

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NOTES:**About Duchenne muscular dystrophy**

Duchenne muscular dystrophy is a rare genetic disease that predominantly affects young boys. Loss of the large protein, dystrophin, in muscle leads to persistent damage to muscle. DMD is a progressive disease, with gradual loss of muscle and weakness over 20 years leading to loss of walking abilities, and shortened lifespan.

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 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 [1,2]. 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. Phase 1 studies in adult volunteers [3], and Phase 2a studies in 48 DMD boys [4] showed biomarker studies consistent with a partial agonist mechanism of action, with dose-responsive improvements in both efficacy and safety biomarkers. Dose-finding studies with 24-weeks of vamorolone treatment over a dose range of 0.25 to 6.0 mg/kg/day showed dose-related improvements in multiple measures of muscle strength and endurance [5]. Vamorolone has been granted Orphan Drug status by both FDA and EMA, Fast Track designation by the FDA, and Priority Innovative Medicine designation by the UK MHRA. 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.

[1] [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](#)

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

[3] [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.](#)

[4] [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.](#)

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

About the Cooperative International Neuromuscular Research Group (CINRG)

CINRG was founded in 2000 as an international academic clinical trial network, with a focus on pediatric neuromuscular disease. CINRG has enrolled over 1,500 patients into clinical research studies. Recent studies include the CINRG Duchenne Natural History Study (DNHS) with 440 DMD patients and over 100 healthy peers

followed by expert neuromuscular physicians in 20 sites in 10 countries. See www.cinrgresearch.org
www.trinds.com