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 Publication of Efficacy, Safety and Tolerability Data with Vamorolone (AGAMREE®) in Patients with Duchenne Muscular Dystrophy in *Neurology*

- *Results from 112 patients with DMD who completed the study confirm maintenance of efficacy and benefits in safety and tolerability of treatment with vamorolone over 48 weeks*
- *AGAMREE® has shown safety benefits in patients switching from standard of care corticosteroids in terms of recovery of bone health and growth*
- *More than 200 patients have now been treated with vamorolone for up to 84 months across clinical studies and access programs*
- *AGAMREE® is the only approved medication in the European Union (EU) for treating all patients from age 4 years with DMD [1], and the first DMD treatment approved across the U.S., EU and UK*

Pratteln, Switzerland, February 14, 2024 – Santhera Pharmaceuticals (SIX: SANN) announces the publication of the paper "*Efficacy and Safety of Vamorolone Over 48 Weeks in Boys With Duchenne Muscular Dystrophy*" in the peer-reviewed journal *Neurology* [2]. The publication reports the results of the 48-week treatment with vamorolone in patients with DMD in the VISION-DMD study, supporting the long-term efficacy and safety profile of vamorolone and concluding that vamorolone was generally well tolerated, consistent with the 24-week study findings, as published previously in *JAMA Neurology* [3].

The *Neurology* publication states:

"Vamorolone is a dissociative corticosteroid that selectively binds to the glucocorticoid receptor and has shown similar efficacy and reduced safety concerns in comparison with prednisone in Duchenne muscular dystrophy (DMD) [3]. This study [VISION-DMD] was conducted to determine the efficacy and safety of vamorolone over 48 weeks and to study crossover participants (prednisone to vamorolone; placebo to vamorolone).

A total of 121 participants with DMD were randomized. Vamorolone at a dose of 6 mg/kg/d showed maintenance of improvement for all motor outcomes to week 48 (e.g., for primary outcome, time to stand from supine [TTSTAND] velocity, week 24 least squares mean [LSM] [SE] 0.052 [0.0130] rises/s vs week 48 LSM [SE] 0.0446 [0.0138]). After 48 weeks, vamorolone at a dose of 2 mg/kg/d showed similar improvements as 6 mg/kg/d for North Star Ambulatory Assessment (NSAA) (vamorolone 6 mg/kg/d–vamorolone 2 mg/kg/d LSM [SE] 0.49 [1.14]; 95% CI −1.80 to 2.78, p = 0.67), but less improvement for other motor outcomes. The placebo to vamorolone 6 mg/kg/d group showed rapid improvements after 20 weeks of treatment approaching benefit seen with 48-week 6 mg/kg/d of vamorolone treatment for TTSTAND, time to run/walk 10 m, and NSAA. There was significant improvement in linear growth after crossover in the prednisone to vamorolone 6 mg/kg/d group, and rapid reversal of prednisone-induced decline in bone turnover biomarkers in both crossover groups. There was an increase in BMI after 24 weeks of treatment that then stabilized for both vamorolone groups.

Improvements of motor outcomes seen with 6 mg/kg/d of vamorolone at 24 weeks of treatment were maintained to 48 weeks of treatment. Vamorolone at a dose of 6 mg/kg/d showed better maintenance of effect compared with vamorolone at a dose of 2 mg/kg/d for most (3/5) motor outcomes. Bone morbidities of prednisone (stunting of growth and declines in serum bone biomarkers) were reversed when treatment transitioned to vamorolone."

AGAMREE® is the first and only medicinal product for DMD to have received full approval in the EU and, following approval in the U.S. last October and in the UK in January, it is the first authorized treatment for patients with the disease in all three territories.

About AGAMREE® (vamorolone)

Vamorolone is a novel drug with a mode of action based on binding to the same receptor as glucocorticoids but modifying its downstream activity and is not a substrate for the 11-β-hydroxysteroid dehydrogenase (11β-HSD) enzymes that may be responsible for local tissue amplification and corticosteroid-associated toxicity in local tissues [3-5]. This mechanism has shown the potential to 'dissociate' efficacy from steroid safety concerns and therefore vamorolone is positioned as an alternative to existing corticosteroids, the current standard of care in children and adolescent patients with DMD [3-5].

In the pivotal VISION-DMD study, vamorolone met the primary endpoint Time to Stand (TTSTAND) velocity versus placebo (p=0.002) at 24 weeks of treatment and showed a good safety and tolerability profile [4]. The most commonly reported side effects were cushingoid features, vomiting, weight increase and irritability. Side effects were generally of mild to moderate severity.

Currently available data show that vamorolone, unlike corticosteroids, has no restriction of growth [6] and no negative effects on bone metabolism as demonstrated by normal bone formation and bone resorption serum markers [7].

AGAMREE (vamorolone), an orphan medicinal product, is approved for use in the United States (Prescribing Information), the European Union (Summary of Product Characteristics) and the United Kingdom.

References:

[1] Applicable drug labeling: Summary of Product Characteristics (SmPC). English. German.
[2] Dang UJ et al. (2024) Neurology 2024;102:e208112. doi.org/10.1212/WNL.0000000000208112. Link.
[3] Guglieri M et al (2022). JAMA Neurol. 2022;79(10):1005-1014. doi:10.1001/jamaneurol.2022.2480. Link.
[4] Liu X et al (2020). Proc Natl Acad Sci USA 117:24285-24293
[5] Heier CR et al (2019). Life Science Alliance DOI: 10.26508
[6] Ward et al., WMS 2022, FP.27 - Poster 71. Link.
[7] Hasham et al., MDA 2022 Poster presentation. Link.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a rare inherited X-chromosome-linked disease, which almost exclusively affects males. DMD is characterized by inflammation which is present at birth or shortly thereafter. Inflammation leads to fibrosis of muscle and is clinically manifested by progressive muscle degeneration and weakness. Major milestones in the disease are the loss of ambulation, the loss of self-feeding, the start of assisted ventilation, and the development of cardiomyopathy. DMD reduces life expectancy to before the fourth decade due to respiratory and/or cardiac failure. Corticosteroids are the current standard of care for the treatment of DMD.

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. The Company has an exclusive license from ReveraGen for all indications worldwide to AGAMREE® (vamorolone), a dissociative steroid with novel mode of action, which was investigated in a pivotal study in patients with Duchenne muscular dystrophy (DMD) as an alternative to standard corticosteroids. AGAMREE for the treatment of DMD is approved in the U.S. by the Food and Drug Administration (FDA), in the EU by the European Medicines Agency (EMA), and in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA). Santhera has out-licensed rights to vamorolone for North America to Catalyst Pharmaceuticals and for China to Sperogenix Therapeutics. The clinical stage pipeline also includes lonodelestat to treat cystic fibrosis (CF) and other neutrophilic pulmonary diseases. For further information, please visit www.santhera.com.

AGAMREE® is a trademark of Santhera Pharmaceuticals.

For further information please contact:

public-relations@santhera.com or
Eva Kalias, Head Investor Relations & Communications
Phone: +41 79 875 27 80
eva.kalias@santhera.com

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