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CONNECTION

October 2020

Edasalonexent at the World Muscle Society Annual Conference

This week at the World Muscle Society virtual conference we and our collaborators shared information on edasalonexent, which is currently in Phase 3 development for Duchenne muscular dystrophy. Learn more about our poster presentations and edasalonexent here:

New Preclinical Research Indicates that Edasalonexent Could Have Positive Effects on Cardiac Function and Preserve Bone Health

Exploring Cardiac Effects

Persistent NF-kB activation in Duchenne can lead to negative effects on the heart, such as cardiac dysfunction. In a preclinical study performed in the laboratory of Pradeep Mammen, M.D., who is the Medical Director of the Neuromuscular Cardiomyopathy Clinic and Director of Translational Research for the Advanced Heart Failure and Transplant Cardiology Program at UT Southwestern Medical Center, the NF-kB inhibitor edasalonexent prevented the development of DMD-associated cardiomyopathy. Edasalonexent reduced the cardiac hypertrophy apparent in these mice, reduced myocardial fibrosis and prevented the development of DMD-associated cardiomyopathy.

Exploring Bone Health

In Duchenne, persistent NF-kB activation drives inflammation and fibrosis, leading to the loss of muscle function and disease progression. Reduced skeletal muscle function in Duchenne results in reduced bone strength. Steroids activate the glucocorticoid receptor and can further negatively impact bone health.

In a preclinical study of *mdx* mice with Frank Rauch, M.D., from Shriners Hospitals for Children – Canada, edasalonexent was seen to maintain bone density and bone strength in a mouse model of DMD. Consistent with these results, edasalonexent treatment in cells inhibited NF-kB and as expected did not impact the glucocorticoid receptor, while prednisolone strongly activated the glucocorticoid receptor.

Baseline Characteristics of Boys Enrolled in the Phase 3 PolarisDMD Trial Before Treatment

The NSAA is a validated measure of physical function designed for use in ambulatory boys affected by Duchenne, and it is the primary endpoint of our Phase 3 PolarisDMD trial studying edasalonexent. In PolarisDMD, we enrolled boys ages 4 to 7, up to 8th birthday, who had not been on steroids for at least 6 months. We saw reliable and consistent NSAA scores between both pre-treatment measurements at screening and baseline, which support no significant learning effect between visits, even at the youngest ages.

An additional evaluation of data from patients at baseline before treatment was shared by Leanne Ward, M.D., FRCPC, Scientific Director from the Ottawa Pediatric Bone Health Research Group. Before treatment, lean body mass index (a marker for muscle mass) was reduced in young boys affected by Duchenne and correlated with reduced muscle function. An analysis of the same patients was also presented earlier in September by Dr. Stefan Jackowski in the same group, and showed that Duchenne has a negative impact on bone strength, including low bone density and mild vertebral fractures at an early stage in Duchenne prior to any treatment.

Long-Term Safety Results with Edasalonexent from the MoveDMD Trial

We also have seen that edasalonexent was well-tolerated throughout our multi-year MoveDMD trial and open-label extension. The most common side effect was diarrhea, which was generally mild and transient. Edasalonexent does not impact the glucocorticoid receptor, and there was no evidence of adrenal insufficiency up to 150 weeks, as measured by cortisol and ACTH levels. Boys also grew along the growth curves of boys who are not affected by Duchenne, resulting in BMIs trending toward the average for unaffected boys. Edasalonexent also demonstrated potential for bone health preservation with low fracture incidence rate in MoveDMD. In the MoveDMD trial, we did not see the adverse effects associated with high-dose steroids.

ABOUT EDASALONEXENT

Edasalonexent is an orally-administered small molecule designed to inhibit NF-kB. Activated NF-kB is a key link between the lack of dystrophin and resulting manifestation and progression of Duchenne. By inhibiting NF-kB in Duchenne, edasalonexent has the potential to limit muscle degeneration, promote muscle regeneration, and reduce inflammation and fibrosis. Edasalonexent is being developed as a monotherapy and for use with other therapies, such as exon-skipping. We believe that based on its mechanism of action, edasalonexent has the potential for use with other approaches in development, such as gene therapy.

The Phase 3 PolarisDMD trial and GalaxyDMD open-label extension trial are both ongoing. Top-line results from the Phase 3 trial are expected in the fourth quarter of 2020.

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For questions: advocacy@catabasis.com

Follow us on social media: @CatabasisPharma.

The information provided here is for parents and caregivers of boys with Duchenne muscular dystrophy. Edasalonexent is an investigational drug that is not yet approved in any territory.

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