MoveDMD Phase 2 Data Supports Design of PolarisDMD, a Phase 3 Study of Edasalonexent, a Novel NF-κB Inhibitor

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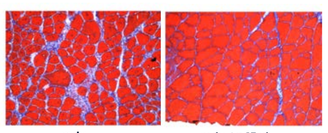
BACKGROUND

Edasalonexent Inhibits NF-κB

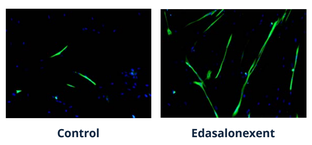
- **NF-κB pathway is the key link between loss of dystrophin and disease progression in DMD**

(Akima et al., *Neuromuscular Disease*, 2012)

- **Edasalonexent: NF-κB inhibition suppressed inflammation and fibrosis, and decreased muscle degeneration and enhanced muscle regeneration**



Inhibition of NF-kB by 50% reduces fibrosis



Human myocyte growth and differentiation in the context of inflammation is positively impacted by edasalonexent

(Yin, et.al., *Muscle Nerve* 2017)

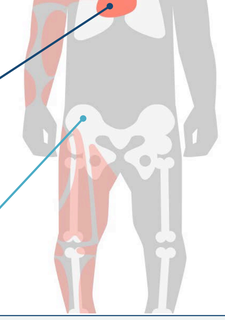
NF-κB Inhibition Provides Potential for Broad Therapeutic Benefit in Duchenne Muscular Dystrophy

Activated NF-κB leads to disease progression in DMD

Skeletal Muscle
Loss of ambulation, upper limb function, respiratory failure

Heart
Cardiomyopathy

Bone
Fractures



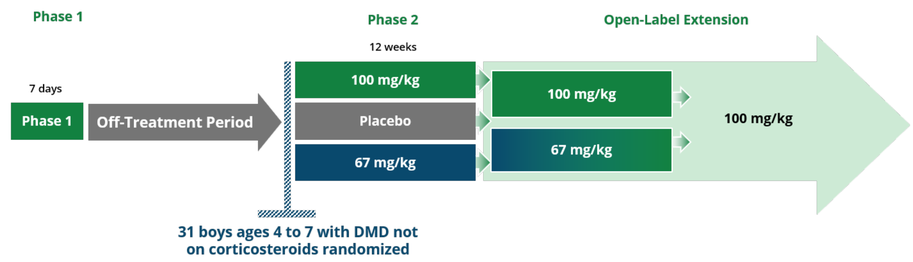
Vision for edasalonexent, an NF-κB inhibitor

Goal: Improve skeletal muscle function

Goal: Preserve cardiac function

Goal: Reduce risk of fractures

MoveDMD Trial Was Designed to Enable Phase 3



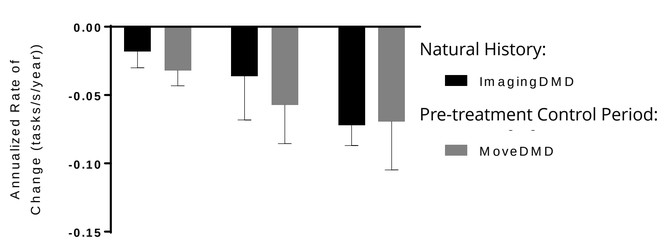
- **Integrated multi-part trial design to evaluate efficacy, safety, tolerability**
  - Assessments included North Star Ambulatory Assessment, age-appropriate timed function tests, MRI
- **Off-treatment control period measurements between Phase 1 and Phase 2**
  - Provides internal control for pre-specified MoveDMD analyses
  - Compared off-treatment control period disease progression with available natural history data
- **Open-label extension enabled assessment of safety and efficacy following longer term treatment**

NATURAL HISTORY DATA

Boys in the MoveDMD Trial Were Declining in Function Prior to Treatment Similar to Natural History

- **The declines in function in the MoveDMD off-treatment period were similar to those in the observational ImagingDMD study in boys up to their 8th birthday who were not on steroids.**

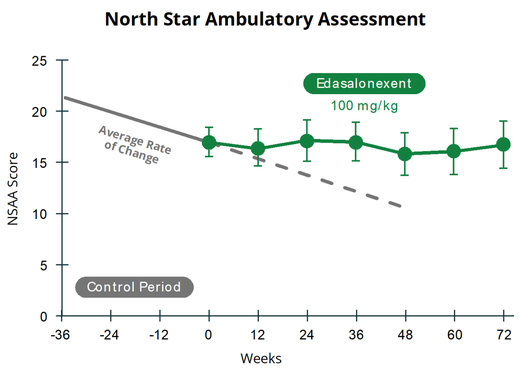
Functional Decline in Boys in ImagingDMD and MoveDMD Not Receiving Steroids or Edasalonexent



Means ± SEM shown

MoveDMD RESULTS

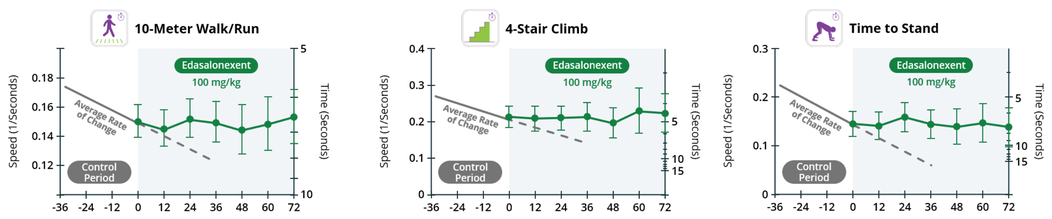
North Star Ambulatory Assessment Score, a Measure of Overall Function in Young Boys, Stabilized with Edasalonexent Treatment Compared to Off-Treatment Control Period



Means ± SEM shown

Speed on All Timed Function Tests Stabilized with Edasalonexent Treatment, Consistent with Effect on NSAA

- **Disease progression on edasalonexent improved compared with rate of change during off-treatment control period**



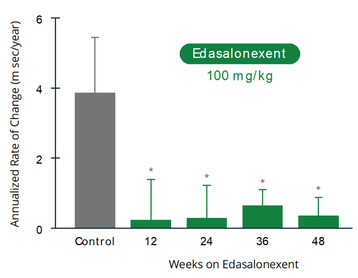
Means ± SEM shown
Includes data of all boys initially started on 100 mg/kg dose (n=16)

MoveDMD RESULTS

Edasalonexent Significantly Improved Rate of Change of MRI T2

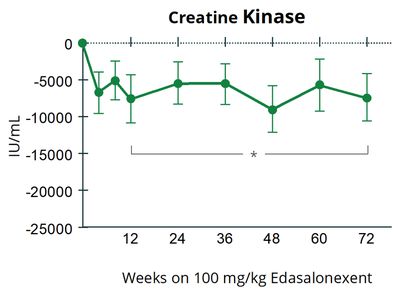
- **On edasalonexent, the rate of change for the MRI T2 composite of the 5 lower leg muscles improved significantly compared to the rate of change during the off-treatment control period (p<0.05 for 12, 24, 36, and 48 weeks)**
- **Stabilization of MRI T2 is consistent with slowing of disease progression also observed in function assessments**

MRI T2: Composite of 5 Lower Leg Muscles



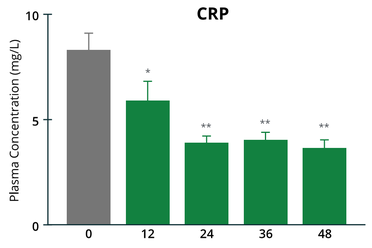
Means ± SEM shown
* p<0.05 for repeated measure mixed model comparison with off-treatment period

Biomarkers Showed Significant Decrease with Edasalonexent Treatment



- **All muscle enzymes (CK, ALT, AST and LDH) showed sustained decrease after 12 weeks (p<0.05)**
- **Consistent positive impact on muscle supportive of an edasalonexent benefit**

Means ± SEM shown
* p<0.05 for change from baseline after 12 weeks



- **C-reactive protein (CRP), a well-characterized blood test marker that provides a global assessment of inflammation is elevated in DMD**
- **CRP approximately 3-fold higher in boys affected by DMD compared to unaffected boys (Anderson, 2017)**
- **In MoveDMD, CRP significantly decreased from baseline throughout 48 weeks of 100 mg/kg edasalonexent**

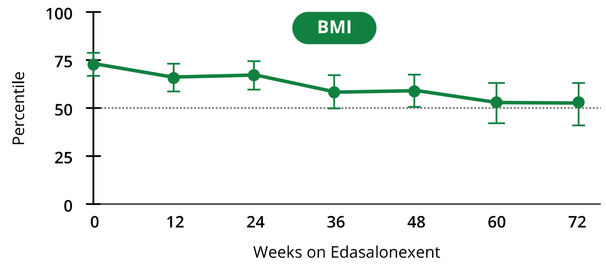
Means ± SEM shown * p ≤ 0.05,
** p ≤0.001 for comparison with pre-treatment baseline measurement

Anderson, et al. (2017). *Pediatr Cardiol* 38(8): 1606-1612.

Safety: Growth Continues as Expected

- **Well tolerated in 50+ patient years of exposure**
  - Well tolerated, with majority of adverse events mild in nature and mostly gastrointestinal
- **Growth: Age-appropriate increase in weight and height**
  - Height increased an average of 2.1 inches/year, while weight increased by an average of 2.9 lbs/year, both in line with typical height and weight increases of unaffected boys

Percentiles Compared to CDC Growth Charts



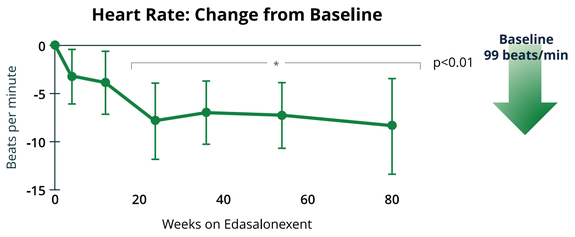
Means ± SEM shown

MoveDMD RESULTS

Elevated Resting Heart Rate Characteristic of DMD Decreased to Age-Normative Values

- **In DMD, heart rate does not decrease with age from 6-12 (Thomas, 2012)**
- **Age-normative value is ~92 beats per minute (Fleming, 2011)**
- **In MoveDMD, ECG heart rate decreased on average from baseline of 99 to 92 beats per minute**
- **Heart rate by physical examination showed similar trends**
  - No significant changes in systolic or diastolic blood pressure

Heart Rate: Change from Baseline

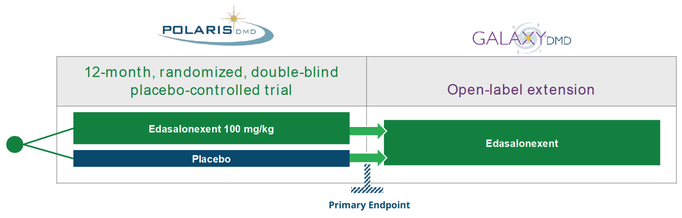


Means ± SEM shown

Thomas, et al. *Pediatr Cardiol.* 2012 33(7):1175-9
Fleming, (2011). *The Lancet* 377(9770): 1011-1018.

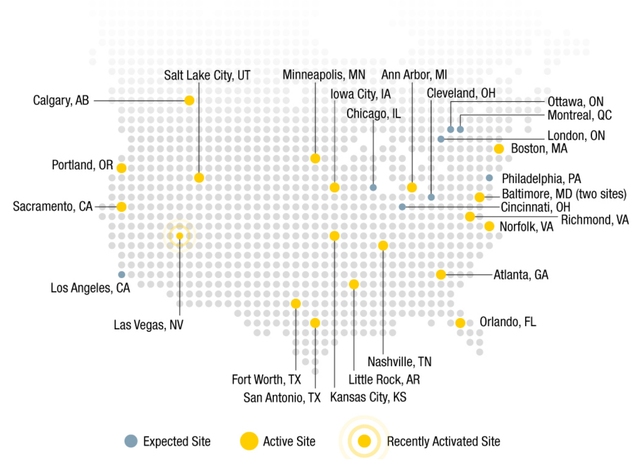
PolarisDMD

PolarisDMD: Global Phase 3 Registration Trial for Edasalonexent



- **Study Population**
  - All mutations, age 4 to 7 (up to 8th birthday), steroid naïve or off steroids for ≥ 6 months
- **Visits / key assessments every 3 months**
  - Primary: Change in North Star Ambulatory Assessment
  - Key secondary: Age-appropriate timed function tests
  - Safety measures
  - Assessments of growth, cardiac, and bone health
  - No biopsy or 6 minute walk test
- **Enrollment of approximately 125 boys, 2:1 randomization**
- **After the 52 week placebo-controlled period, patients may elect to continue in the open-label study, GalaxyDMD**

Many Sites Active and Enrolling Patients



- **Clinical trial sites across US, Canada, Australia, Europe, and Israel**

Presented at the 2019 MDA Clinical & Scientific Conference, April 13-17, Orlando, FL

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