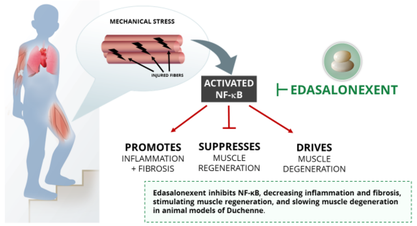
MoveDMD®: Phase 2 Trial of Edasalonexent, an NF-κB Inhibitor, in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy

Richard Finkel, MD[1], Krista Vandenborne, PT PhD[2], H. Lee Sweeney, PhD[2], Erika L. Finanger, MD[3], Gihan I. Tennekoon, MBBS MRCS LCRP[4], Perry Shieh, MD PhD[5], Rebecca J. Willcocks, PhD[2], Glenn Walter, PhD[2], William Rooney, PhD[3], Sean C. Forbes, PhD[2], William T. Triplett, BSc[2], Sabrina W. Yum, MD[4], Maria Mancini, MHP[6], James MacDougall, PhD[6], Angelika Fretzen, PhD[6], Pradeep Bista, PhD[6], Andrew Nichols, PhD[6], Joanne M. Donovan, MD PhD[6]

[1] Nemours Children's Health System, Orlando, FL; [2] University of Florida Health, Gainesville, FL; [3] Oregon Health Sciences University, Portland, OR; [4] The Children's Hospital of Philadelphia, Philadelphia, PA; [5] University of California, Los Angeles, Los Angeles, CA; [6] Catabasis Pharmaceuticals, Cambridge, MA

Background & Study Design

Edasalonexent Inhibits NF-κB and Slows Muscle Degeneration and Stimulates Muscle Regeneration

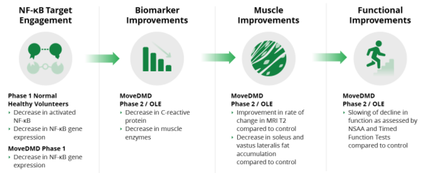


Edasalonexent inhibits NF-κB, decreasing inflammation and fibrosis, stimulating muscle regeneration, and slowing muscle degeneration in animal models of Duchenne.

Hammers, et al. JCI Insight 2016 1(21): e90341

1

Edasalonexent: Translation from Target Engagement to Functional Improvements in Duchenne



Phase 1 Normal Healthy Volunteers
- Decrease in activated NF-κB
- Decrease in NF-κB gene expression

MoveDMD Phase 1
- Decrease in NF-κB gene expression

MoveDMD Phase 2 / OLE
- Decrease in C-reactive protein
- Decrease in muscle enzymes

MoveDMD Phase 2 / OLE
- Improvement in rate of change in MRI T2 compared to control
- Decrease in soleus and vastus lateralis fat accumulation compared to control

MoveDMD Phase 2 / OLE
- Slowing of decline in function as assessed by NSAA and Timed Function Tests compared to control

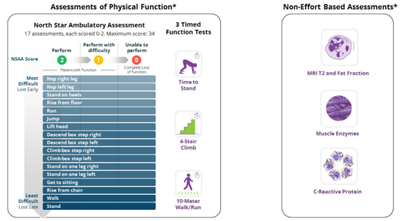
2

MoveDMD Trial Design

- **Integrated 3-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**
  - Provided internal control for pre-specified MoveDMD analyses
  - To confirm consistency of patient off-treatment control period disease progression with available natural history data
- **Phase 2 showed favorable trends towards the slowing of disease progression after 12 weeks with no safety issues**
- **Open-label extension enabled assessment of safety and efficacy following longer term treatment**

3

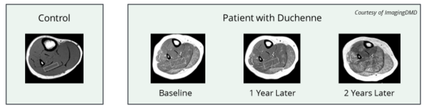
MoveDMD Trial Endpoints: Multiple Measures of Physical Function and Biomarkers



*Assessed before initiation of active treatment and every 12 weeks during open-label extension

4

MRI is a Non-Invasive Approach to Assess Disease Progression in Duchenne



- **MoveDMD incorporated both Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS)**
- **MRI T2 measures both inflammation and fat content**
  - MRI T2 is elevated from a young age and increases with age as fat increases
  - Changes in MRI T2 correlate with changes in function[9] and loss of functional milestones
- **MRS Fat Fraction measures fat content**
  - Changes in MRS Fat Fraction correlate with changes in function[9] and loss of functional milestones

[9] Willcocks et al. 2016. Ann. Neurol., Willcocks et al. 2014. Ann. Neurol.

5

Results

Changes in Fat Fraction on Edasalonexent Consistent with Slowing of Disease Progression

MRS Fat Fraction Change from Baseline

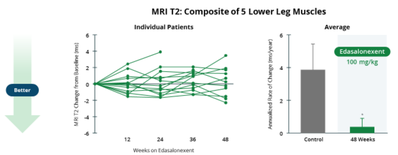
Muscle	MoveDMD Off-Treatment Control Period Annualized Rate	MoveDMD 48 weeks on Edasalonexent	ImagingDMD Natural History Study* 1 Year Change
Soleus (calf)	2.6%	0.85%	3%
Vastus lateralis (thigh)	10.4%	5.9%	7%

- Rate of increase in Fat Fraction of the soleus and vastus lateralis was substantially decreased as compared to the off-treatment control period following 48 weeks of edasalonexent
- Increases in Fat Fraction correlate with declines in function and predict future loss of functional milestones*
- In the ImagingDMD natural history study, boys were largely on steroids

*Willcocks et al. 2016. Ann. Neurol., Willcocks et al. 2014. Ann. Neurol

6

Edasalonexent Significantly Improved Rate of Change of MRI T2

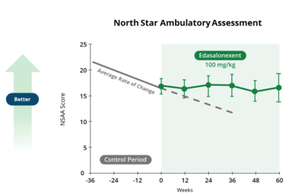


- On edasalonexent, the rate of change for the MRI T2 of lower leg muscles improved significantly compared to the rate of change during the off-treatment control period[9]
- Stabilization of MRI T2 is consistent with slowing of disease progression also observed in functional assessments

Means ± SEM shown; * p<0.05 for repeated measure mixed model comparison with off-treatment period; † p<0.05 for 12, 24, 36 and 48 weeks

7

North Star Ambulatory Assessment Score Stabilized with Edasalonexent Treatment

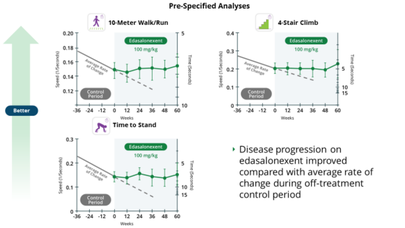


- Disease progression on edasalonexent improved compared with average rate of change during off-treatment control period

Means ± SEM shown

8

All Timed Function Test Speeds Stabilized with Edasalonexent Treatment



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

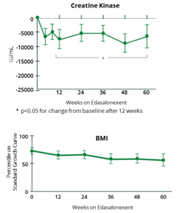
Means ± SEM shown

9

Safety & Tolerability

Edasalonexent: Well Tolerated Without Safety Signals

- No safety signals in MoveDMD trial to date
- Well tolerated, with majority of adverse events being mild in nature, mostly gastrointestinal
- No adverse trends in hematology, chemistry, renal or adrenal function, calcium and phosphate
- Growth: Age-appropriate increases in weight and height
- Heart rate decreased toward normal values at this age



10

Summary

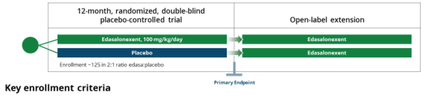
Summary: Edasalonexent Substantially Slowed Predicted Disease Progression in MoveDMD Study

- **Clinically meaningful slowing of disease progression on edasalonexent over more than 1 year compared to off-treatment control period**
  - North Star Ambulatory Assessment stabilized
  - All timed function tests stabilized (10-meter walk/run, 4-stair climb and time to stand)
- **MRI measures support positive edasalonexent treatment effects over 48 weeks**
  - Muscle MRI T2 significantly improved during edasalonexent treatment versus off-treatment control period progression
  - Increases in Fat Fraction decreased compared to the off-treatment control period and to that expected for natural history on corticosteroids
- **No safety signal and well tolerated over more than 1 year**
  - Height, weight and BMI growth patterns continued to be similar to unaffected boys
- **Supportive of Phase 3 clinical trial**

11

Phase 3 Plans

Positive MoveDMD Data Support Phase 3 Registration Trial for Edasalonexent



- **Key enrollment criteria**
  - Age 4 to 7th birthday
  - Able to complete timed function tests
  - Not on corticosteroids for at least 6 months
  - Not on other investigational therapies for at least 1 month, can be on stable eteplirsen
- **Visits / key assessments every 3 months**
  - North Star Ambulatory Assessment, Timed Function Tests, Muscle Strength
  - Safety measures
  - Assessments of growth, cardiac and bone health
  - No biopsy or 6 minute walk test
- **Expected Locations: US, Canada, Europe, Israel and Australia**

12

Conclusions

Edasalonexent: Potential to Slow Disease Progression for All Those Affected by Duchenne

- Investigational oral disease-modifying agent for all patients with Duchenne, regardless of mutation type
- Edasalonexent substantially slowed disease progression compared to control
- Preparing to initiate Phase 3 POLARIS DMD trial in H2 2018
- Potential as monotherapy and also exploring potential to combine with dystrophin-targeted and other therapies

POLARIS DMD

13

Acknowledgments

We would like to thank the patients and families, patient groups, and ImagingDMD Investigators and study staff.

For Questions:
DMDtrials@catabasis.com

Parent Project Muscular Dystrophy

Sign up for the Catabasis Quarterly newsletter on Catabasis.com

Jett Foundation · MDA · Cure Duchenne™

Presented at PPMD Annual Conference | June 2018 | Scottsdale, Arizona

catabasis