MoveDMD®: Positive Effects of Edasalonexent, an NF-κB Inhibitor, in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy in Phase 2 Study with an Open-Label Extension

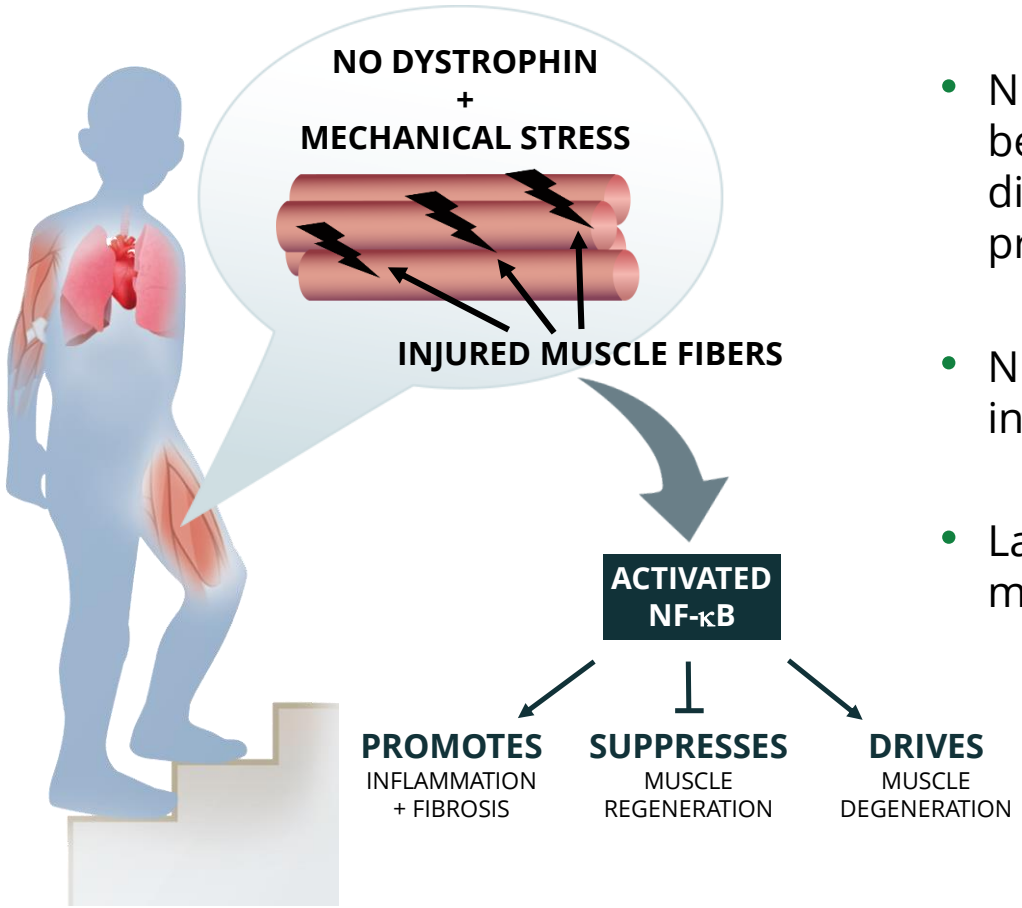
Richard Finkel, MD[1,]; Krista Vandenborne, PT, PhD[2], H Lee Sweeney, PhD. [2], Erika Finanger, MD[3], Gihan Tennekoon, MBBS, MRCS, LCRP [4], Perry Shieh, MD, PhD [5], Rebecca J. Willcocks, PhD [2], Sean C Forbes, PhD [2], William T. Triplett, BSc [2], Sabrina W. Yum, MD [4], Maria Mancini, MHP [6], Angelika Fretzen, PhD [6], Joanne 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,

Disclosures

- The clinical trial was sponsored by Catabasis Pharmaceuticals, Inc.
- Richard Finkel, Krista Vandenborne, H Lee Sweeney, Erika Finanger, Gihan Tennekoon, Perry Shieh, Rebecca J Willcocks, Sean C Forbes, William T Triplett, and Sabrina W Yum received research support from Catabasis
- Richard Finkel, H Lee Sweeney, Erika Finanger, and Perry Shieh received honoraria from Catabasis
- Maria Mancini, Angelika Fretzen, and Joanne Donovan are employees of Catabasis and hold stock in Catabasis

Edasalonexent Inhibits NF-κB, a Fundamental Driver of Disease Progression in DMD

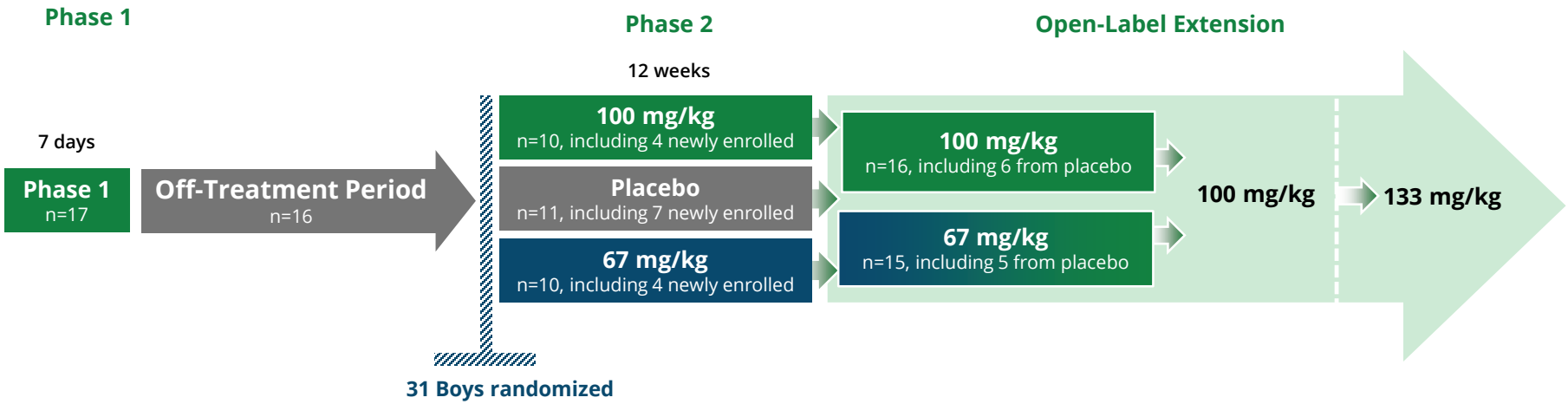


- NF-κB pathway is a key link between loss of dystrophin and disease manifestation and progression in DMD
- NF-κB is known to be upregulated in DMD from infancy
- Lack of dystrophin combined with mechanical stress activates NF-κB

Edasalonexent is an oral small molecule that inhibits NF-κB and improves skeletal, diaphragm and cardiac disease in mouse and dog models of DMD

Kumar, et al. FASEB J 2003 17(3):17: 386-96.
Peterson, et al. Curr Top Dev Bio. 2011; 96: 85-119.
Hammers, et al. JCI Insight 2016;1:e90341.

MoveDMD Trial: An Integrated Multi-Part Trial Design



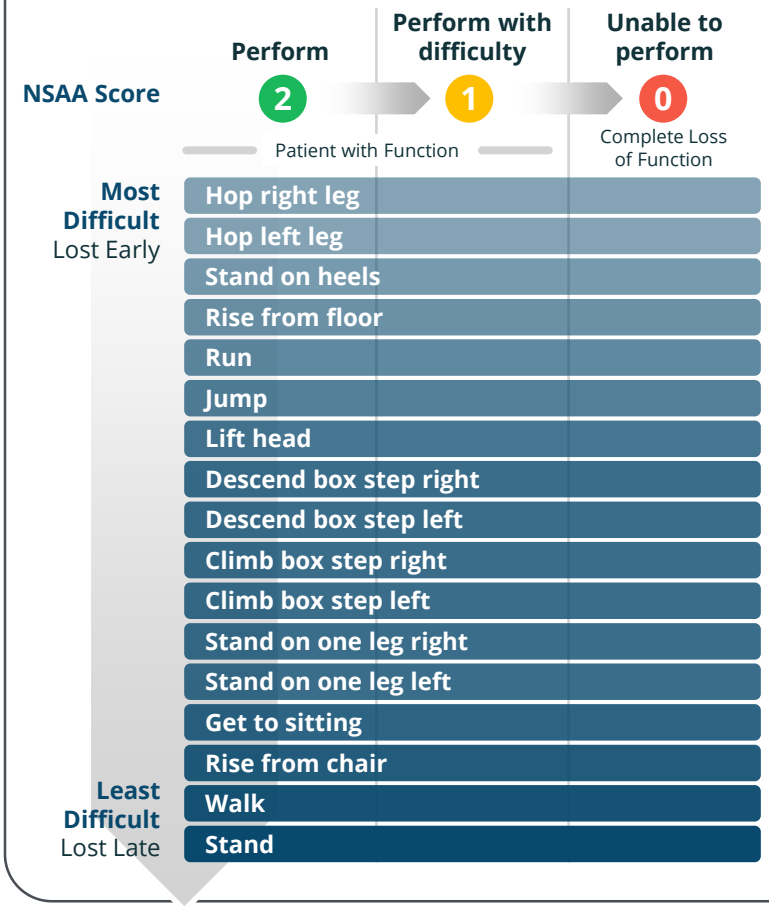
- **Supports evaluation of efficacy, safety/tolerability, target engagement, and dose response**
- **4 to 7 year-old steroid naïve boys with DMD were enrolled**
- **Off-treatment control period measurements between Phase 1 and commencement of dosing in Phase 2/open-label extension**
  - Provides internal control (run-in) for pre-specified MoveDMD analyses
  - To confirm consistency of patient off-treatment control period disease progression with available natural history data
- **Open-label extension**
  - Enables assessment of safety and efficacy following longer term treatment
  - Data includes boys reaching at least 48 weeks after initiation of active treatment

MoveDMD Trial Endpoints Multiple Measures of Physical Function and Biomarkers

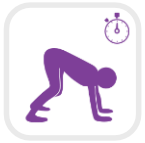
Assessments of Physical Function*

North Star Ambulatory Assessment

17 assessments, each scored 0-2. Maximum score: 34



3 Timed Function Tests



Time to Stand

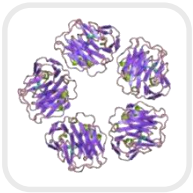
4-Stair Climb

10-Meter Walk/Run

Non-Effort Based Assessments*

MRI T2 and Fat Fraction

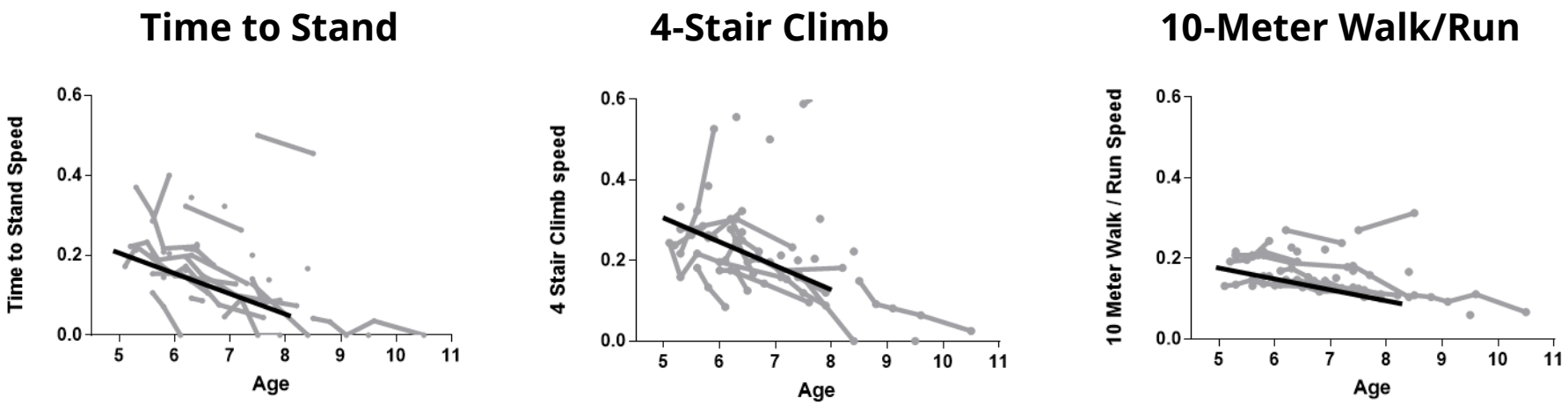
Muscle Enzymes



C-Reactive Protein

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

Boys in the MoveDMD Trial Were Declining in Function Prior to Treatment Similar to Those in Natural History Study of DMD

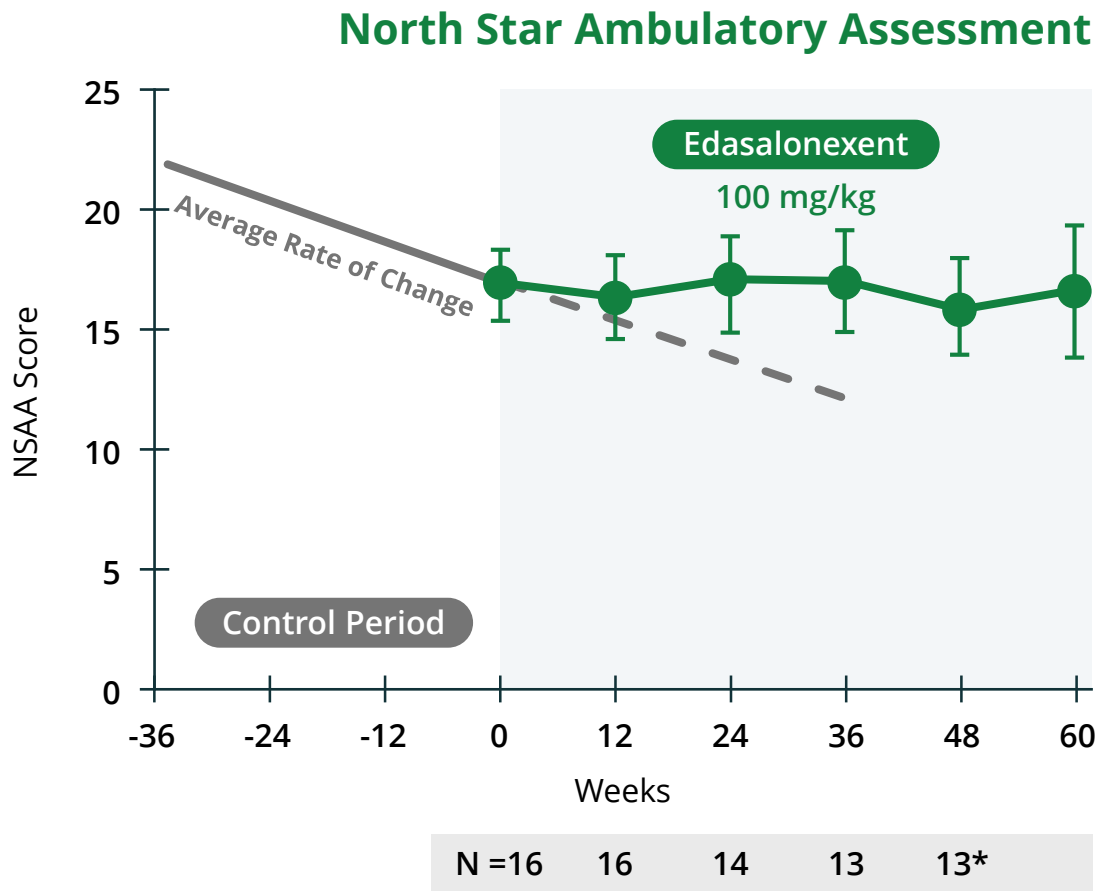


Boys (ages 5-8.5 yo) not on corticosteroids (n=28)

Rate of change in MoveDMD off-treatment (n=23)

- The ImagingDMD natural history study (Willcocks et al., 2014) performed annual timed function tests in young boys with DMD
- Boys enrolled in the MoveDMD study under same data collection protocols generally had declines consistent with observations in the ImagingDMD natural history study.

North Star Ambulatory Assessment Score Stabilized with Edasalonexent Treatment



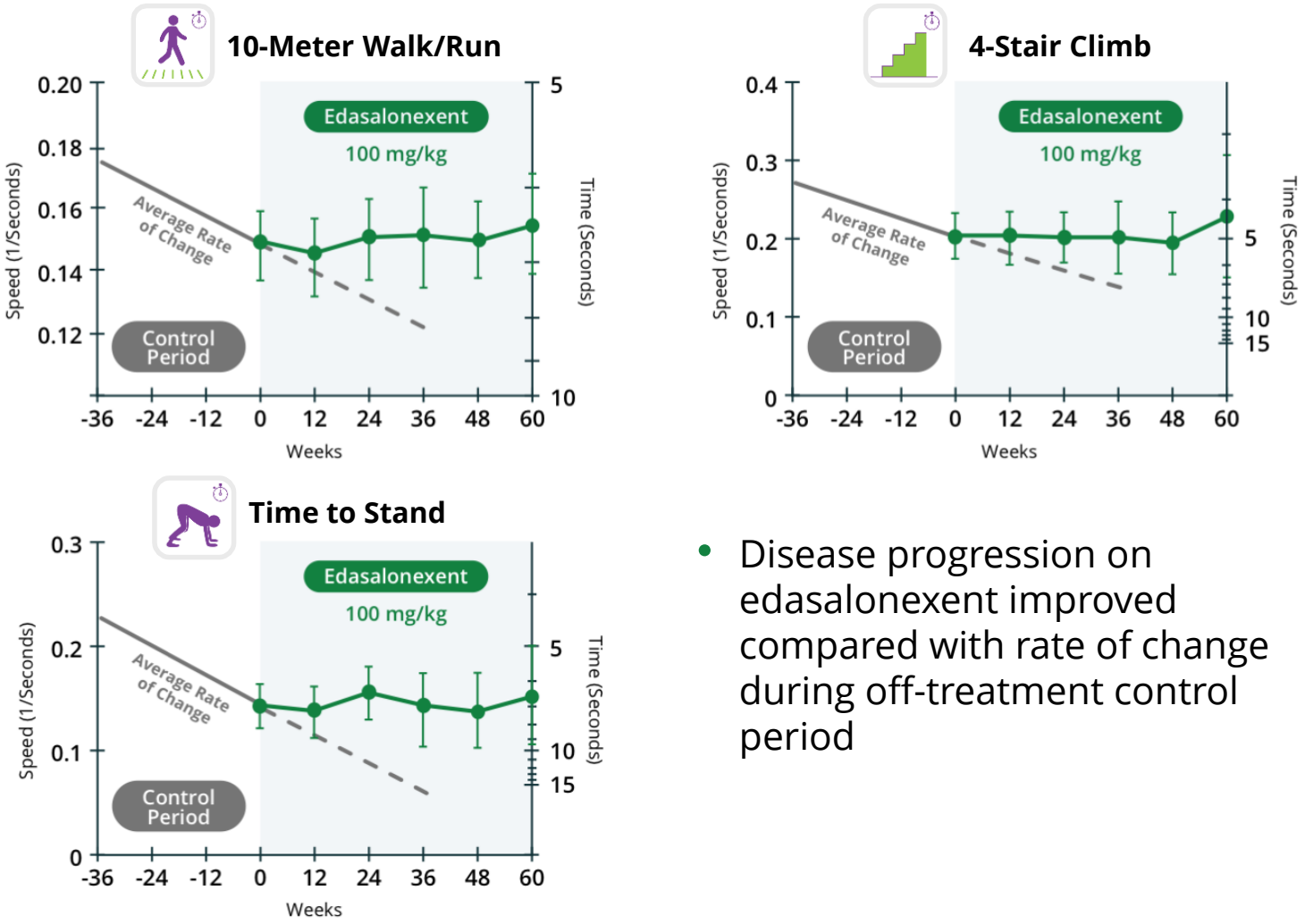
- Disease progression on edasalonexent improved compared with rate of change during off-treatment control period

- 3 discontinued for steroid use (n=2) or no reason given (n=1) before 48 weeks; all remaining patients completed >48 weeks after initiation of therapy, and the 8 patients who reached 60 weeks as of data cut-off are included.

Means ± SEM shown; p NS

All Timed Function Tests Speed Stabilized with Edasalonexent Treatment

Pre-Specified Analyses

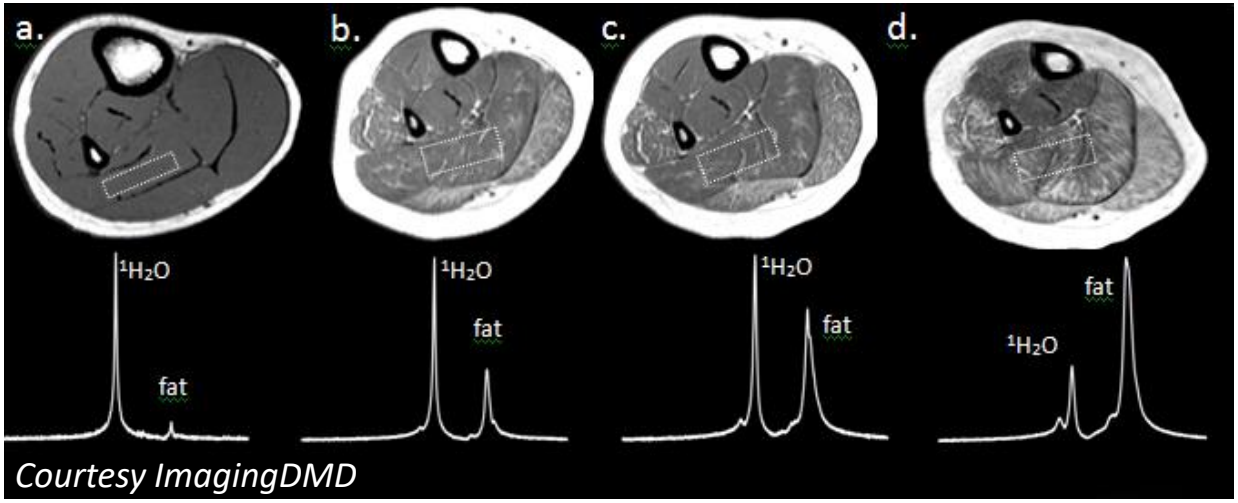


- Disease progression on edasalonexent improved compared with rate of change during off-treatment control period

3 discontinued for steroid use (n=2) or no reason given (n=1) before 48 weeks; all remaining patients completed >48 weeks after initiation of therapy, and the 8 patients who reached 60 weeks as of data cut-off are included.

Means ± SEM shown; p NS

MRI Is a Non-Invasive Approach to Assess Disease Progression in DMD



Courtesy ImagingDMD

a. Control

b. DMD patient baseline

c. DMD patient 1 year later

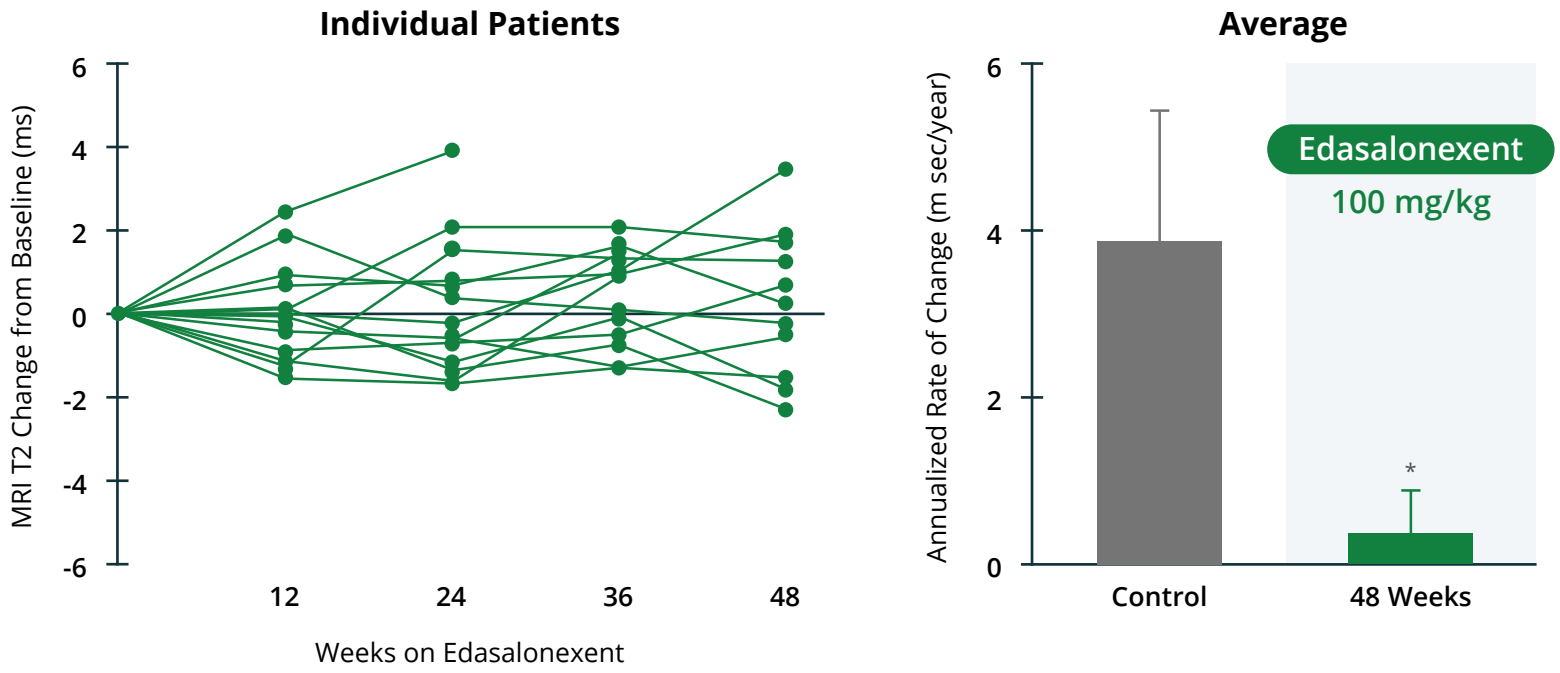
d. DMD patient 2 years later

- **MRI T2 measures combined inflammation and fat**
  - MRI T2 elevated from a young age and increases with age as fat increases
- **MR Spectroscopy measures inflammation and fat fraction independently**
  - Fat fraction increases with age while MRS T2 measures only the inflammatory component
- **MoveDMD incorporated both MRI and MRS**
  - Primary MRI assessment was composite of T2 of 5 lower leg muscles
  - Fat fraction and MRS T2 also measured in lower leg (soleus) and upper leg (vastus lateralis)
- **Changes in MRI T2 and fat fraction are known to correlate with changes in function**
  - Increases in both measures strongly correlate with worse performance on timed function tests$^{\phi}$ and predict future loss of functional milestones

$^{\phi}$ Willcocks et al, 2016, Ann. Neurol., Willcocks et al, 2014, Ann. Neurol

Edasalonexent Significantly Improved Rate of Change of MRI T2

MRI T2: Composite of 5 Lower Leg Muscles



- 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

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

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

MR Spectroscopy
Change in Fat Fraction from Baseline

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

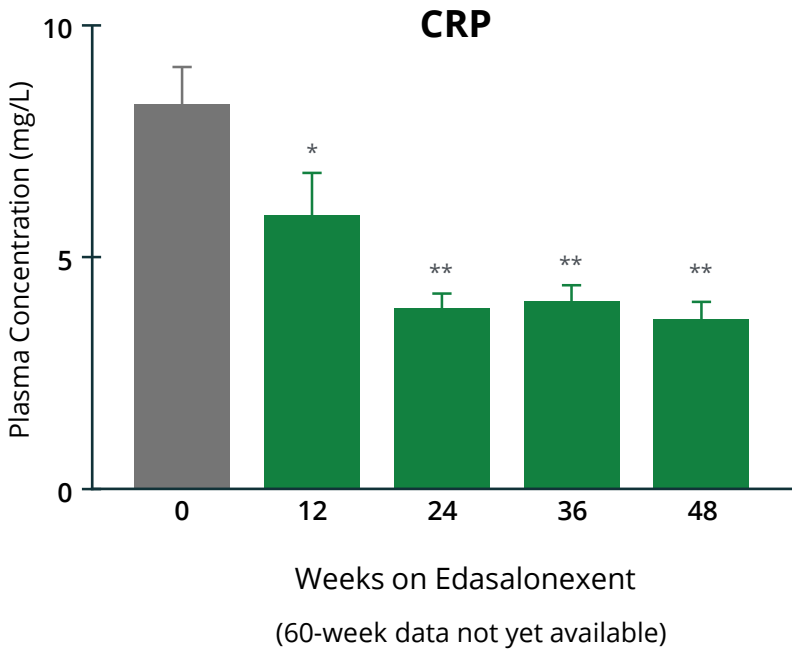
- Following 48 weeks of edasalonexent the rate of increase in fat fraction of the soleus and vastus lateralis was substantially decreased as compared to the off-treatment control period
- In the ImagingDMD natural history study, boys were largely on steroids

Baseline fat fraction in the soleus was 9.3% and in the VL 13.1%
At 48 weeks, MRS T2, reflecting inflammation only, decreased by -1.1 and -1.2 msec for the soleus and VL, respectively.

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

Edasalonexent Significantly Reduced Plasma C-Reactive Protein Compared with Pretreatment Baseline

- C-reactive protein (CRP) is a well-characterized blood test marker that provides a global assessment of inflammation
- CRP is elevated in DMD
  - CRP approximately 3-fold higher in boys affected by DMD compared to unaffected boys[†]
- In MoveDMD, CRP significantly decreased from baseline through 48 weeks of 100 mg/kg edasalonexent
  - No change in CRP following 12 weeks of placebo (8.3 ± 0.7 to 9.7 ± 0.8)

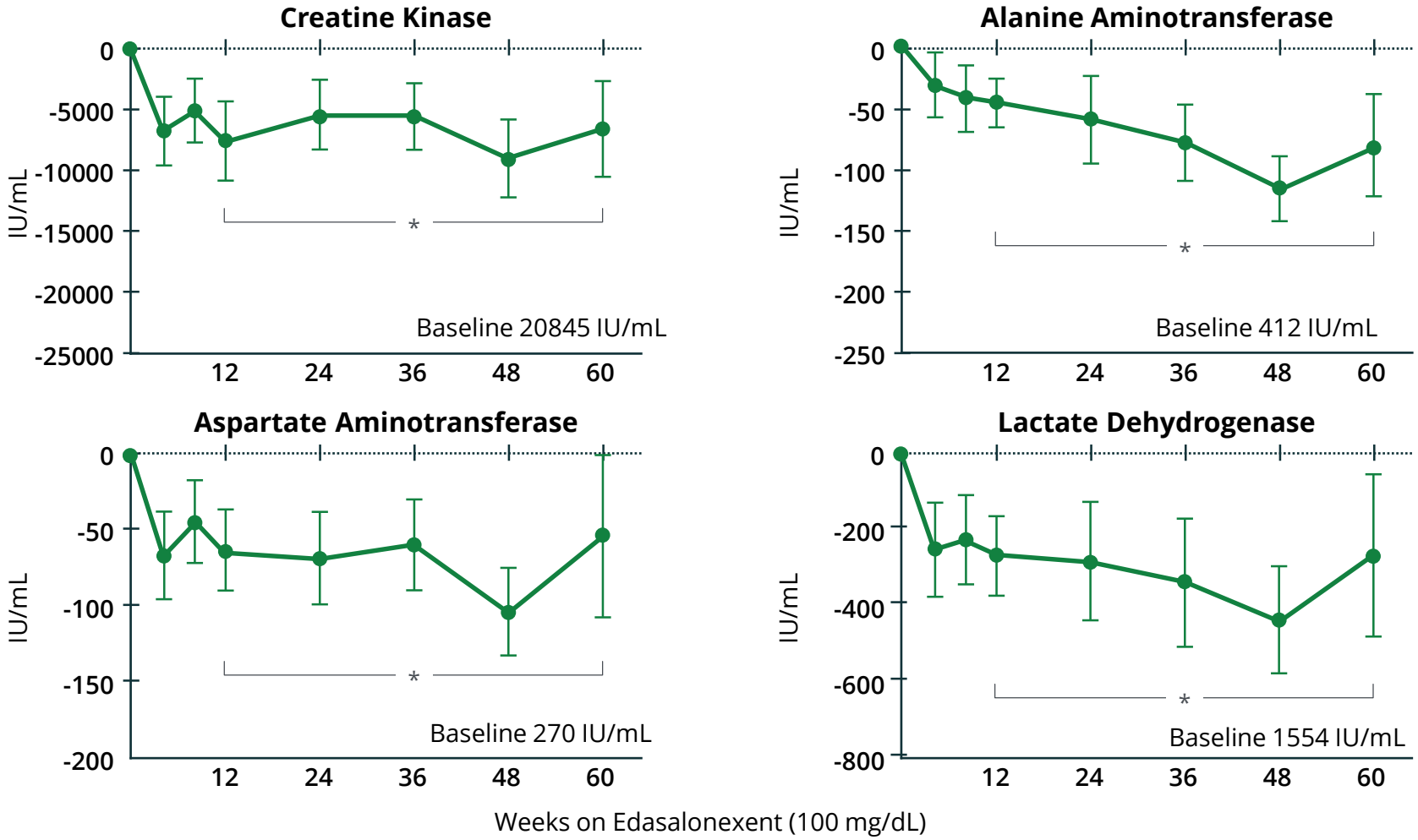


Means ± SEM shown; * p≤0.05, ** p≤0.001 for comparison with pre-treatment baseline measurement

[†] Anderson et al, 2017, Pediatric Cardiology

Muscle Enzymes Significantly Decreased from Baseline on Edasalonexent

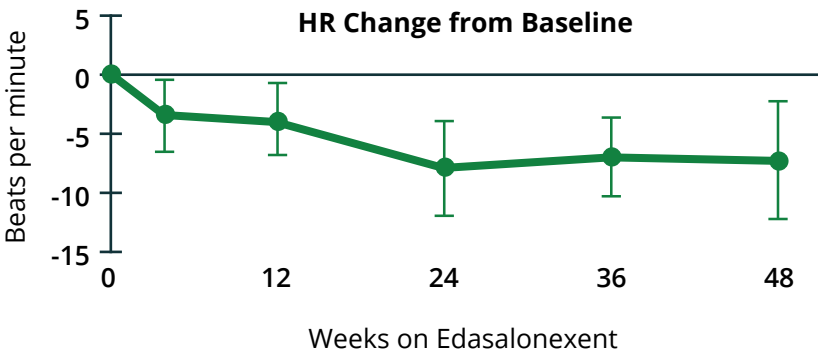
- Plasma muscle enzymes are elevated 10 to 100 fold in DMD, indicative of leakage from damaged myocytes
- Decrease is consistent with positive impact on muscle and supportive of an edasalonexent benefit



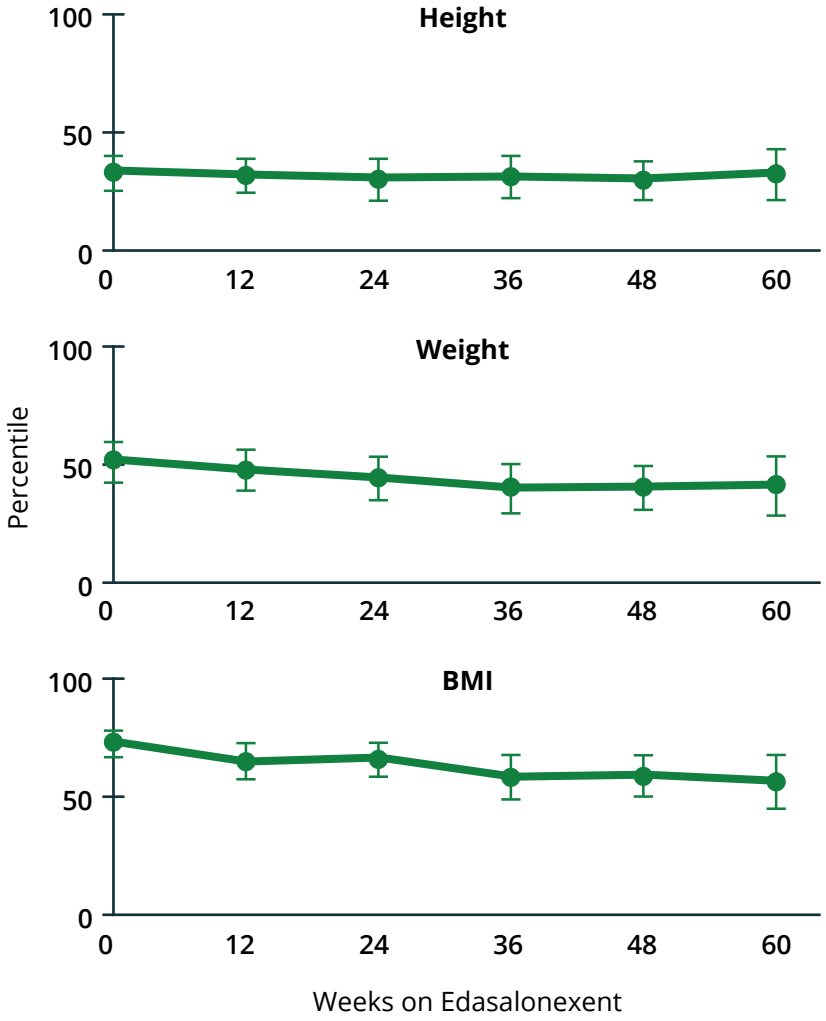
Means ± SEM shown; * $p<0.05$ for change from baseline after 12 weeks

Edasalonexent Was Well Tolerated with No Safety Signals

- **No safety signals in MoveDMD trial to date**
- **Well tolerated, with majority of adverse events being mild in nature, mostly gastrointestinal**
  - Most common treatment-related adverse events were mild diarrhea
  - No serious treatment-related adverse events or dose reductions
- **No adverse trends in hematology, chemistry, renal or adrenal function, calcium and phosphate**
- **Growth: Age appropriate increases in weight and height**
- **ECG heart rate decreased toward age-normative values**



Percentiles Compared to CDC Growth Charts



Conclusions: In MoveDMD Open-Label Extension Edasalonexent Substantially Slowed Predicted DMD Disease Progression

- **Clinically meaningful slowing of disease progression on edasalonexent over >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 48 weeks of 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 >1 year**
  - Height, weight and BMI growth patterns continued to be similar to unaffected boys
- **Supportive of Phase 3 clinical trial**