Edasalonexent, an NF-κB Inhibitor In Development as a Potential Disease-Modifying Therapy for Duchenne Muscular Dystrophy

Andrew Nichols, Catabasis Pharmaceuticals

New Directions in Biology and Disease of Skeletal Muscle Conference

New Orleans, June 25 2018

Forward Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, including statements regarding our expectations and beliefs about our business, future financial and operating performance, product development plans and prospects, including statements about future clinical trial plans including, among other things, statements about our plans to commence a single global Phase 3 trial in Duchenne muscular dystrophy, or DMD, to evaluate the efficacy and safety of edasalonexent for registration purposes, and our plans to continue to evaluate data from the open-label extension of our MoveDMD® clinical trial of edasalonexent for the treatment of DMD. The words “believe”, “anticipate”, “plans,” “expect”, “could”, “should”, “will”, “would”, “may”, “intend” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements contained in this presentation and in remarks made during this presentation and the following Q&A session are subject to important risks and uncertainties that may cause actual events or results to differ materially from our current expectations and beliefs, including: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of our product candidates, including the final trial design of our planned Phase 3 trial in DMD; availability and timing of results from preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; expectations for regulatory approvals to conduct trials or to market products, including our expected target product profile for edasalonexent in DMD; our ability to obtain financing on acceptable terms and in a timely manner to fund our planned Phase 3 trial in DMD to evaluate the efficacy and safety of edasalonexent for registration purposes; availability of funding sufficient for our foreseeable and unforeseeable operating expenses and capital expenditure requirements; other matters that could affect the availability or commercial potential of our product candidates; and general economic and market conditions and other factors discussed in the “Risk Factors” section of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, which is on file with the Securities and Exchange Commission, and in other filings that we may make with the Securities and Exchange Commission in the future. In addition, the forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

Acknowledgements

- **Patients and families**
- **Patient groups**
- **Nemours Children's Hospital**
  - Richard Finkel, MD
- **ImagingDMD & University of Florida**
  - Krista Vandenborne, PT PhD
  - H. Lee Sweeney, PhD
  - Rebecca J. Willcocks, PhD
  - Glenn Walter, PhD
  - Sean C. Forbes, PhD
  - William T. Triplett, BSc
- **Oregon Health Sciences University**
  - Erika L. Finanger, MD
  - William Rooney, PhD
- **The Children's Hospital of Philadelphia**
  - Gihan I. Tennekoon, MD
  - Sabrina W. Yum, MD
- **University of California**
  - Perry Shieh, MD PhD
- **Catabasis Pharmaceuticals**
  - Joanne Donovan, MD PhD
  - Maria Mancini, MHP
  - Angelika Fretzen, PhD
  - Pradeep Bista, PhD
  - Michael Zimmer, PhD
  - Feng Liu, PhD
  - John Reilly, PhD
  - Hanlan Liu, PhD
  - James MacDougall, PhD

Parent Project Muscular Dystrophy

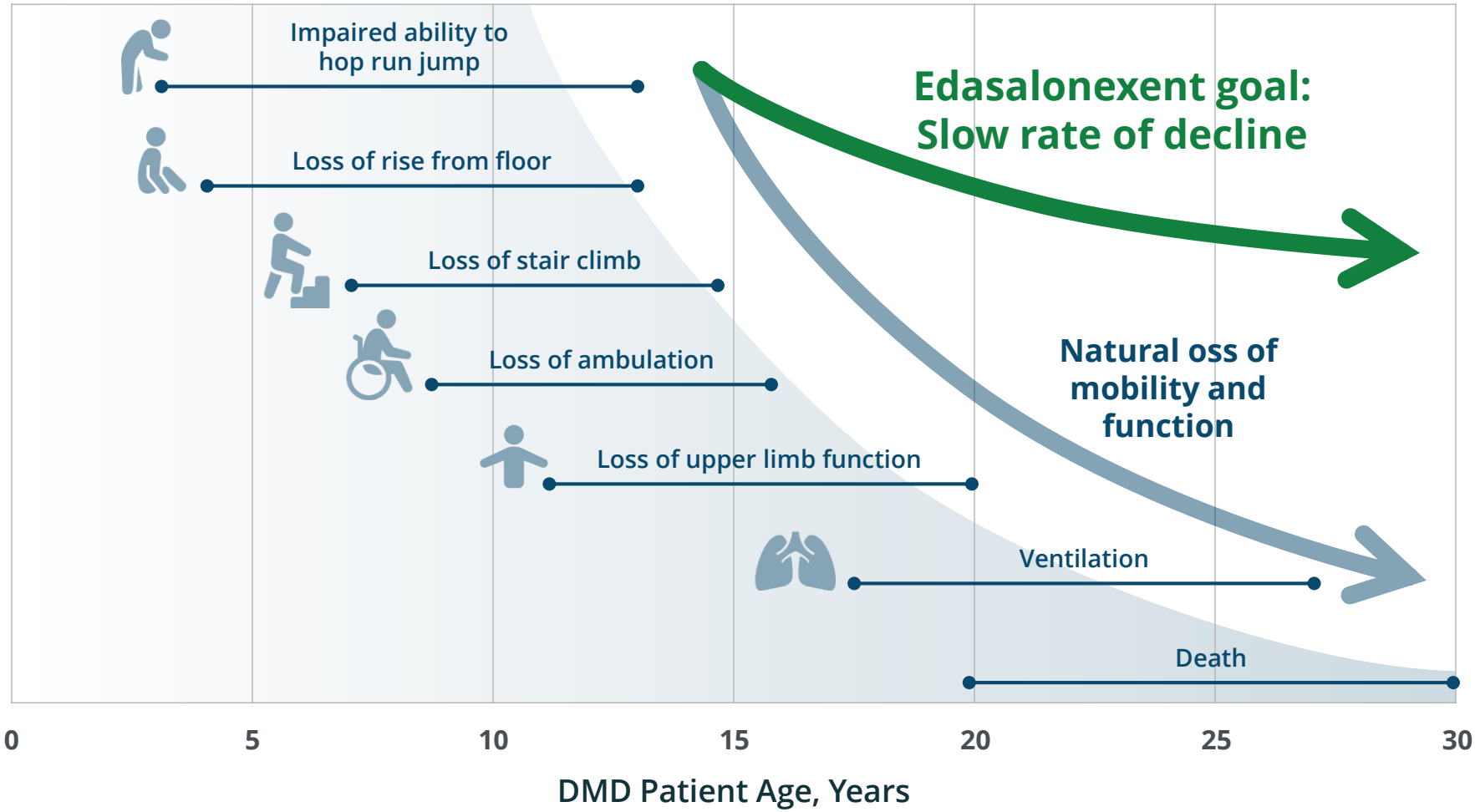
Jett Foundation

MDA

Cure Duchenne™

DMD Progresses Through a Predictable Cascade of Discrete Losses of Function and Mobility Milestones to Disablement and Death

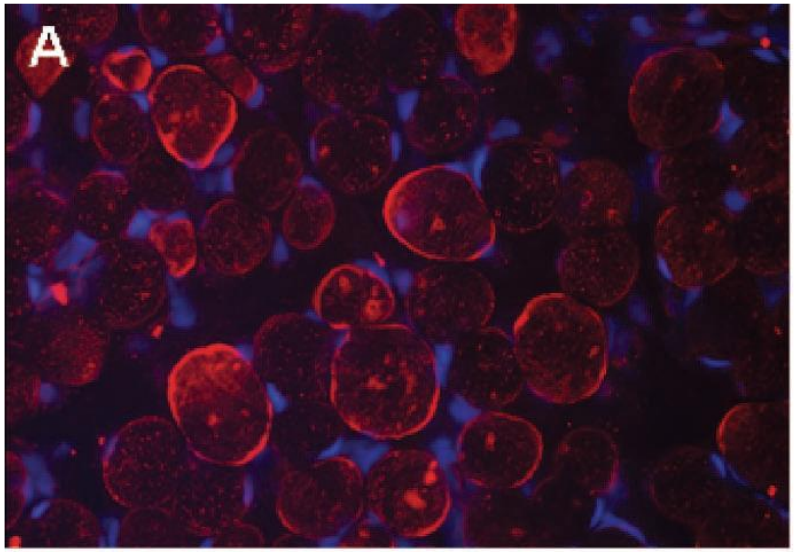
Typical DMD Disease Progression and Goal of Edasalonexent Therapy



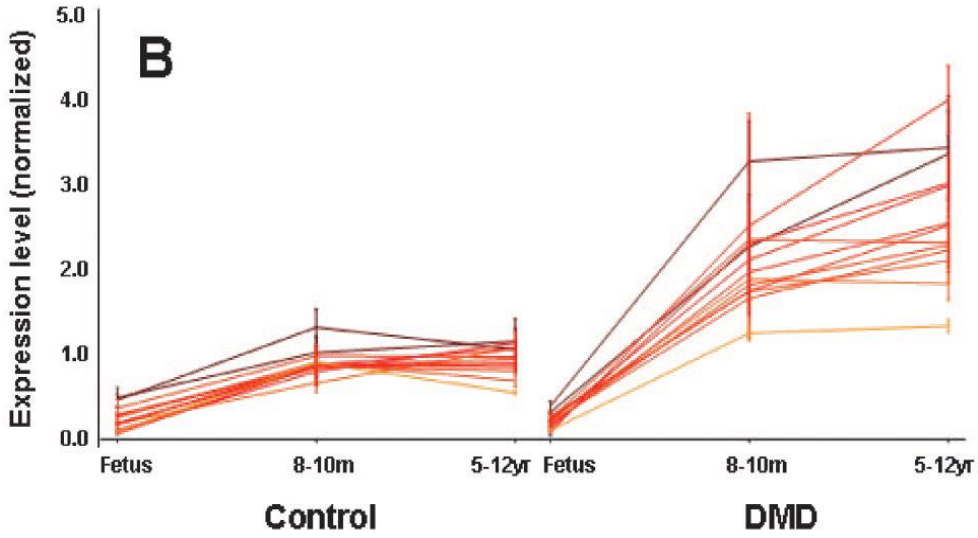
Adapted from presentation by Dr. Craig McDonald, UC Davis NeuroNEXT Program Director, University of California

NF-κB: The Key Driver of Muscle Inflammation, Damage and Fibrosis in DMD is Activated Early in Disease Before Onset of Symptoms

Activated NF-κB (p65) in DMD muscle biopsy



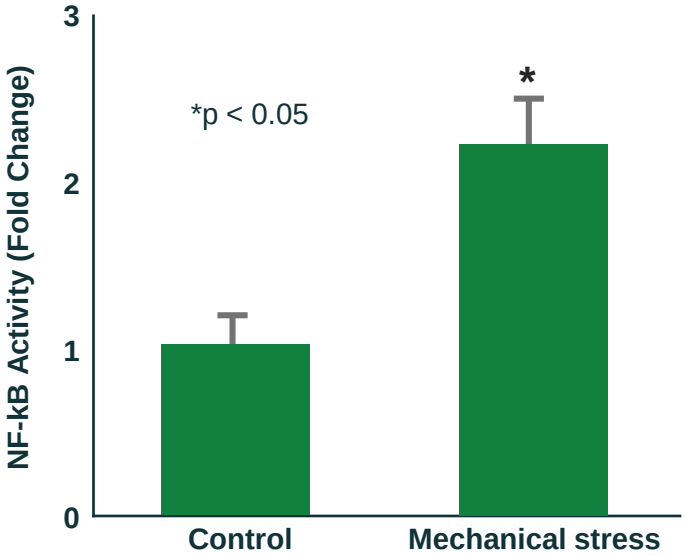
Early activation of inflammatory genes in DMD muscle



Modified from:
Early onset of inflammation and later involvement of TGFbeta in Duchenne muscular dystrophy
Chen et al., Neurology 65:826-834, 2005

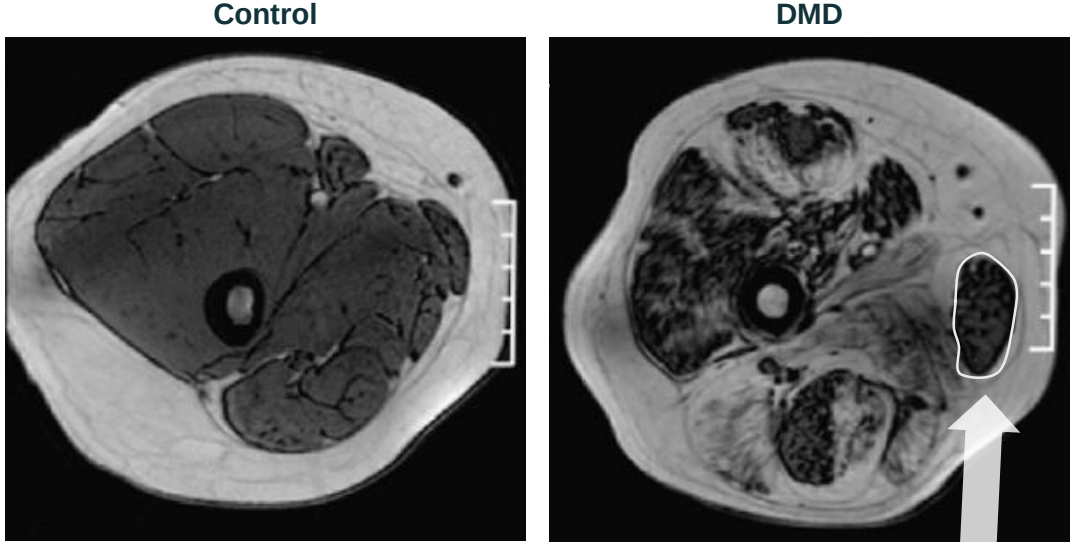
Central Role of NF-κB: Lack of Dystrophin is Necessary but Not Sufficient for DMD Disease Progression

Mechanical stress activates NF-κB in mouse diaphragm



Replacement of muscle with fat and fibrosis

Cross section of mid-thigh muscle in boys age 12 - 14

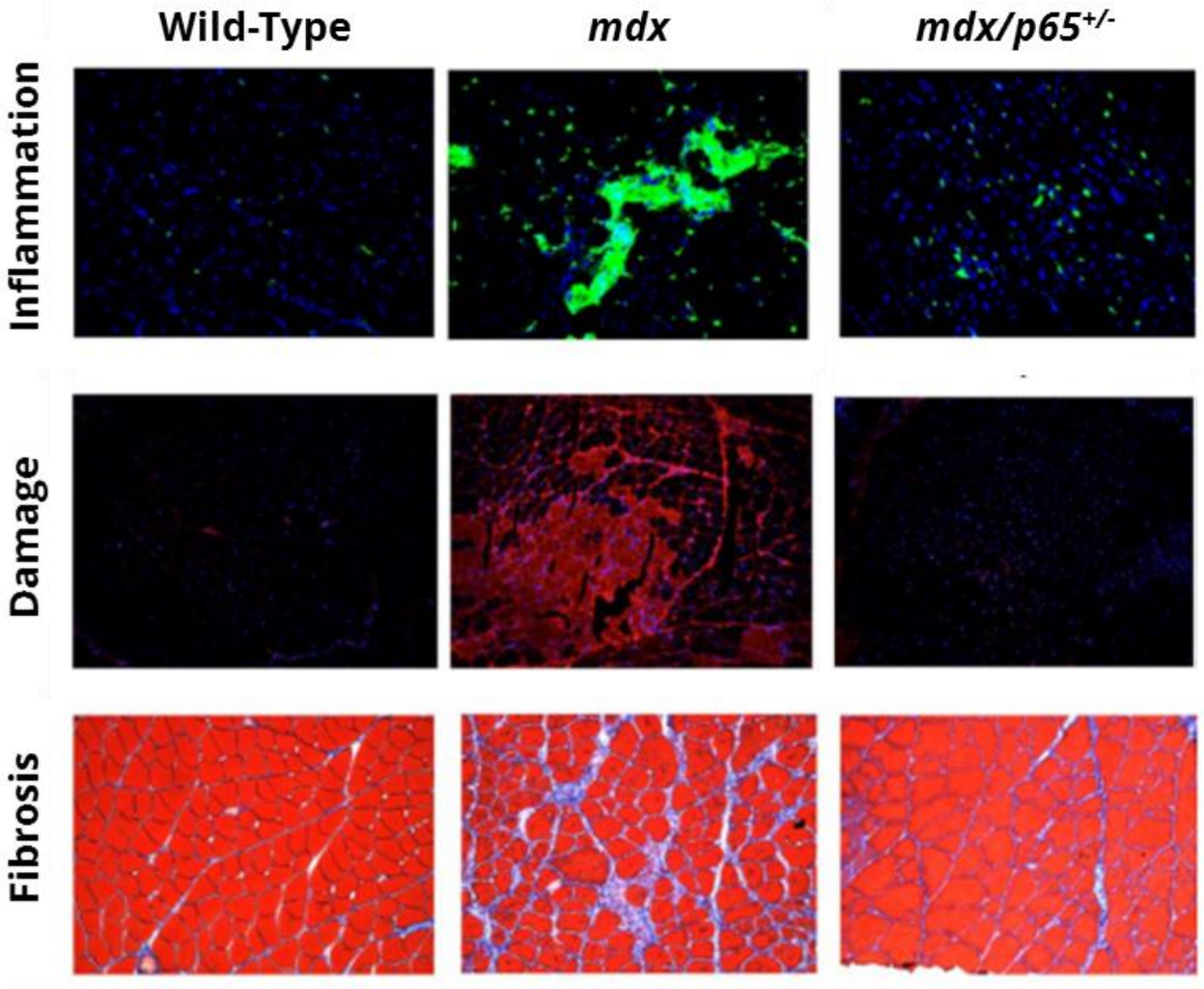


Muscles with no dystrophin but less mechanical stress are protected from degradation

"The absence of dystrophin alone is necessary but not sufficient to cause the patterned fibrosis, inflammation and failure of muscle regeneration characteristic of dystrophinopathy" **– John Porter, past CEO, Parent Project Muscular Dystrophy**

Kumar *et al* FASEB J 2003 17:386
Akima *et al* Neuromuscul Disord 2012 22(1):16-25
Porter *et al* Hum Mol. Genet 2003 12 (15):1813-1821

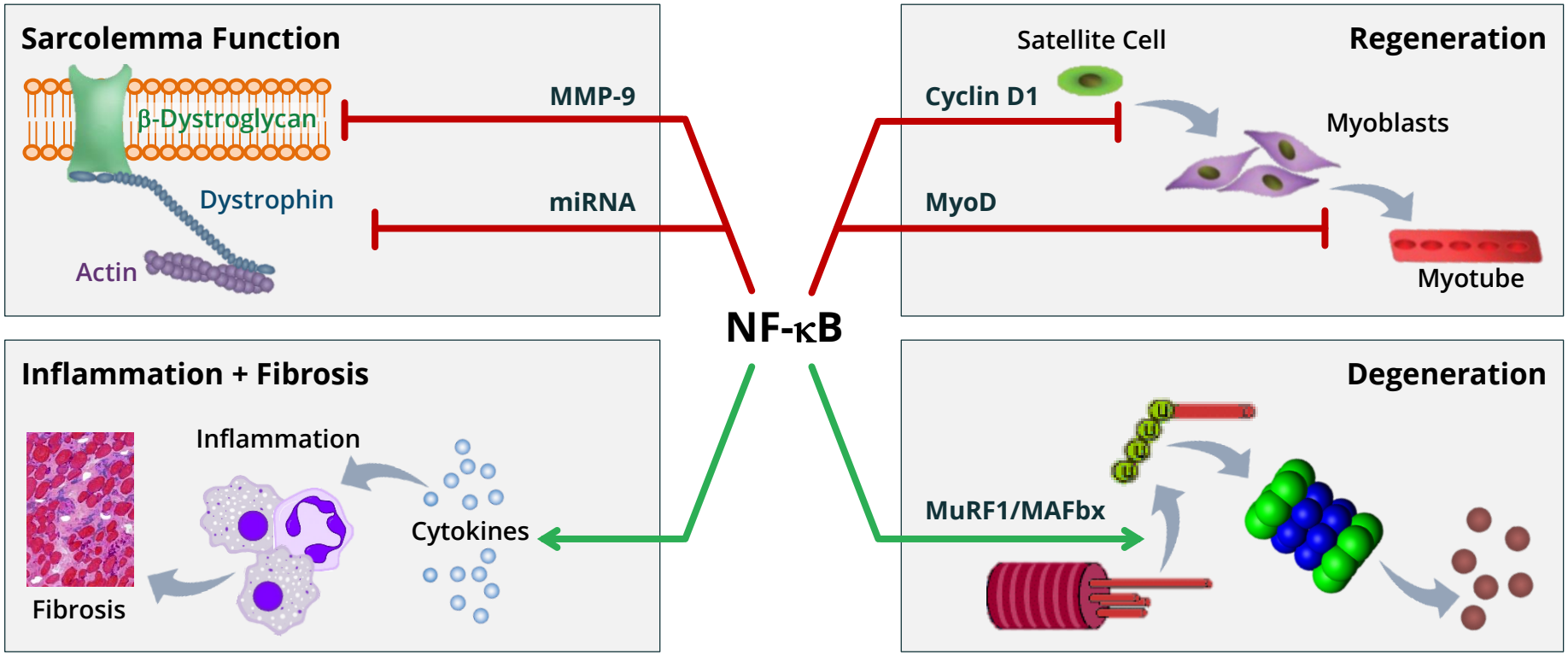
Inhibition of NF-κB by 50% (*p65*$^{+/-}$) Reduces Muscle Inflammation, Damage and Fibrosis in *mdx* Mice



Modified from:
Genetic ablation of P65 subunit of NF-κB in mdx mice to improve muscle physiological function
Yin et al., Muscle Nerve 56:759-767, 2017

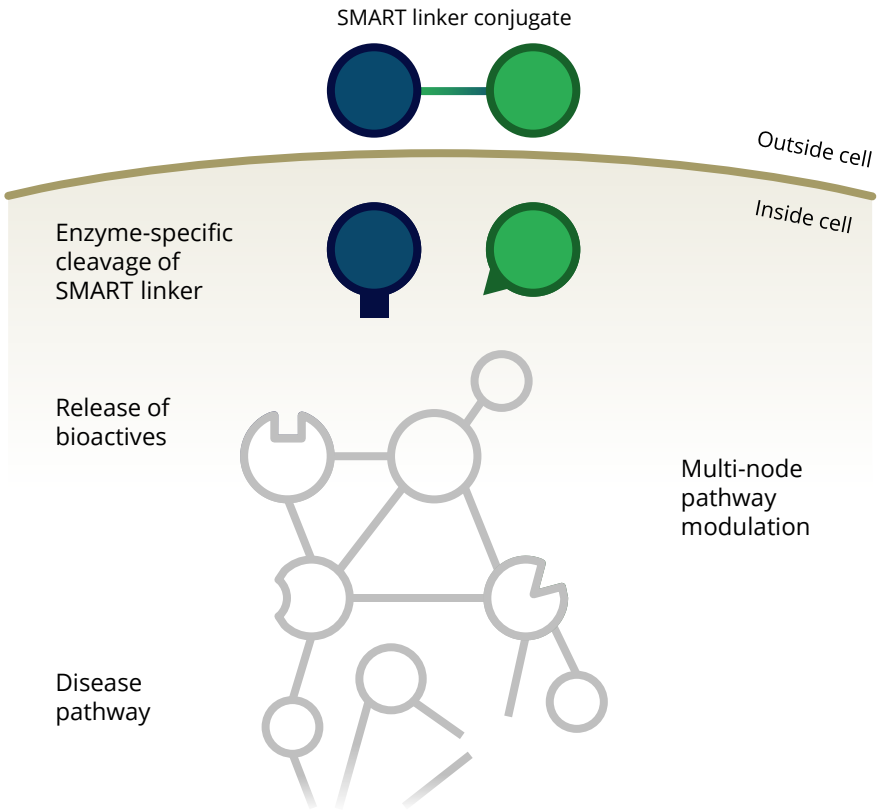
Pathogenic Role of Activated NF-κB in Muscle Diseases

Duchenne muscular dystrophy, Becker muscular dystrophy, others

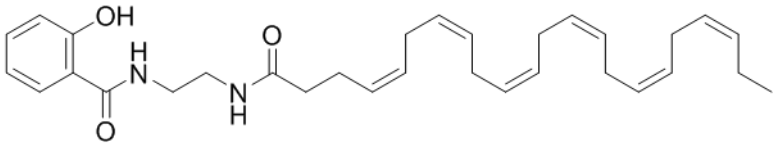


The Catabasis SMART Linker Technology: A New Approach to Difficult Problems

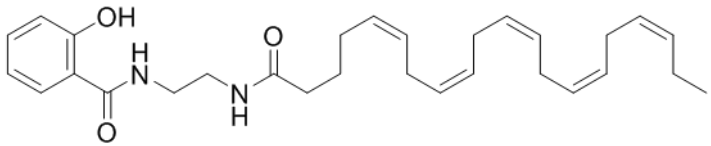
- **Catabasis-amassed IP, technology, and know-how**
  - Conjugation engineering know-how
  - Library of proprietary “SMART linkers”
  - Bioactives can be ‘GRAS’ molecules, Rx or OTC drugs, food ingredients
- **Targeted delivery of bioactives**
  - Conjugates inactive in circulation but actively taken up by cells
  - Bioactives released inside cells by enzymatic cleavage of linkers
  - Bioactives interact with targets for desired activity
- **New IP**
  - Conjugates have composition of matter and method of use patents



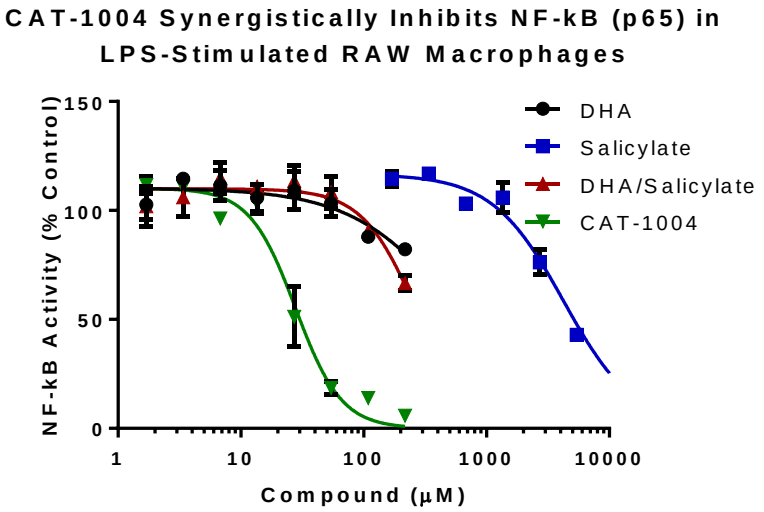
Edasalonexent (CAT-1004) and CAT-1041 are Novel Inhibitors of NF-κB

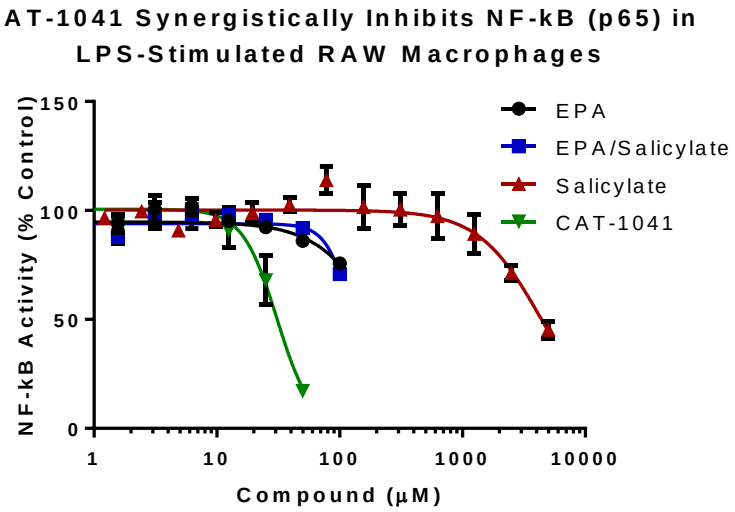


CAT-1004



CAT-1041





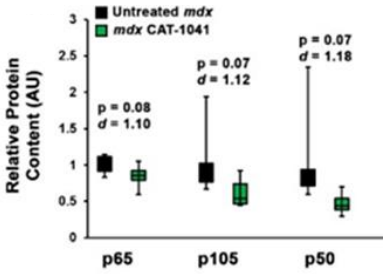
CAT-1041 was used in some preclinical experiments as a proxy for CAT-1004

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

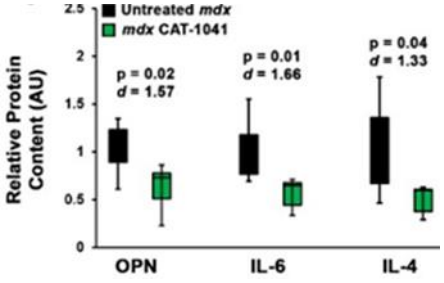
Inhibition of NF-κB, Slows Muscle Degeneration, Stimulates Muscle Regeneration and Improves Function

Inhibiting NF-κB reduces muscle inflammation and fibrosis and improves muscle mass and function in *mdx* mice

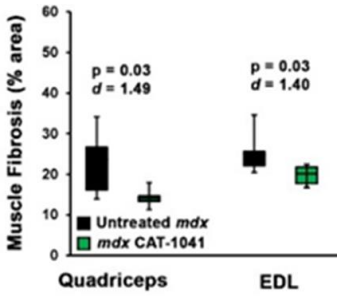
NF-κB Inhibition



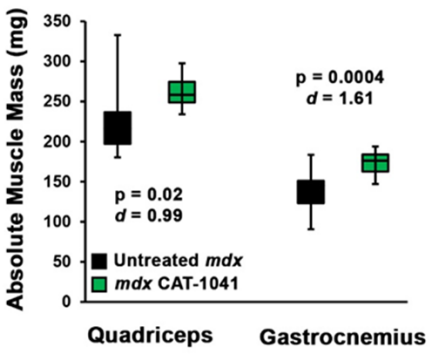
Reduced Inflammation



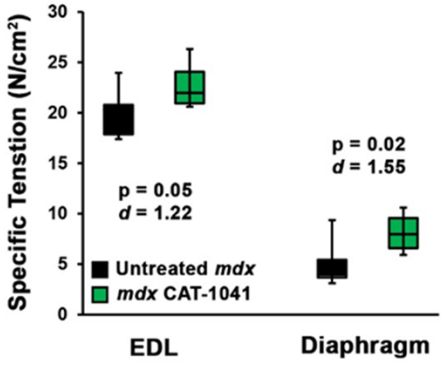
Reduced Fibrosis



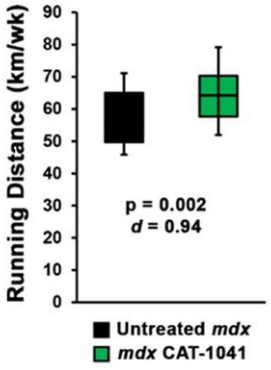
More Muscle



Improved Strength



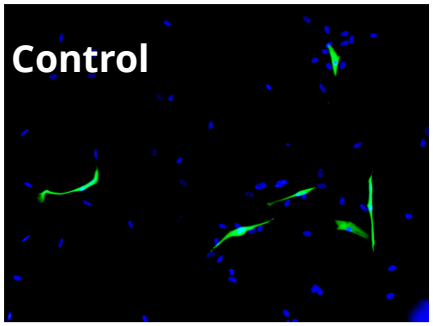
Increased Activity

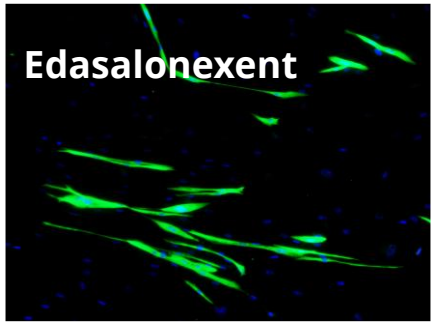


mdx mice treated with CAT-1041 at 0.75% in diet for 6 months

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

Edasalonexent positively impacts human myocyte growth and differentiation





Blue = Nucleus
Green = Myosin heavy chain

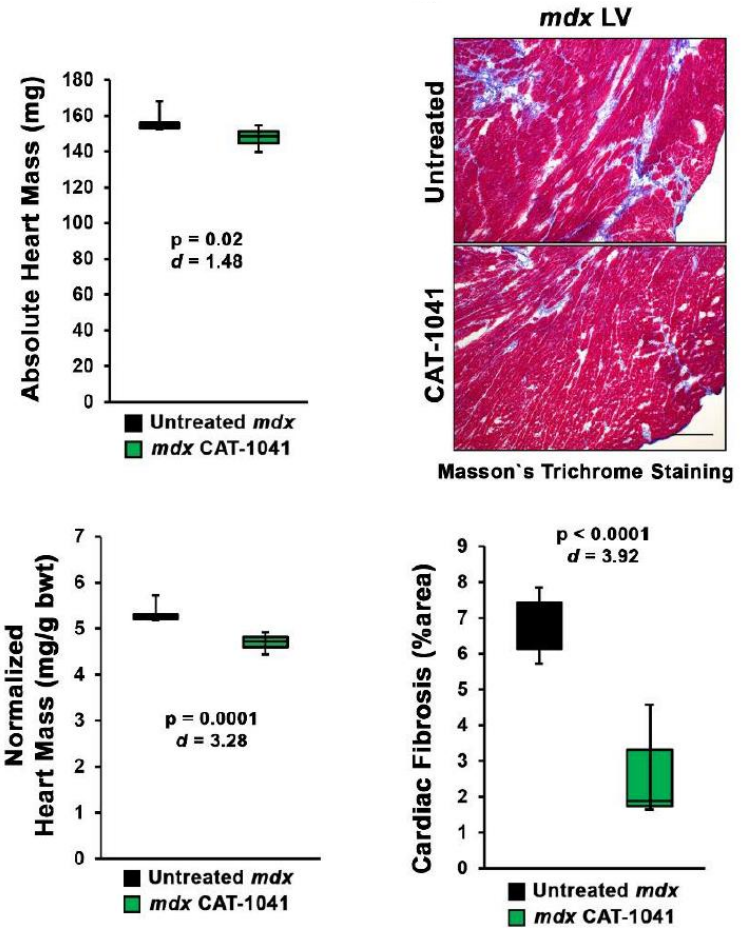
Human myotube formation

Nichols, et al. Neuromuscular Disorders 2017 27: S215

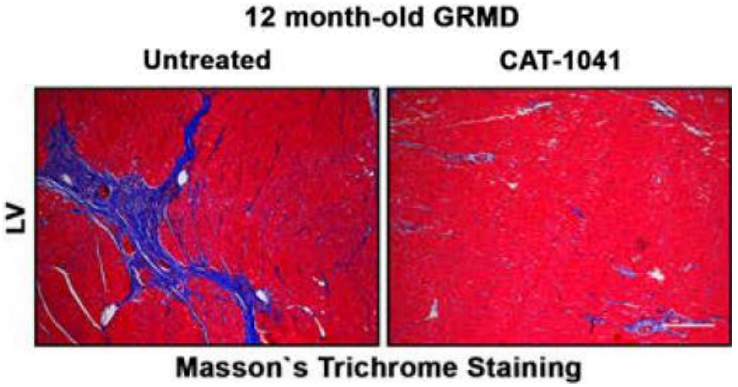
catabasis

Potential for Positive Cardiac Effects in DMD

Inhibiting NF-κB reduces cardiac hypertrophy and fibrosis in *mdx* mice



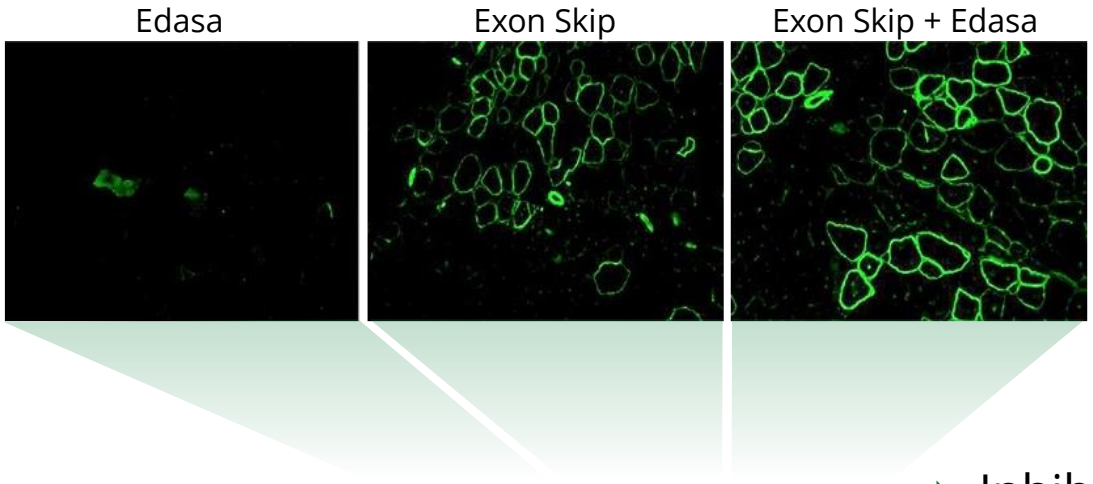
Inhibiting NF-κB reduces cardiac fibrosis in GRMD dog

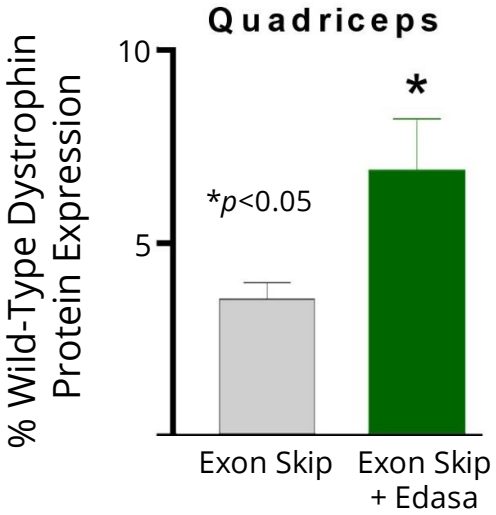


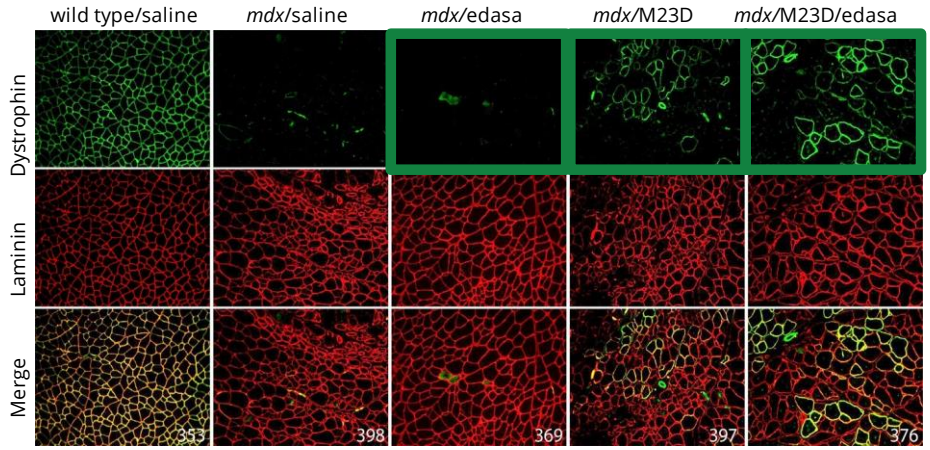
- Inhibition of NF-κB strongly reduces cardiac fibrosis and reduces cardiac hypertrophy in models of DMD
- Edasalonexent has the potential to reduce cardiomyopathy, the leading cause of mortality, in DMD

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

Edasalonexent Increases Dystrophin Expression in Combination with Exon-Skipping in *mdx* Mice







M23D: exon skipping specific for *mdx*

Edasalonexent administered at 1% in diet

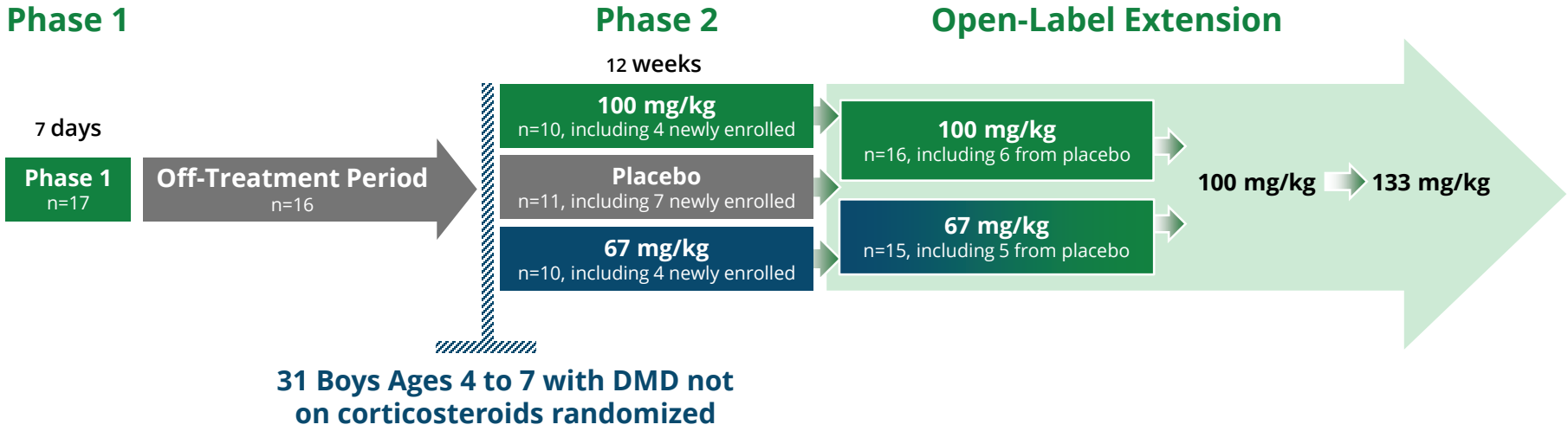
- Inhibition of NF-κB by edasalonexent enhances dystrophin production with sarcolemmal localization in combination with exon skipping therapy in *mdx* mice
- Edasalonexent may enhance dystrophin expression in combination with dystrophin-targeted therapies in DMD and as monotherapy in BMD

Nichols, et al. Neuromuscular Disorders 2017 27: S215

Edasalonexent Clinical Development Program: From First-in-Human to Efficacy in MoveDMD®

Study	Design	Population	Duration	Results
CAT-1004-101	First-in-human single ascending-dose, randomized, double-blind, placebo-controlled	Adults (N=52)	Single-dose	Positive safety data and determined PK parameters
CAT-1004-102	Multiple ascending-dose, randomized, double-blind, placebo-controlled	Adults (N=44)	14 days	Positive safety and NF-kB inhibition data
CAT-1004-103	Single-dose biomarker study comparing edasalonexent to equimolar ratio of component bioactives	Adults (N=9)	Single-dose	Demonstrated NF-kB inhibition with single dose
CAT-1004-201 (MoveDMD)	**Phase 1:** Multiple ascending-dose, open-label	DMD Boys (N=17)	7 days	Positive PK and safety in patients
	Off-treatment control period	DMD Boys (n=23)	3-13 months	Demonstrated disease progression during control period for boys in MoveDMD trial
	Phase 2: Randomized, double-blind, placebo-controlled	DMD Boys (N=31)	12 weeks	Numerical improvement in functional assessments and MRI at 100 mg/kg
	Open-Label Extension	DMD Boys (N=31)	>60 weeks	Long term safety and slowing of disease progression observed. Statistically significant reductions in muscle enzymes and C-reactive protein

MoveDMD Trial Was Designed to Enable Phase 3

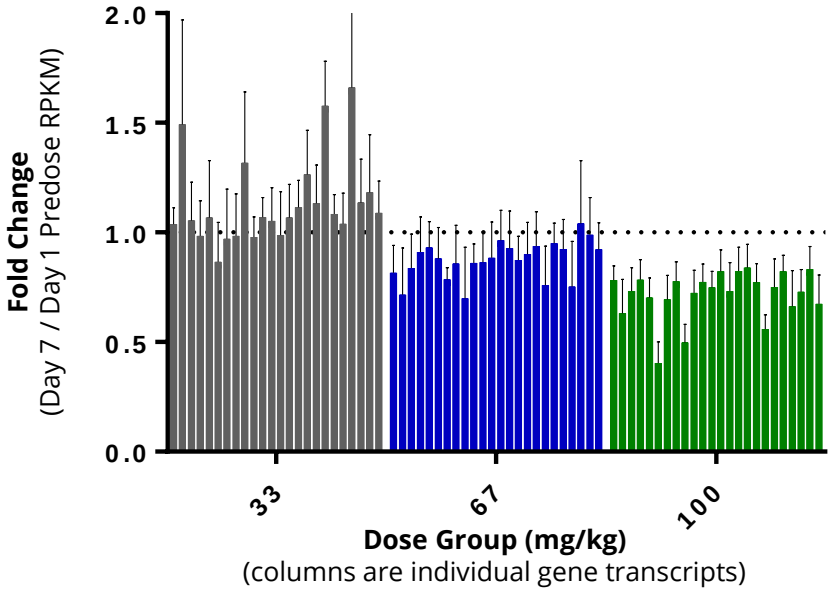


- **Integrated multi-part trial design**
  - Supports evaluation of efficacy, safety/tolerability, target engagement, and dose response
- **Off-treatment control period measurements between Phase 1 and commencement of dosing in Phase 2/open-label extension**
  - Provides internal control for pre-specified 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

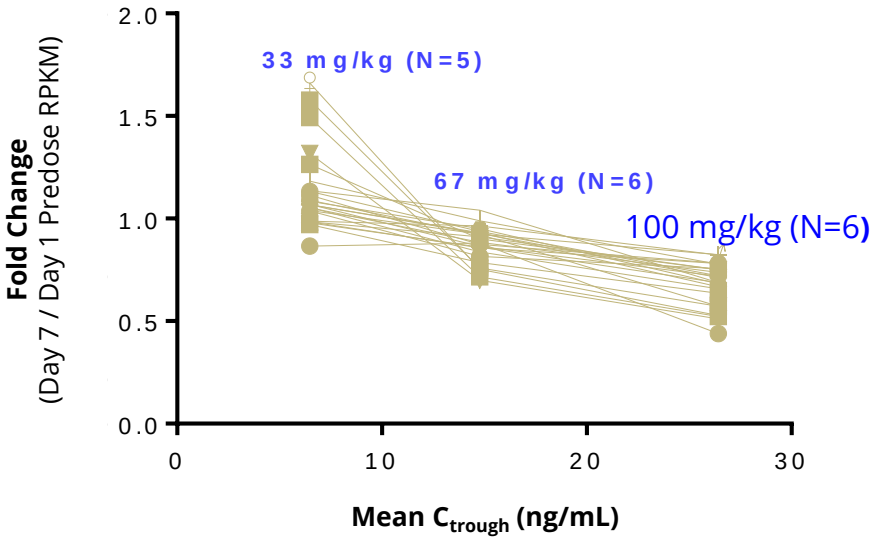
MoveDMD Phase 1 PK/PD Analysis and Preclinical Modeling Suggest that Pharmacodynamics and Efficacy are Driven by C_{trough}

Edasalonexent produces dose-related reductions in NF-κB regulated and inflammation-related gene transcripts

Change in NF-κB Gene Transcripts Following Edasalonexent Treatment



Mean C_{trough} vs. Inhibition of 24 NF-κB Targeted Genes



- C_{trough} and time over threshold is a driver of efficacy in preclinical models and in the clinic
- Preclinical efficacy studies and clinical PK/PD analysis support a TID dosing regimen for edasalonexent

MoveDMD Trial Incorporated Multiple Measures of Physical Function and Biomarkers

Assessments of Physical Function

North Star Ambulatory Assessment

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

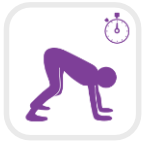
NSAA Sore	Perform	Perform with difficulty	Unable to perform
	2	1	0
	Patient with Function		Complete Loss of Function

Most Difficult Lost Early

- Hop right leg
- Hop left leg
- Stand on heels
- Rise from floor
- Run
- Jump
- Lift head
- Descend box step right
- Descend box step left
- Climb box step right
- Climb box step left
- Stand on one leg right
- Stand on one leg left
- Get to sitting
- Rise from chair
- Walk
- Stand

Least Difficult Lost Late

3 Timed Function Tests



Time to Stand

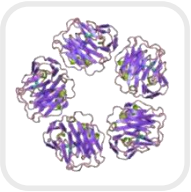
4-Stair Climb

10-Meter Walk/Run

Non-Effort Based Assessments

MRI T2 and Fat Fraction

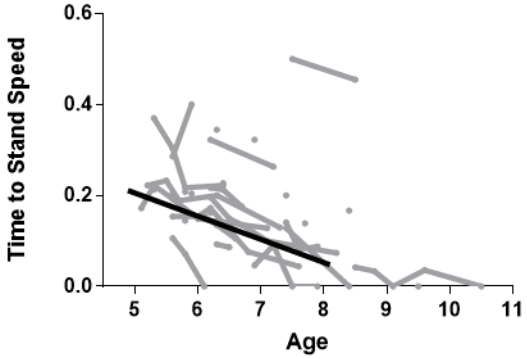
Muscle Enzymes



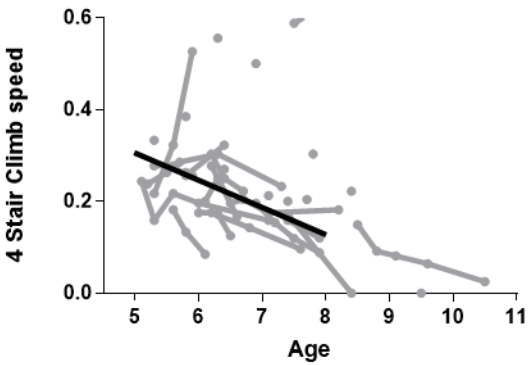
C-Reactive Protein

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

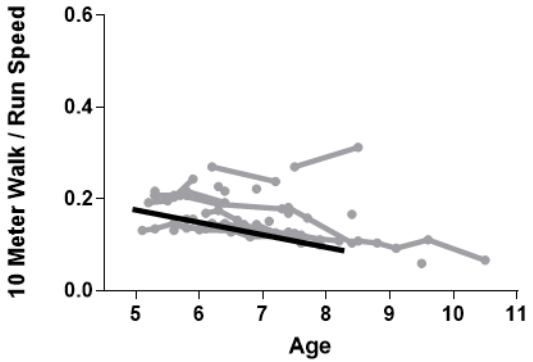
Time to Stand



4-Stair Climb



10-Meter Walk/Run



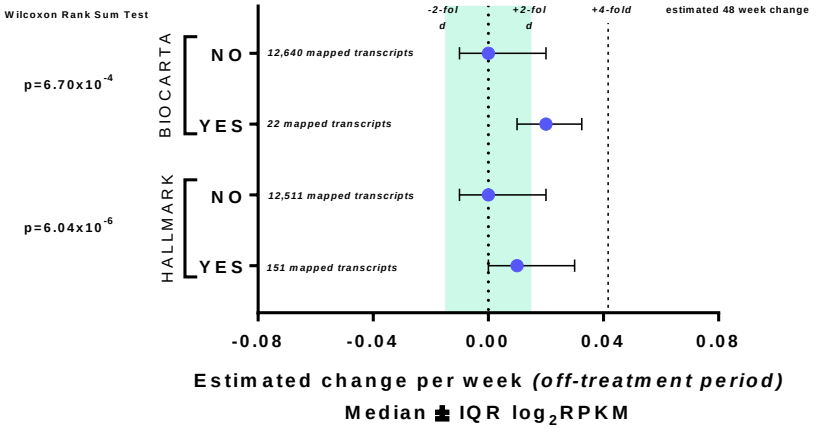
Boys (ages 5-8.5 yo) not on corticosteroids (n=28)

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

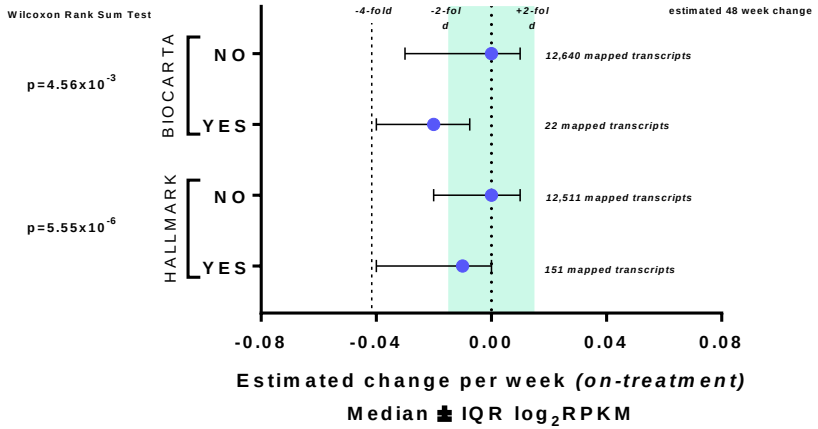
- The ImagingDMD natural history study (Willcocks et al., 2014) performed annual timed function tests in young boys with DMD
- Boys enrolled in the MoveDMD study under same data collection protocols generally had declines consistent with observations in the ImagingDMD natural history study

NF-κB-Regulated Transcripts in Whole Blood Increased During the Off-Treatment Control Period But Were Decreased by Edasalonexent Treatment

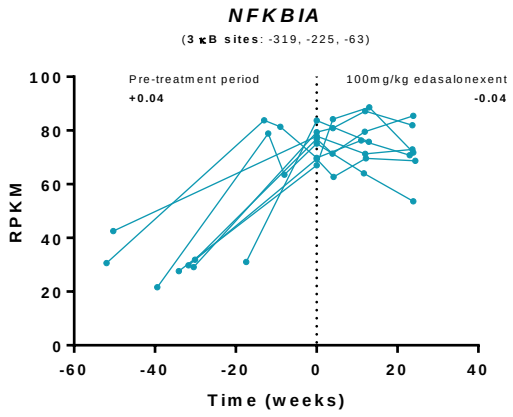
Significant Increase in NF-κB Transcript Gene Sets During Off-Treatment Period

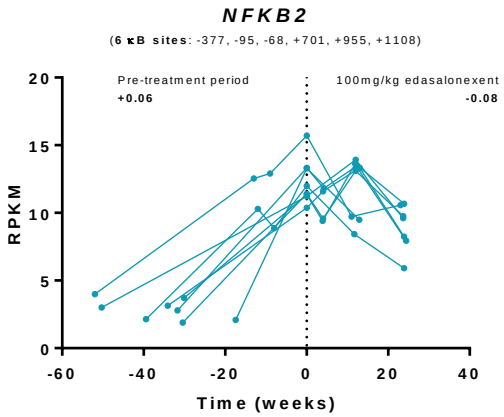


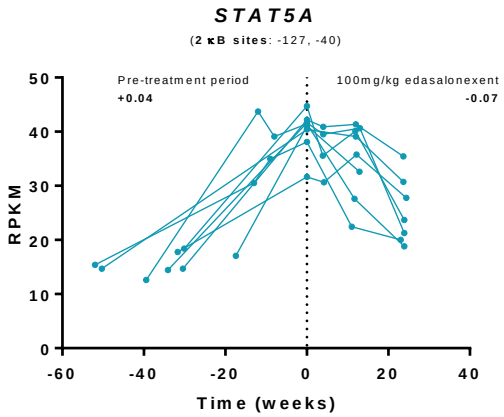
Significant Decrease in NF-κB Transcript Gene Sets With Edasalonexent Treatment



Patient Level NF-κB Transcripts Increased During Off-Treatment and Decreased With Edasalonexent Treatment





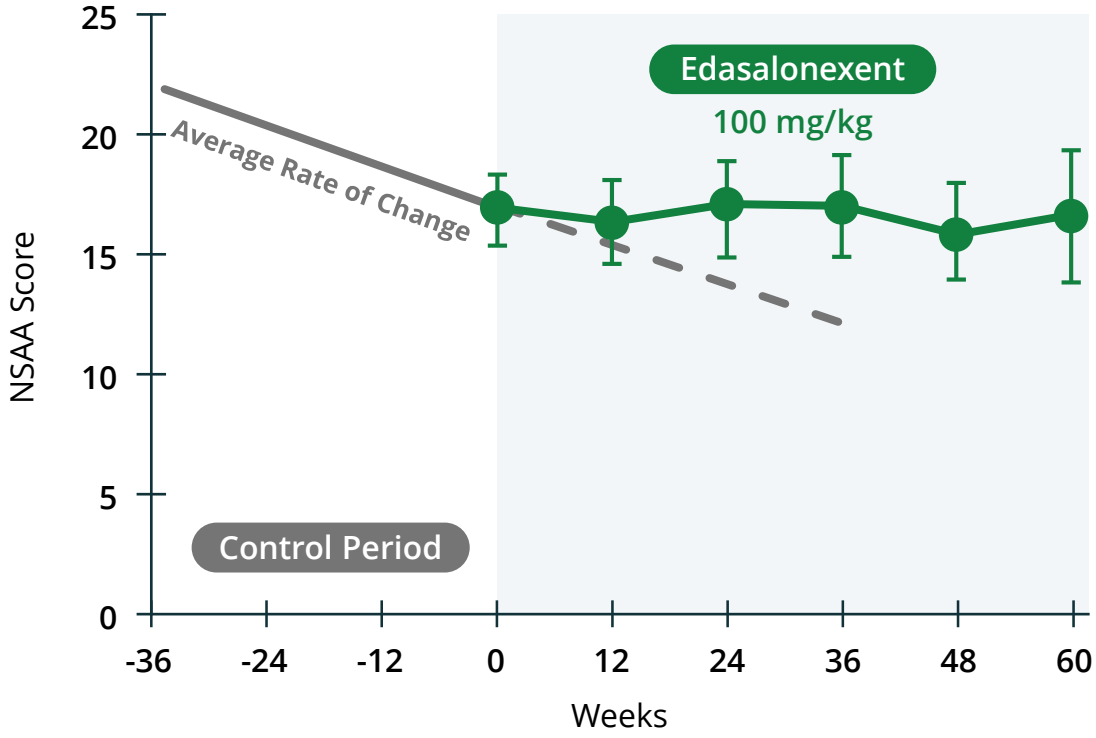


catabasis

Data analyzed for 8 boys who participated in Phase 1 and were treated with 100 mg/kg Edasalonexent in Phase 2

North Star Ambulatory Assessment Score, a Measure of Overall Function in Young Boys, Was Stabilized with Edasalonexent Treatment

North Star Ambulatory Assessment

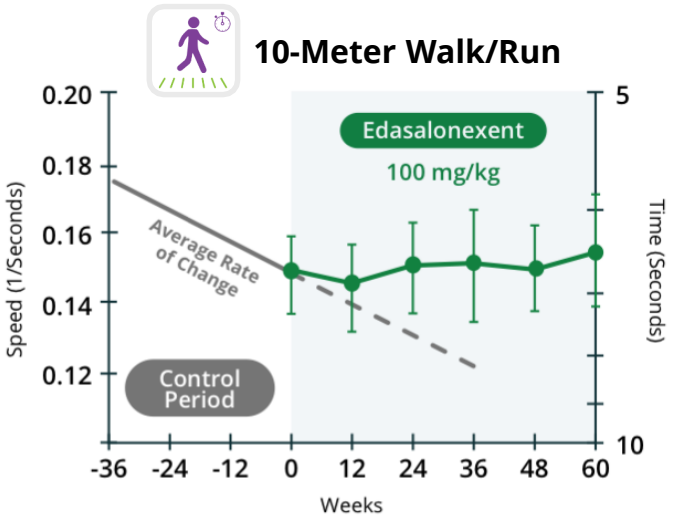


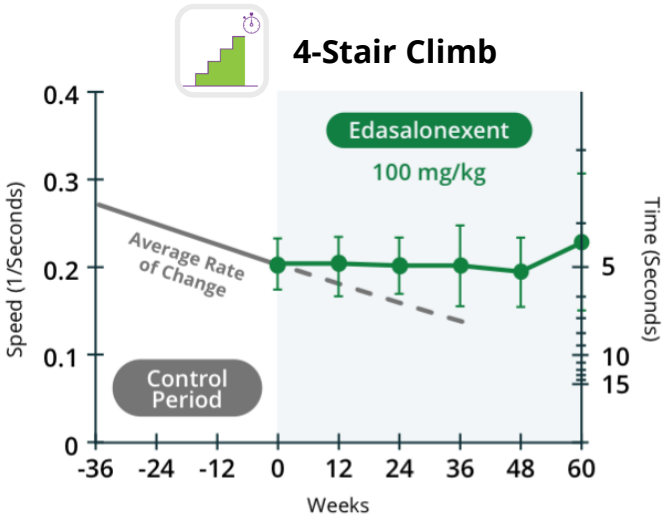
- Disease progression on edasalonexent improved compared with rate of change during off-treatment control period

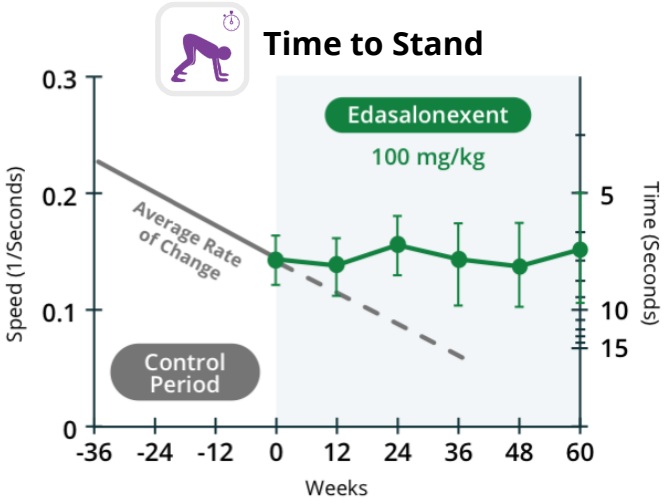
Means ± SEM shown

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

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







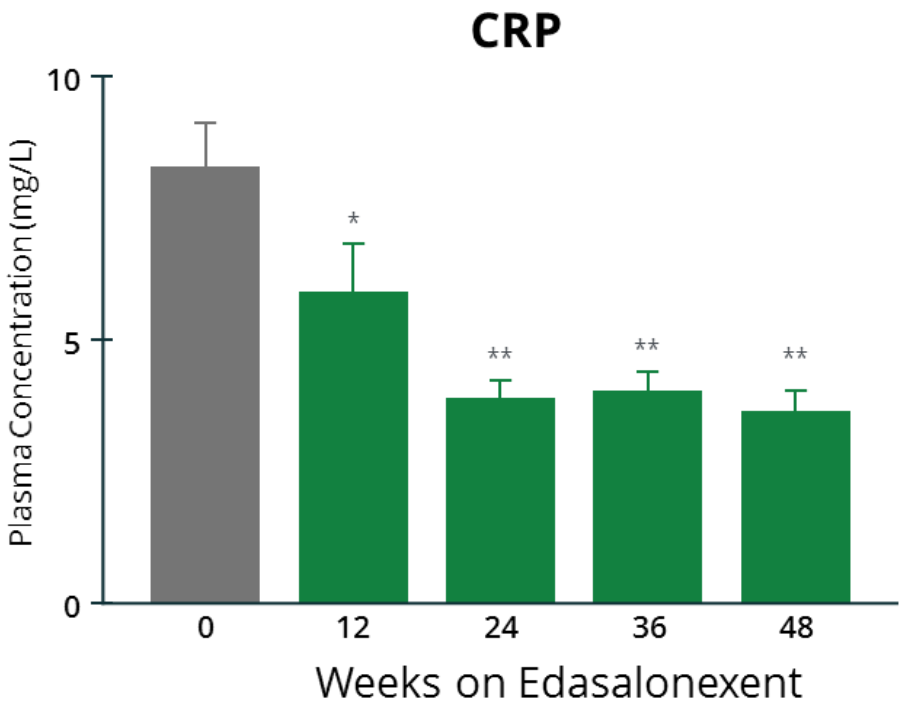
- Disease progression on edasalonexent improved compared with rate of change during off-treatment control period

Means ± SEM shown

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

Edasalonexent Produced Statistically Significant Reduction in Inflammation as Assessed by Plasma C-Reactive Protein

- C-reactive protein (CRP) is a well-characterized blood test marker that provides a global assessment of inflammation
- CRP is elevated in DMD
  - CRP is approximately 3-fold higher in boys affected by DMD compared to unaffected boys†
- In MoveDMD, there was a statistically significant CRP reduction from baseline through 48 weeks of 100 mg/kg edasalonexent treatment

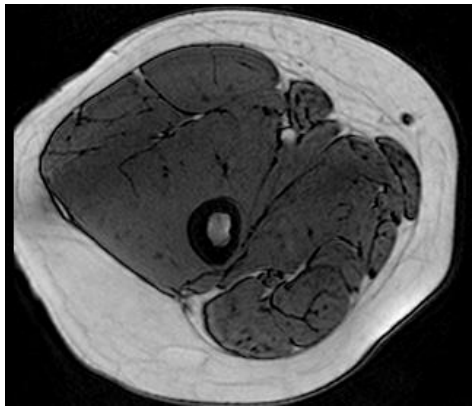


Means ± SEM shown; * p≤0.05, ** p≤0.001 for comparison with pre-treatment baseline measurement

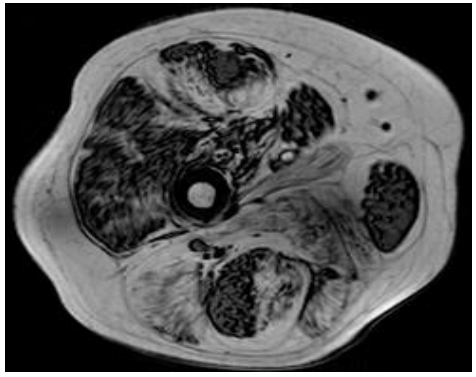
† Anderson et al, 2017, Pediatric Cardiology

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

Unaffected



DMD



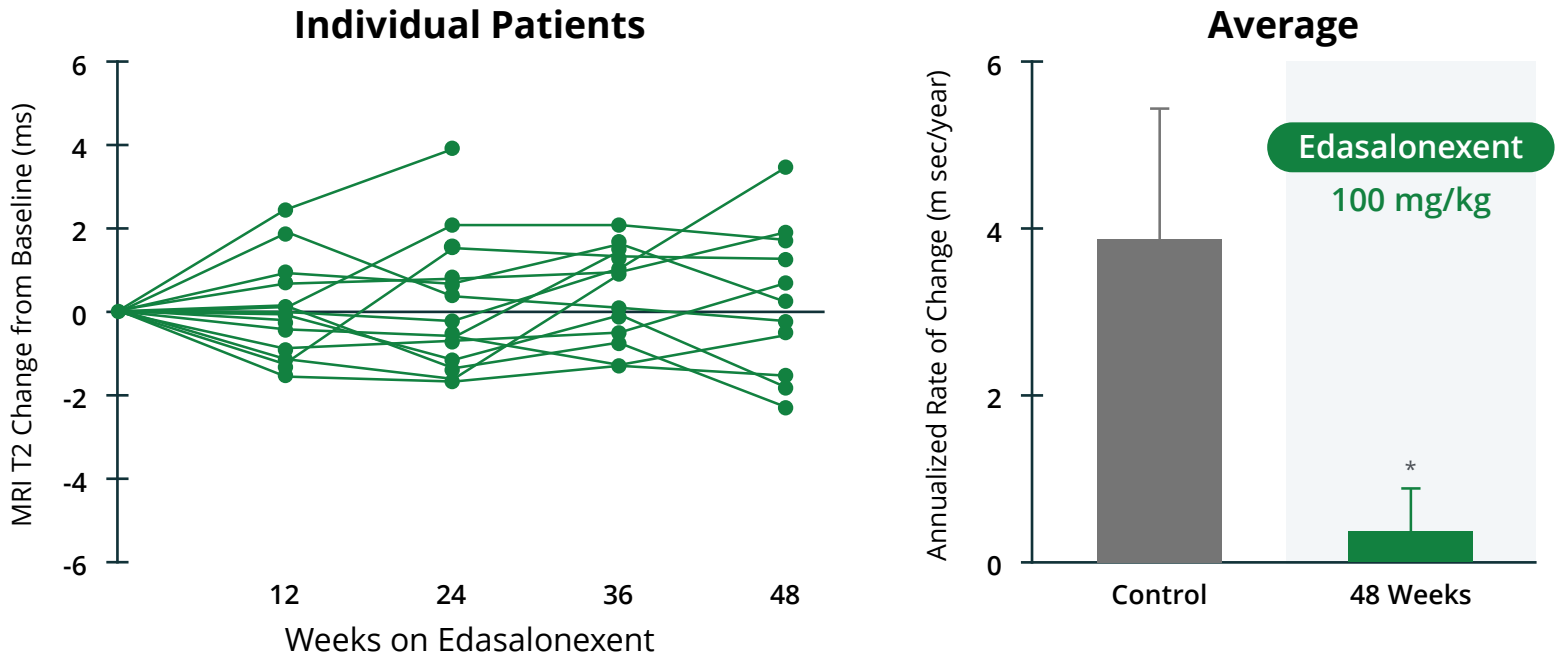
MRI T1 images from thigh

- **MRI T2 and MRS fat fraction in DMD**
  - Magnetic resonance can be used to assess inflammation and fat fraction
  - MRI T2 is elevated and increases with age
  - Fat fraction increases with age
- **MoveDMD incorporated both MRI and MRS**
  - Composite MRI T2 of 5 lower leg muscles was the primary MRI assessment
  - Fat fraction and MRS T2 also measured in lower (soleus) and upper leg (vastus lateralis)
- **Changes in MRI T2 and fat fraction 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 abilities

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

Edasalonexent Produced Statistically Significant Improvement in 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 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

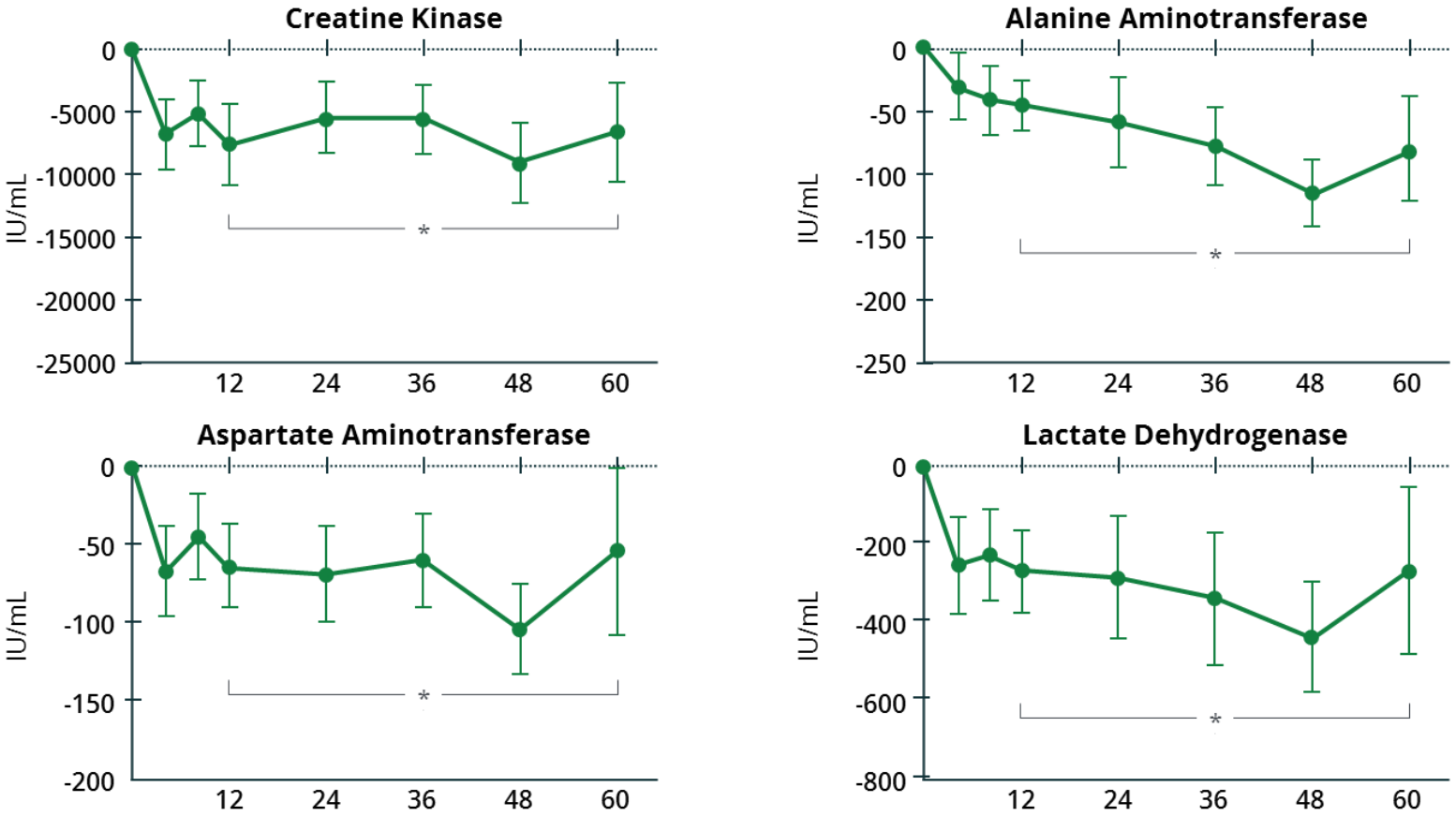
Muscle	MoveDMD Off-Treatment Control Period Annualized Rate	MoveDMD 48 weeks on Edasalonexent	ImagingDMD Natural History Study* 1 Year Change
Soleus	2.6%	0.85%	3%
Vastus lateralis	10.4%	5.9%	7%

- Following 48 weeks of edasalonexent treatment 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 ImagingDMD natural history study, boys were largely on chronic steroids
- At 48 weeks, MRS T2, reflecting inflammation only, decreased by -1.1 and -1.2 msec for the soleus and VL, respectively

Baseline fat fraction in the soleus was 9.3% and in the VL 13.1%
*Willcocks et al, 2016, Ann. Neurol., Willcocks et al, 2014, Ann. Neurol

Statistically Significant Reduction in Muscle Enzymes on Edasalonexent Treatment

- 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 health and supportive of an edasalonexent benefit

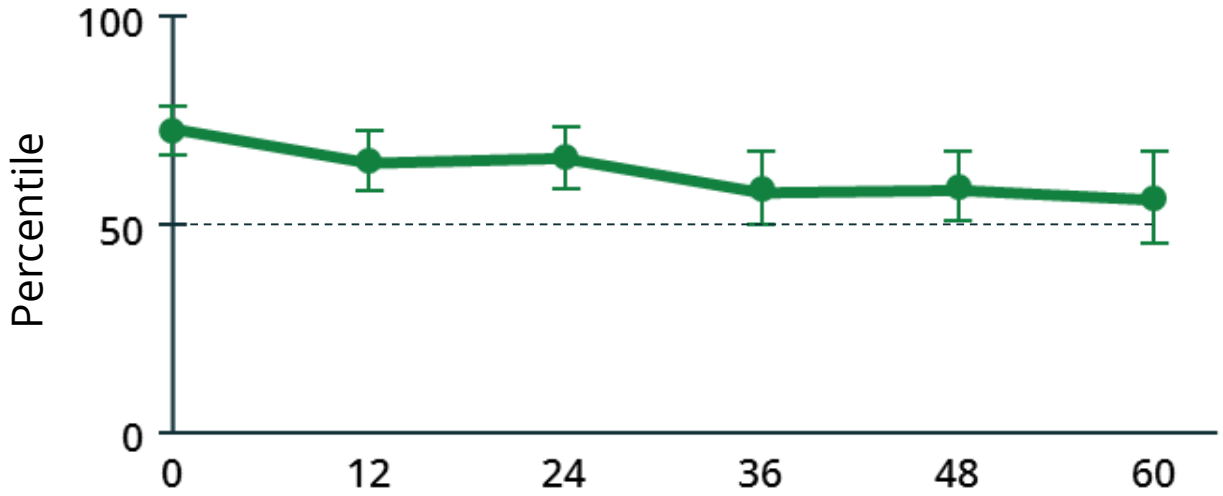


Means ± SEM shown; * p<0.05 for change from baseline after 12 weeks

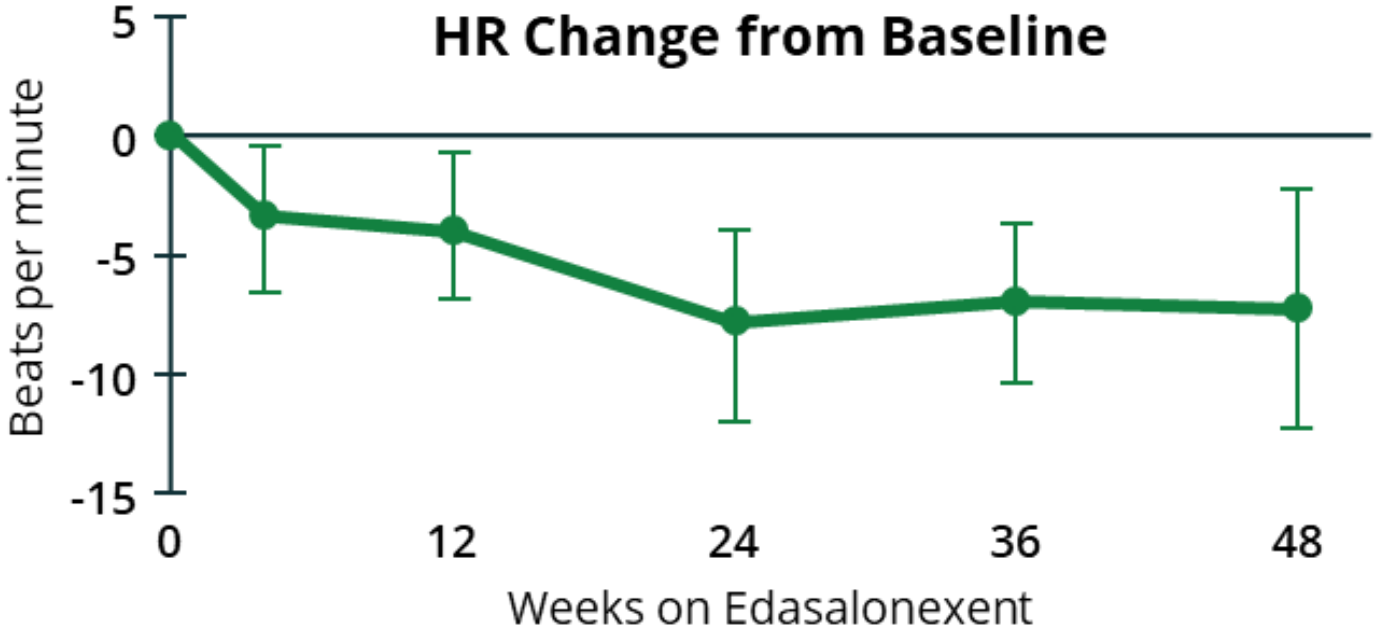
Edasalonexent Has Been Well Tolerated with No Safety Signals; Normal Growth Observed

- No safety signals 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
  - Favorably differentiated from typical profile associated with corticosteroid standard of care, which includes weight gain and curtailed growth

BMI Compared to CDC Growth Charts



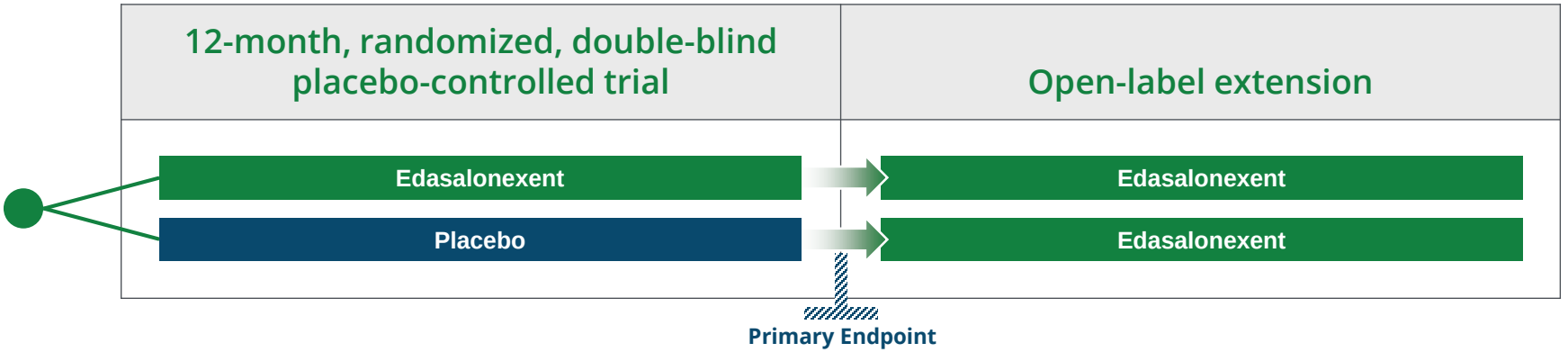
Edasalonexent Has Potential to Have Positive Effects on Cardiomyopathy in DMD



- Cardiac failure is a leading cause of mortality in DMD
- In young boys, tachycardia is the first manifestation of cardiac disease in patients with DMD
- In MoveDMD trial, ECG heart rate decreased toward age-normative values
- In DMD, fibrosis leads to cardiac dysfunction
  - In *mdx* mouse and GRMD dog, edasalonexent reduces cardiac fibrosis

Thomas, e.al. *Pediatr Cardiol.* 2012 33(7):1175-9. Hammers, et al. *JCI Insight* 2016 1(21): e90341

Positive MoveDMD Data Support the Planned Global Phase 3 Registration Trial for Edasalonexent



- **Key Phase 3 trial components, including patient population and endpoints, previously evaluated in MoveDMD trial**
- **Enrollment of approximately 125 boys, 2:1 randomization, accounting for dropouts**
- **Study Population**
  - Anticipated to be all mutations, age 4 to 7, steroid naïve or off steroids for ≥6 months
- **Endpoints consistent with FDA guidance**
  - At 12 months
  - Primary: Change in North Star Ambulatory Assessment
  - Key secondary: Age-appropriate timed function tests
  - Additional assessments planned to include cardiac and bone measures
- **Preparing for Phase 3 clinical trial**

MoveDMD® Open-Label Extension Results: Edasalonexent Preserved Muscle Function and Slowed DMD Disease Progression

- **Clinically meaningful slowing of disease progression on edasalonexent compared to off-treatment control period through more than 1 year of treatment**
  - North Star Ambulatory Assessment stabilized
  - Timed function tests stabilized (10-meter walk/run, 4-stair climb and time to stand)
- **Additional measures of muscle health support positive edasalonexent effects**
  - Statistically significant improvement in muscle MRI T2 versus off-treatment control period
  - Statistically significant decrease in muscle enzymes compared to baseline
  - Statistically significant decrease in CRP, a marker of systemic inflammation, compared to baseline
- **No safety signal and well tolerated**
  - Height, weight and BMI growth patterns similar to unaffected boys

Edasalonexent: A Potential Disease-Modifying Foundational Therapy in DMD

- **Disease-modifying non-steroid oral therapy**
  - Intended for all patients, regardless of mutation type
  - Inhibit muscle degeneration, enhance regeneration
  - Benefits in skeletal muscle, diaphragm and heart
- **Preparing for single Phase 3 trial for registration**
  - In MoveDMD® trial, edasalonexent preserved muscle function and slowed disease progression
- **Potential foundational therapy**
  - Initiate upon diagnosis
  - Potential as monotherapy and may enhance efficacy of dystrophin upregulation approaches

Developing a potential NEW Standard of Care in Duchenne

- **Favorably differentiated tolerability profile from standard of care**
- **Strong IP position and wholly owned**