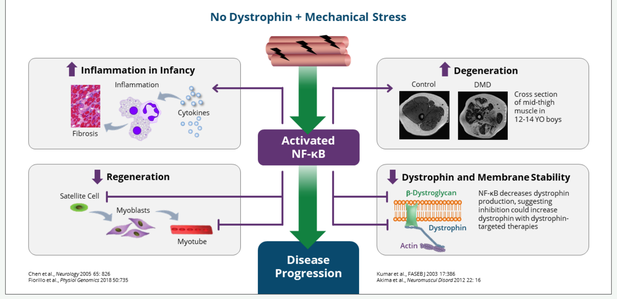
# Edasalonexent Treatment in Young Boys with Duchenne Muscular Dystrophy Is Associated with Age-Normative Growth and Normal Adrenal Function


Erika L. Finanger, MD[1]; Richard Finkel, MD[2]; Krista Vandenborne, PT, PhD[3]; H Lee Sweeney, PhD[3]; Gihan Tennekoon, MBBS, MRCS, LCRP[4]; Perry Shieh, MD, PhD[5]; Sabrina W. Yum, MD[4]; Maria Mancini, MHP[6]; James MacDougall, PhD[6]; Joanne Donovan, MD, PhD[6]

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


## Background

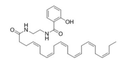
### Activation of NF-κB in Duchenne Muscular Dystrophy Is a Key Factor in Disease Progression




Chen et al., Neurology 2005 65: 826
Fiorillo et al., Physiol Genomics 2018 50:735
Kumar et al., FASEB J 2003 17:386
Acima et al., Neuromuscul Disord 2012 22: 16

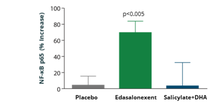
### Edasalonexent Inhibits NF-κB, a Key Driver of Muscle Disease in Duchenne

- Edasalonexent is an orally-administered small molecule

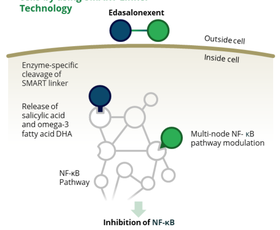


- Edasalonexent has a unique pharmacological profile that inhibits NF-κB better than its individual components

**Edasalonexent Synergistically Inhibits NF-κB (p65) in Adult Humans**

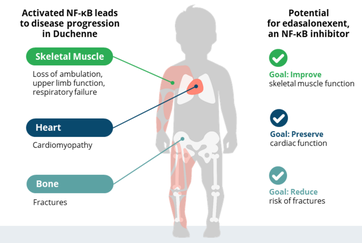



- Edasalonexent is a unique molecule delivering Salicylic Acid and DHA into cells by using SMART Linker Technology




Donovan et al. J Clin Pharmacol 2017 57:627-639

### Edasalonexent: Potential for Broad Therapeutic Benefit




**In Duchenne, the loss of dystrophin leads to chronic activation of NF-κB, which is a key driver of skeletal muscle and cardiac disease progression**

## Study Design

### Design of MoveDMD®, a Phase 1/2 Trial with Open-Label Extension

- **Study Objectives**
  - Safety and PK in pediatric patients with Duchenne
  - Proof of concept using MRI to assess changes in muscle health
  - Long-term safety and effects on age-appropriate functional measures to enable design of Phase 3 study
- **Study Population**
  - Age 4 up to 8th birthday not currently being treated with corticosteroids
  - Able to perform timed function tests and MRI
- **Design**
  - Phase 1: 1-week open-label to assess safety and PK, with initial assessments of function and MRI
  - Off-treatment period of ~6 months prior to Phase 2
  - Phase 2: 12-week placebo-controlled period of 67 mg/kg and 100 mg/kg doses of edasalonexent
  - Open-label extension up to 150 weeks


- **Prespecified Analysis Plan**
  - 12-week placebo-controlled period evaluated MRI T2, North Star Ambulatory Assessment, timed-function tests, and safety
  - Additional comparison of rates of change during off-treatment control period versus on edasalonexent treatment

## Results

In Phase 2 MoveDMD Trial and Open-Label Extension:

### Safety: Edasalonexent was Well-Tolerated

- **Well-tolerated for up to 150 weeks**
- **Majority of adverse events mild in nature**
  - Most common related adverse event was diarrhea, generally mild and transient
  - No serious adverse events on treatment (one on placebo)
- **No adverse trends in chemistry and hematology**

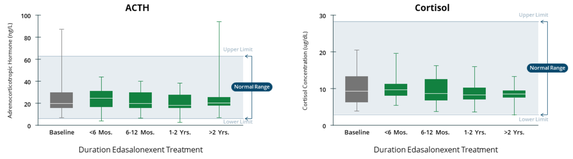
| Treatment-Related Adverse Events >5% | Edasalonexent Overall (N=31) |
|---|---|
| System Organ Class/ Preferred Term | n % |
| Subjects with any treatment-emergent adverse event | 31 (100%) |
| Subjects with any treatment-emergent adverse event related to study treatment | 19 (61.3) |
| Gastrointestinal disorders | |
| Diarrhoea | 16 (51.6%) |
| Abdominal pain upper | 7 (22.6%) |
| Nausea | 3 (9.7%) |
| Vomiting | 3 (9.7%) |
| Abdominal discomfort | 2 (6.5%) |
| Abdominal pain | 2 (6.5%) |
| Faecal incontinence | 2 (6.5%) |
| Faeces soft | 2 (6.5%) |
| Metabolism and nutrition disorders | |
| Decreased appetite | 4 (12.9%) |

In Phase 2 MoveDMD Trial and Open-Label Extension:

### Safety: Edasalonexent was Well-Tolerated

- Edasalonexent does not impact the glucocorticoid receptor
- ACTH is a hormone that triggers the adrenal gland to make cortisol, a hormone that supports the body's response to stress
- We have not seen negative effects on ACTH and cortisol for up to 150 weeks on edasalonexent treatment

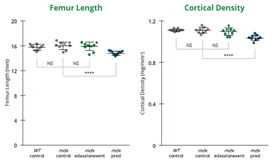
Pituitary gland → ACTH Production → Adrenal Gland → Cortisol Production




Box plot error bars indicate range of results

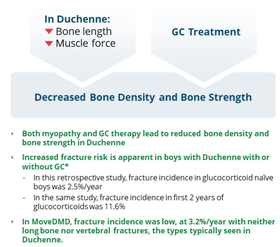
### Potential for Bone Preservation with Edasalonexent

- Unlike glucocorticoids (GC), edasalonexent treatment in a *mdx* mouse model preserves bone length and bone density




**** P<0.0001 vs *mdx* control

Donovan 2019 Bone Symposium oral presentation, Salzburg, Austria




- Both myopathy and GC therapy lead to reduced bone density and bone strength in Duchenne
- Increased fracture risk is apparent in boys with Duchenne with or without GC*
  - In this retrospective study, fracture incidence in glucocorticoid naïve boys was 2.5%/year
  - In the same study, fracture incidence in first 2 years of glucocorticoids was 11.6%
- In MoveDMD, fracture incidence was low, at 3.2%/year with neither long bone nor vertebral fractures, the types typically seen in Duchenne.

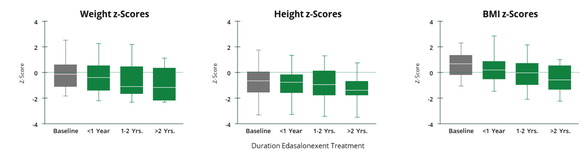
*Joseph, et. al. 2019;29(1):59-66
Rauch & Schoenau, Ped Res 2001 50(3):309-315

In Phase 2 MoveDMD Trial and Open-Label Extension:

### Safety: Growth Continues as Expected Compared to Standard Growth Charts

- **Boys on edasalonexent grew similarly to growth curves for unaffected boys up to 150 weeks**
  - Weight increased by an average of 3 lbs per year
  - Height increased by an average of 2 inches per year
- **BMI is typically elevated in these boys and on edasalonexent treatment, BMI trended down**

**z-Scores Compared to CDC Growth Charts**



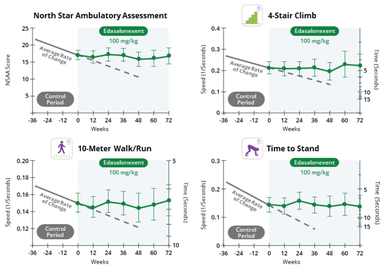

Box plot error bars indicate range of values
Comparison with CDC growth charts: https://www.cdc.gov/growthcharts/clinical_charts.htm

## Results

In Phase 2 MoveDMD Trial and Open-Label Extension:

### Edasalonexent Demonstrated Clinically Meaningful Slowing of Disease Progression Compared to Off-Treatment Period

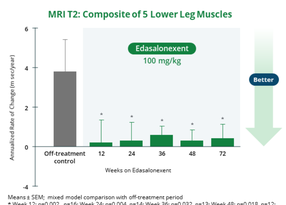
**Sustained stabilization up to 72 weeks on edasalonexent**




Means ± SEM shown. Includes data of all boys initially started on 100 mg/kg dose (n=16) with 11 boys participating through 72 weeks.

In Phase 2 MoveDMD Trial and Open-Label Extension:

### Edasalonexent Improved Rate of Change of MRI T2 Compared to Off-Treatment Control Period

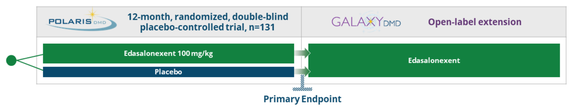



Means ± SEM; mixed model comparison with off-treatment period
* Week 12: p=0.002, n=16; Week 24: p=0.004, n=14; Week 36: p=0.032, n=13; Week 48: p=0.018, n=12; Week 72: p=0.052, n=9

- MRI T2 is tightly correlated with fat fraction and functional measures
- 12-week Phase 2 MRI T2 primary endpoint for treated boys compared to boys in the placebo group was directionally positive although not statistically significant
- Following 72 weeks of edasalonexent, the rate of increase in the composite MRI T2 decreased as compared to the rate of increase during the off-treatment control period
- **Early and sustained response in annualized rate of change**
- Composite of 5 lower leg muscles MRI T2 (soleus, gastrocnemius, anterior and posterior tibialis, peroneals) used to encompass muscles at various stages of disease progression and minimize variability

### Phase 2 MoveDMD Trial Supports Phase 3 Trial Design

- **The global PolarisDMD trial is fully enrolled across all 8 countries where the trial is active**




- **Enrolled 131 boys ages 4-7 (up to 8th birthday)**
  - Not on corticosteroids for at least 6 months
- **2:1 randomization, 67% of boys receive drug initially, all boys have the option to receive drug after 12 months through GalaxyDMD**
- **Clinical trial site visits and key assessments every 3 months**
- **Safety measures including labs every 3 months**
- **Top-line results expected in Q4 2020**

NCT03703882 and NCT03917719

## Conclusion

### Conclusion

- Treatment with edasalonexent was well-tolerated and associated with age-appropriate growth patterns without negative impact on bone health or adrenal function.
- Muscle function and MRI assessments of muscle integrity showed slowing of disease progression compared to an off-treatment control period.
- Edasalonexent is a potential foundational therapy for all patients affected by Duchenne, and is being evaluated in young boys in the Phase 3 PolarisDMD trial to determine whether it can slow disease progression and have positive effects on muscle and cardiac function as well as bone health.


## Acknowledgements

- Patients and families
- Patient groups
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- Site staff
- Catabasis team
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**Questions?** MedInfo@catabasis.com

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