EDG-5506: A Novel Approach to Protect Muscle in Duchenne and Becker Muscular Dystrophy

J Donovan, H Phan, S Collins, L Thaler, N Kilburn, M Mancini, B Barthel, J MacDougall, A Russell
Edgewise Therapeutics, Boulder, CO | Rare Disease Research Atlanta, GA
Presented at Parent Project Italy, Rome, February 2023

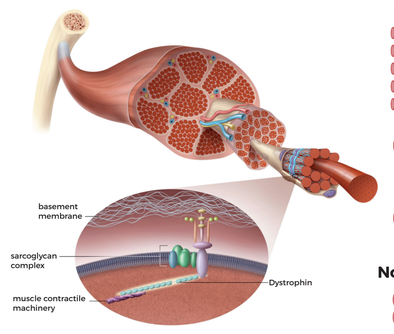
The Edgewise Approach: *Protect suceptible muscle fibers*

Some muscle fibers are more susceptible to damage due to the lack of functional dystrophin

We've made an investigational therapy, **EDG-5506** that is designed to protect these susceptible muscle fibers from damage, regardless of mutation

In diseased animal models, **EDG-5506** protected susceptible muscle fibers and prevented long-term development of damage

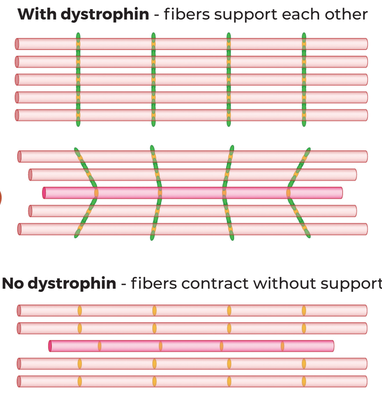
The Dystrophin Complex Helps Prevent Injury in Contracting Fibers



Dystrophin connects contractile proteins to the membrane and surrounding matrix of fibers

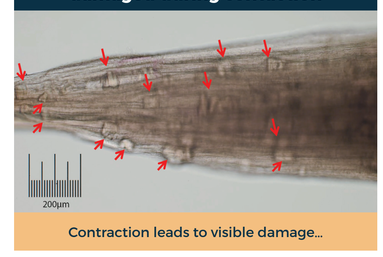
With dystrophin - fibers support each other

No dystrophin - fibers contract without support



EDG-5506 Protects Dystrophic Mouse Muscle

Dystrophic mouse muscle is damaged during contaction



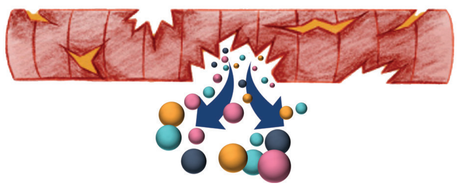
Contraction leads to visible damage...

EDG-5506 protects dystrophic mouse muscle during contraction

With **EDG-5506**, contractions don't cause changes

Claflin, Su and Brooks. U Michigan

Injured Muscles Release Muscle Protein Biomarkers

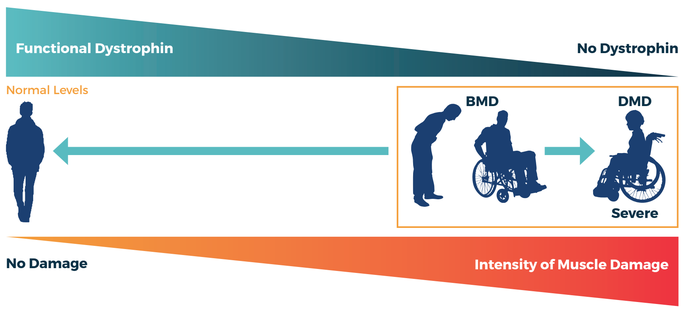


- Creatine Kinase
- Myoglobin
- Fast Troponin
- Many other muscle proteins

Multiple muscle proteins enter the bloodstream and can be measured, which we term biomarkers of muscle damage

BMD and Duchenne Muscular Dystrophy (DMD) Represent Severe Dystrophinopathies

Spectrum of Severity Across Dystrophinopathies



BMD and DMD represent a continuum of the same disease; Edgewise's approach aims to treat across the disease spectrum, regardless of dystrophin mutation

Schematic of Clinical Development of EDG-5506 to Date

Phase 1 in Healthy Adults and Adults with Becker Muscular Dystrophy

ARCH Open-label Study in Becker Muscular Dystrophy

CANYON Phase 2 in Adults and Adolescents with Becker Muscular Dystrophy

LYNX Phase 2 in Children with Duchenne Muscular Dystrophy

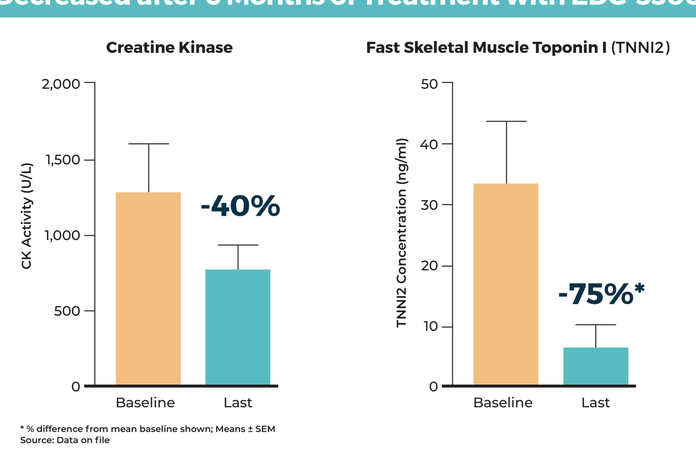
EDG-5506 Phase 1 Trial in Unaffected Adults and Those with Becker Muscular Dystrophy

What do we know about side effects?
- When dosed for two weeks, EDG-5506 was well-tolerated

How is EDG-5506 given?
- EDG-5506 can be taken as an oral tablet once a day that is absorbed well with or without food

Does it get to the muscle?
- EDG-5506 is highly concentrated in muscle compared to the bloodstream, which tells us that it is getting to where it needs to be to protect the muscle

Biomarkers of Muscle Damage in Becker Participants Decreased after 6 Months of Treatment with EDG-5506



* % difference from mean baseline shown; Means ± SEM
Source: Data on file

EDG-5506 Clinical Trials Ongoing

ARCH A 24-month open-label study is ongoing, including adults with Becker who were in the Phase 1 trial (NCT05160415)

CANYON A study in ambulatory adolescent and adult males with Becker is enrolling (ages 12+) (NCT05291091)

LYNX An initial study in ambulatory boys with Duchenne is enrolling (NCT05540860)

Phase 2 Study in Adults and Adolescents with Becker

Population:
- Age 12 to 50 years old, inclusive
- Confirmed mutation in dystrophin gene with characteristic Becker phenotype
- Ambulatory
- Not on corticosteroids

Design:
- 12-month placebo-controlled

Endpoints:
- Biomarker (CK) at 12 months
- Safety
- MRI fat fraction of upper leg
- Functional assessments to include NSAA, NSAD

Phase 2 Dose-Ranging Study in Boys with Duchenne

Population:
- 4 to 9 years old, inclusive
- Confirmed mutation in dystrophin gene with characteristic phenotype
- Ambulatory
- On stable dose of corticosteroids; can be on approved exon-skipping rx

Design:
- 3-month placebo-controlled, followed by 9-month open-label

Endpoints:
- Safety, pharmacokinetics and biomarkers at 3 months
- Functional assessments collected for longer term information

EDG-5506 is Being Developed for Becker and Duchenne Muscular Dystrophy

Taken orally, intended to preserve and improve function in Becker and Duchenne patients with any mutation

Goal to prevent damage to muscle by protecting the most susceptible fast muscle fibers

Potential to be used alone or in combination with other therapeutic approaches for dystrophinopathies

Designed to stop the damage where it begins

The authors are grateful to the participants in the trial.

Disclaimer
EDG-5506 is an investigational drug that is not approved in any territory. The authors are employees or consultants for Edgewise Therapeutics and may hold stock and/or stock options.

Edgewise THERAPEUTICS

At Edgewise, patients are at the core of everything we do.