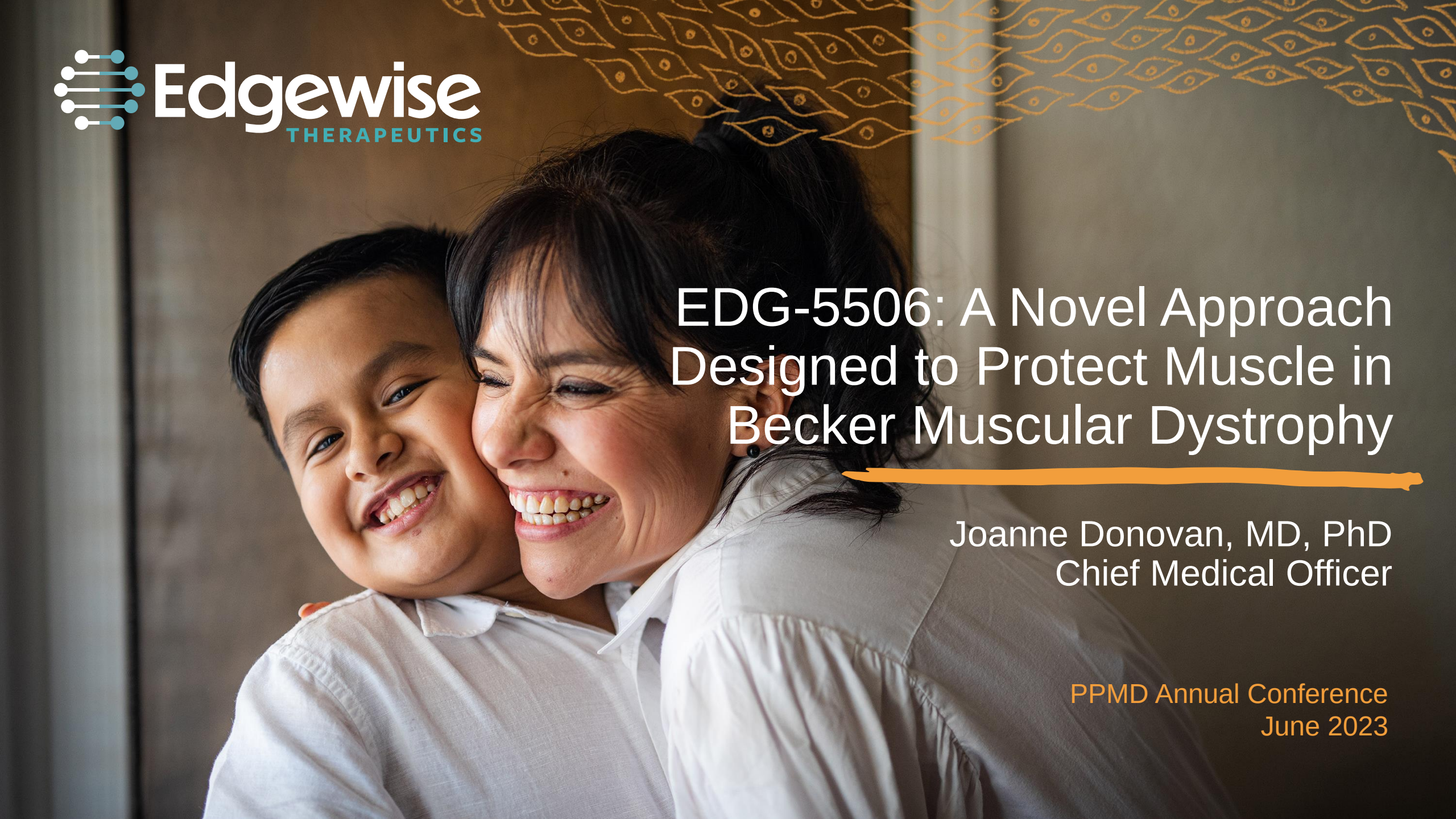


Edgewise THERAPEUTICS

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

Joanne Donovan, MD, PhD
Chief Medical Officer

PPMD Annual Conference
June 2023

Forward-Looking Statements

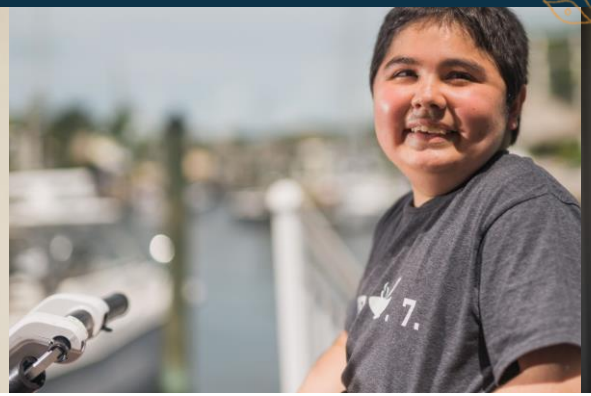
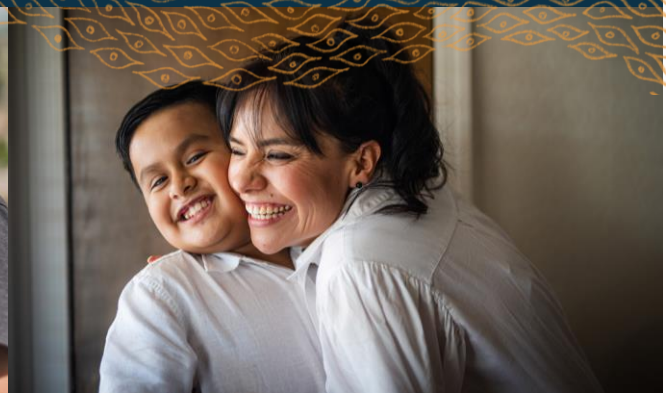
This presentation contains forward-looking statements that involve substantial risks and uncertainties of Edgewise Therapeutics, Inc. ("Edgewise" or the "Company"). All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, and expectations regarding, Edgewise's drug discovery platform; Edgewise's product candidates and programs, including EDG-5506; the expected milestones and timing of such milestones for EDG-5506 including the expected timing of reporting of data for EDG-5506 and clinical trials; statements regarding the market opportunity for Edgewise's product candidates; statements regarding Edgewise's pipeline of product candidates and programs; and statements regarding Edgewise's financial position including its liquidity. In some cases, you can identify forward-looking statements by terminology such as "estimate," "intend," "may," "plan," "potentially" "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: negative impacts of the COVID-19 pandemic on Edgewise's operations, including clinical trials; risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company; Edgewise's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates; changes in Edgewise's plans to develop and commercialize EDG-5506 or any other product candidates; the potential for clinical trials of EDG-5506 or any other product candidates to differ from preclinical, interim, preliminary, topline or expected results; Edgewise's ability to enroll patients in its ongoing and future clinical trials; operating results and business generally; Edgewise's ability to raise funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; Edgewise's reliance on third parties, contract manufacturers and contract research organizations; Edgewise's ability to obtain and maintain intellectual property protection for its product candidates; risks associated with access to capital and credit markets; the loss of key scientific or management personnel; competition in the industry in which Edgewise operates; Edgewise's ability to develop a proprietary drug discovery platform to build a pipeline of product candidates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in documents that Edgewise files from time to time with the Securities and Exchange Commission. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation concerns product candidates that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

EDG-5506 is an investigational agent and is not approved in any territory



Edgewise aims to improve lives of individuals living with rare muscle disorders

Founded in 2017, Edgewise is focused on developing novel therapies for muscular dystrophy, including Becker and Duchenne. We believe our investigational compound, a daily oral pill, could be used alone or in combination with other therapies, regardless of mutation.

The Becker Muscular Dystrophy Landscape

- Becker muscular dystrophy (BMD) is a serious dystrophinopathy with a variable clinical course. However, once declining, individuals irreversibly lose muscle and their disease progresses

- Living with Becker poses multiple challenges. To develop treatments it is critical to listen to the community to understand their lived experience

- In both BMD and DMD, contraction-induced injury in fast muscle fibers is a key aspect of the disease process, and we believe that modulation of fast myosin can protect muscle fibers from contraction-induced injury

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)

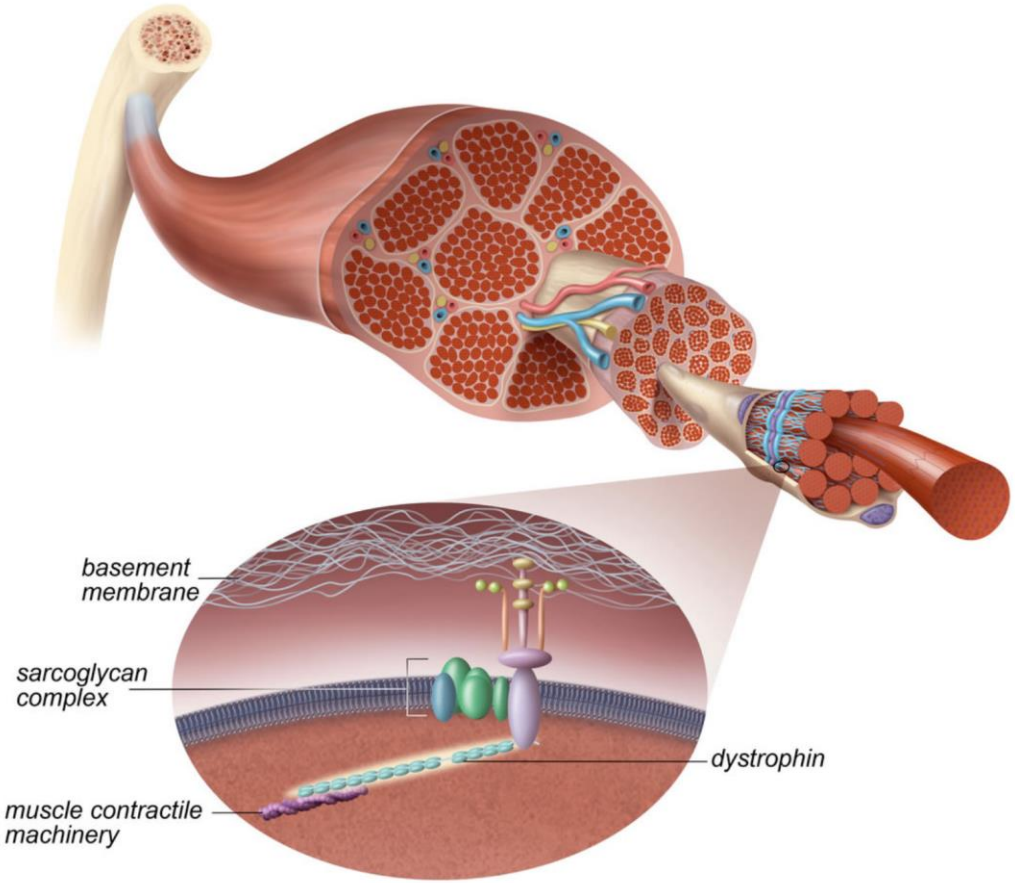
The Edgewise Approach: *Protect susceptible muscle fibers*

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

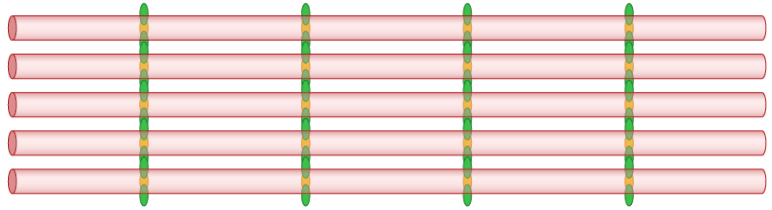
How Does Dystrophic Muscle Break Down?



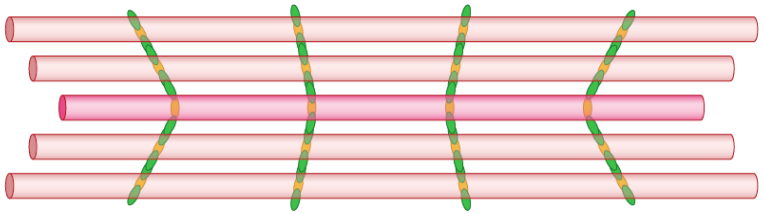
Dystrophin connects contractile proteins to the membrane and surrounding matrix of fibers

With dystrophin – fibers support each other

Rest

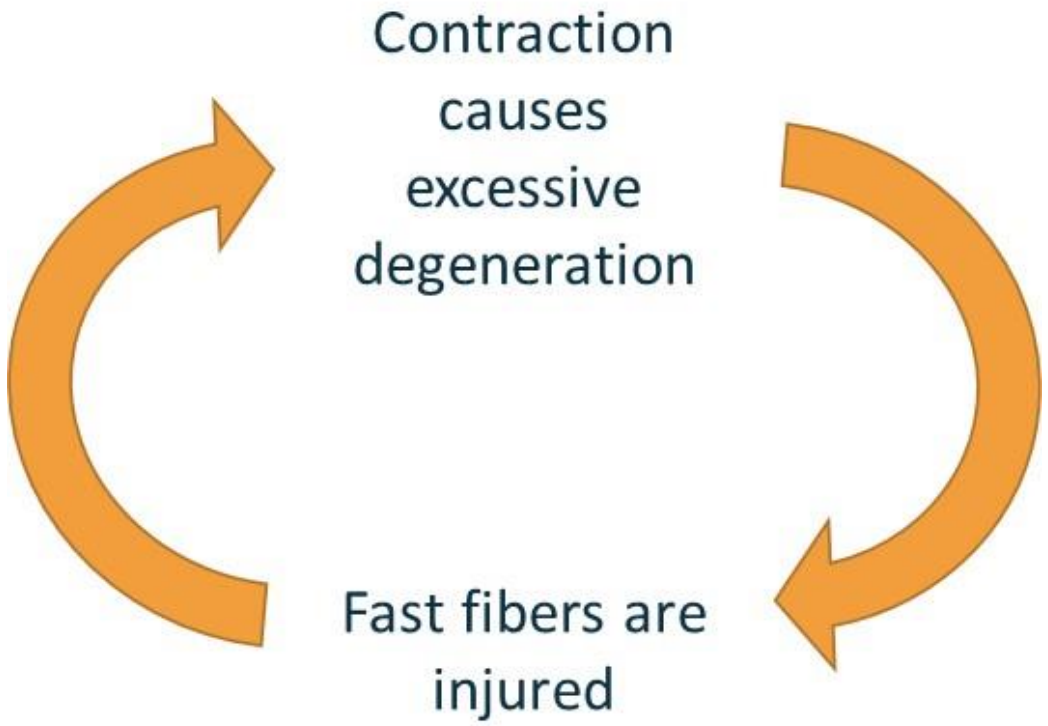


Contraction



Without dystrophin – contraction causes injury

A New Strategy to Rebalance Dystrophic Muscle



Protecting muscle is predicted to preserve function

EDG-5506 Protects Dystrophic Mouse Muscle

Dystrophic mouse muscle is damaged during contraction

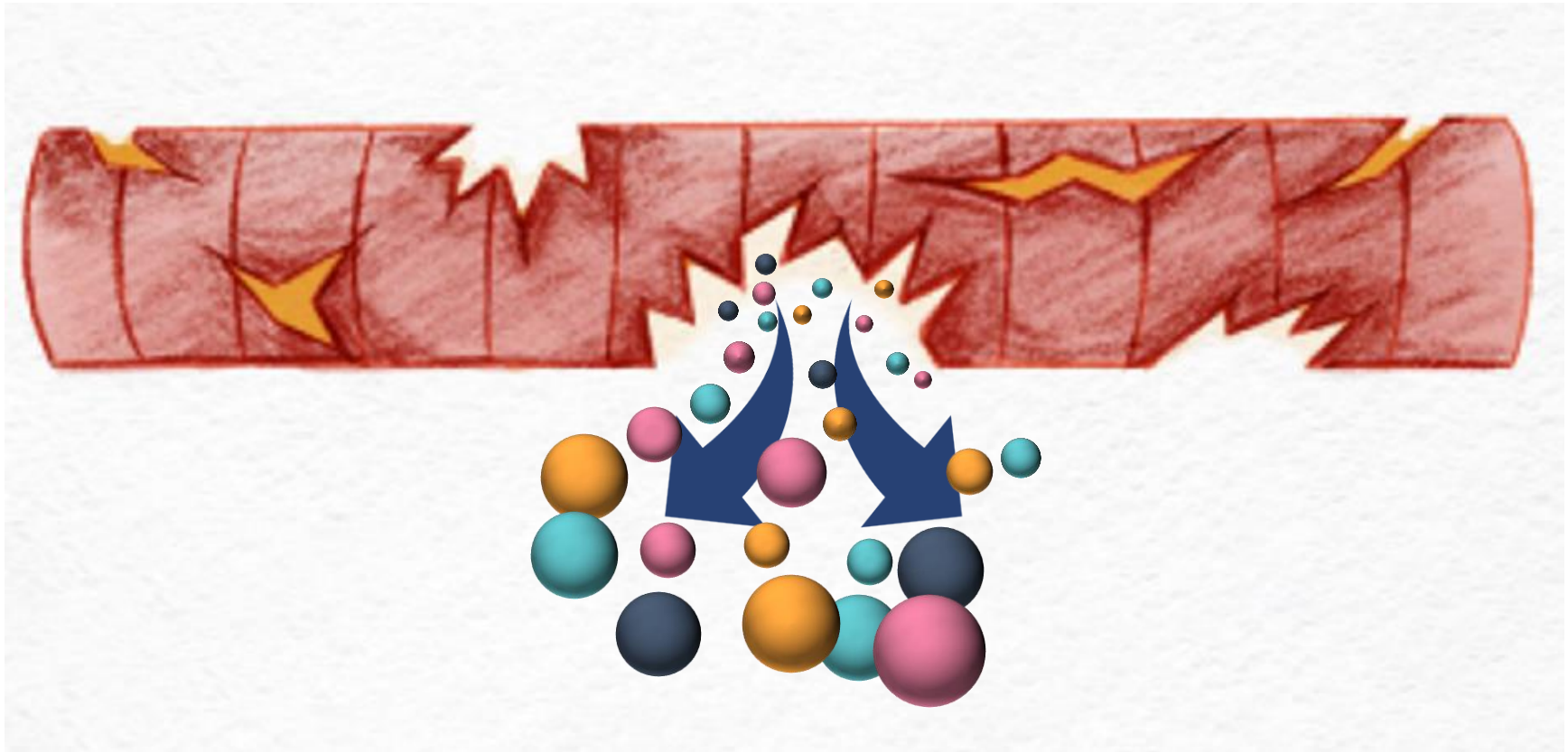
Contraction leads to visible changes…

EDG-5506 protects dystrophic mouse muscle during contraction

With EDG-5506, contractions don’t cause these changes

Claflin, Su and Brooks. U Michigan

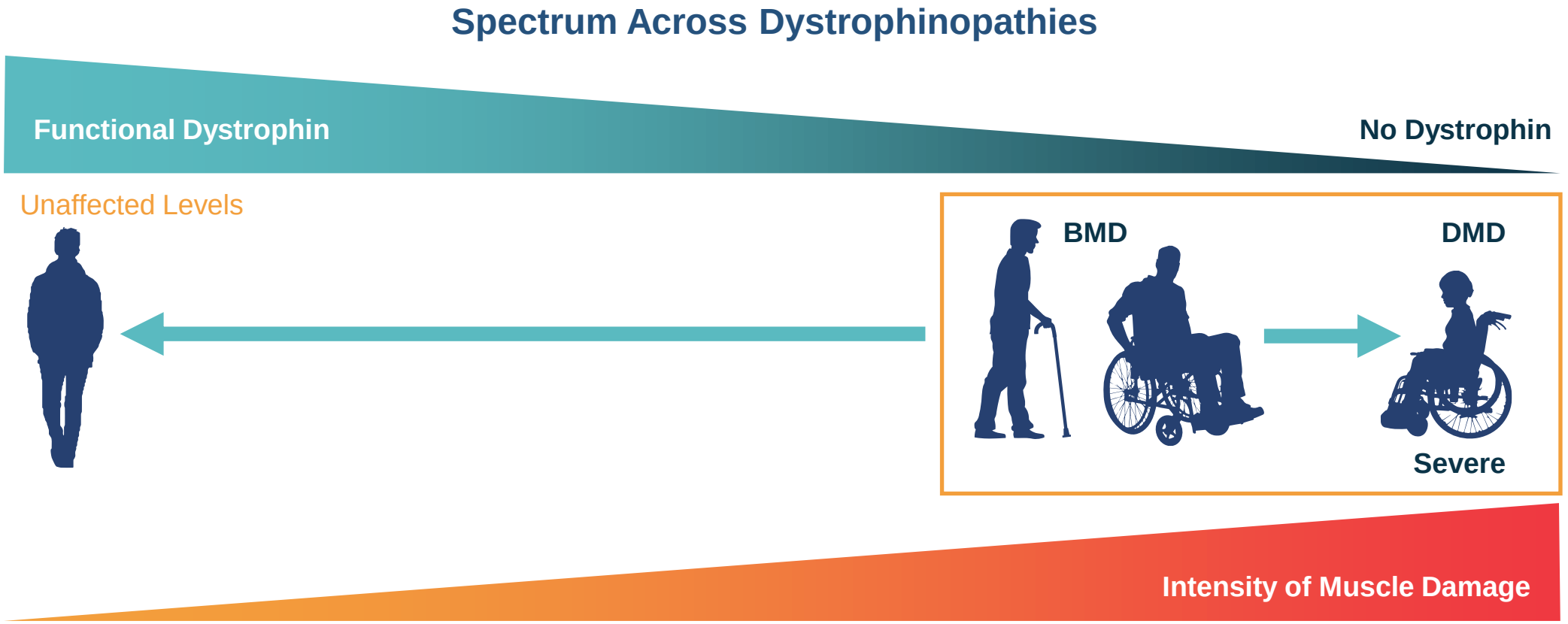
Injured Muscles Release Muscle Protein Biomarkers



- Creatine Kinase
- Myoglobin
- Fast Skeletal Muscle 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) are Related Dystrophinopathies

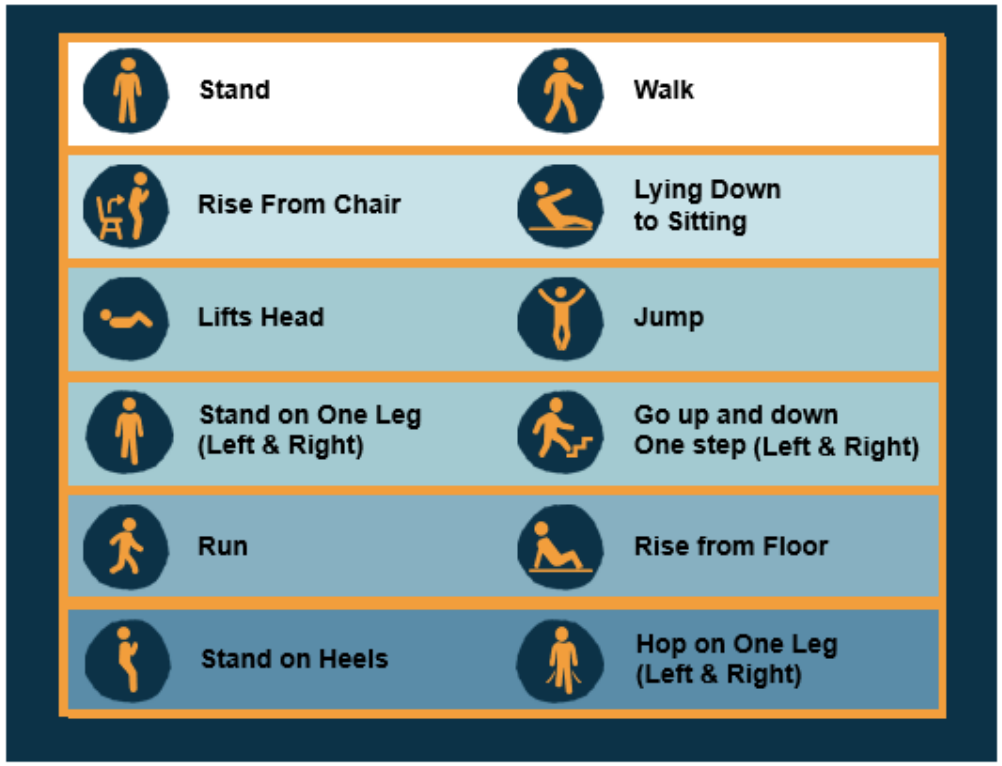


Edgewise's approach aims to prevent muscle breakdown due to lack of functional dystrophin, regardless of mutation

North Star Ambulatory Assessment (NSAA)

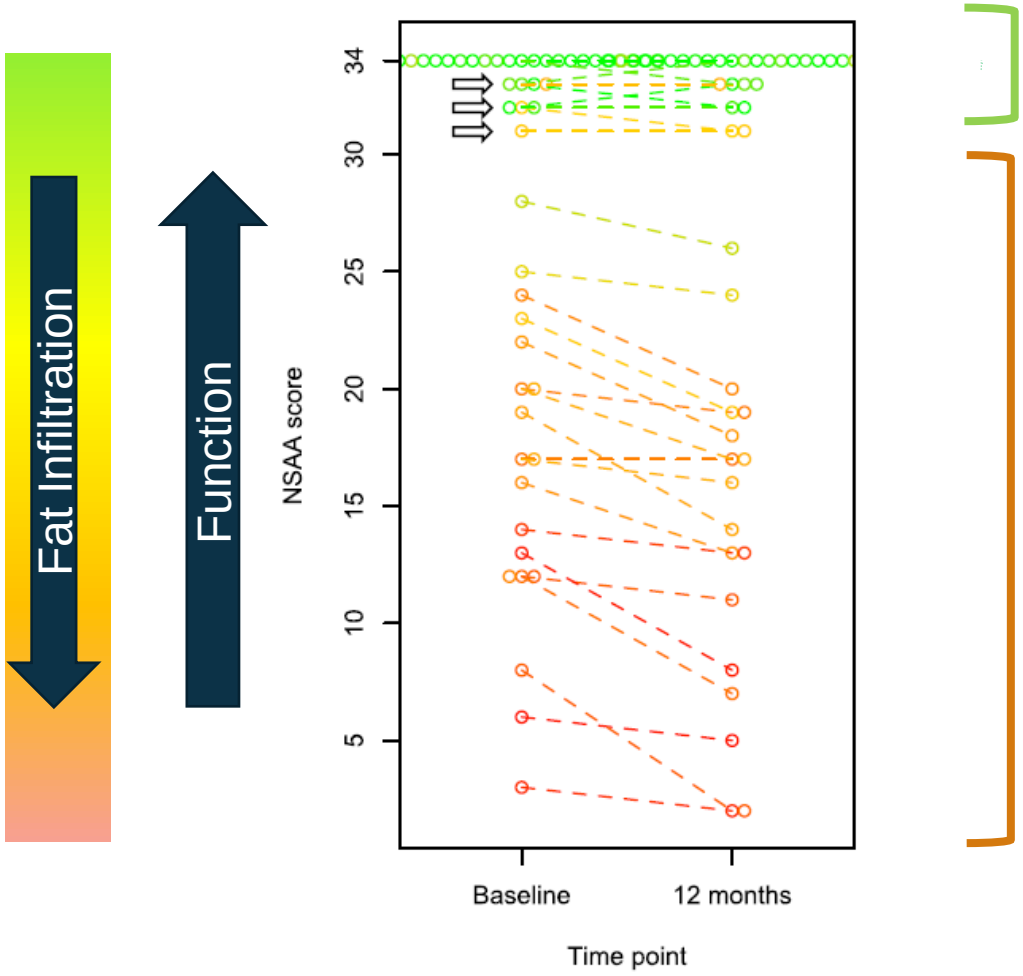
- The NSAA includes 17 different activities that measure function in those who are able to walk
- Each activity is scored on whether the activity can be complete the usual way, with an adjustment because of weakness, or not at all. The maximum score is 34.
- It is used by practitioners and in clinical trials to measure motor function over time.

Snapshot of NSAA skills assessed



BMD: Once Muscle Loss Occurs, Function Progressively Declines

Age doesn't predict function, but function predicts future deterioration



Individuals with NSAA near maximal have low degree of replacement of the muscle by fat and fibrosis, otherwise known as fat infiltration

Individuals with NSAA below 32 have more severe replacement of muscle by fat and fibrosis, and progressive disease over 1 year, with NSAA decreasing an average of 1.2 points annually over a 5-year period

Barp et al., 2017 Sci Reports; Bello, 2016, Sci Reports

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

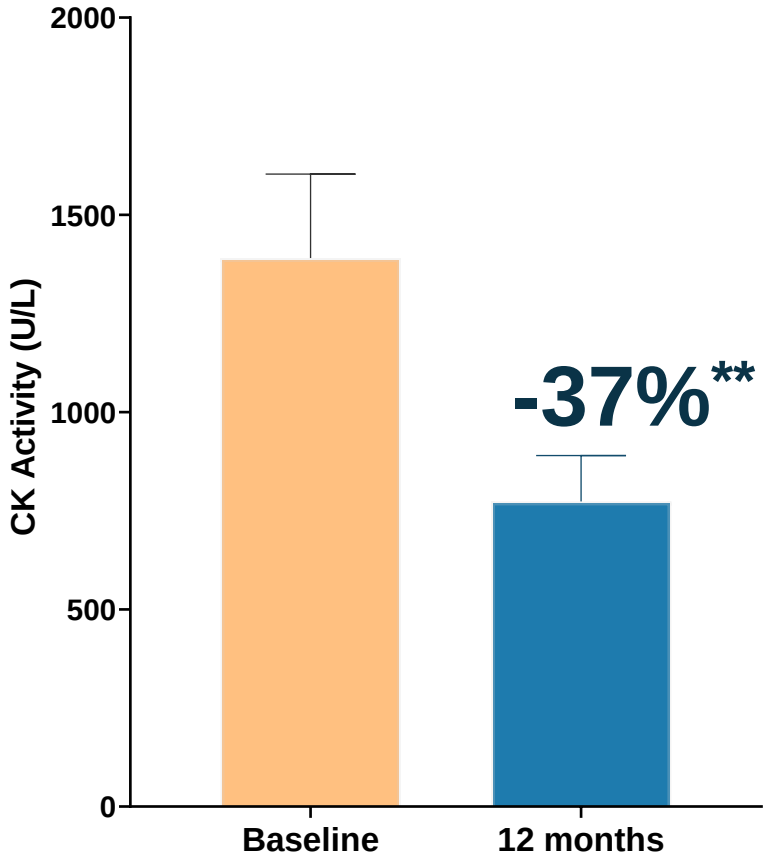
- What do we know about side effects?
  - When dosed for two weeks, EDG-5506 was well-tolerated

- 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

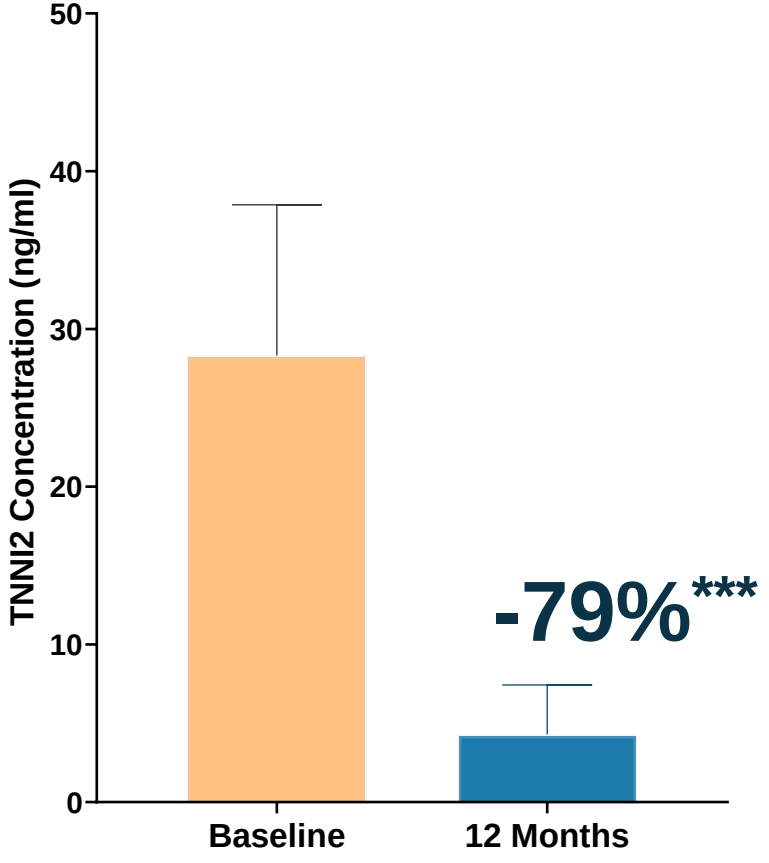
- Does it get to the muscle?
  - EDG-5506 is highly concentrated in muscle compared to the bloodstream, which tells us that it is getting to where it needs to be to protect the muscle

Biomarkers of Muscle Damage in Becker Participants Decreased after 12 Months of Treatment with EDG-5506

Creatine Kinase

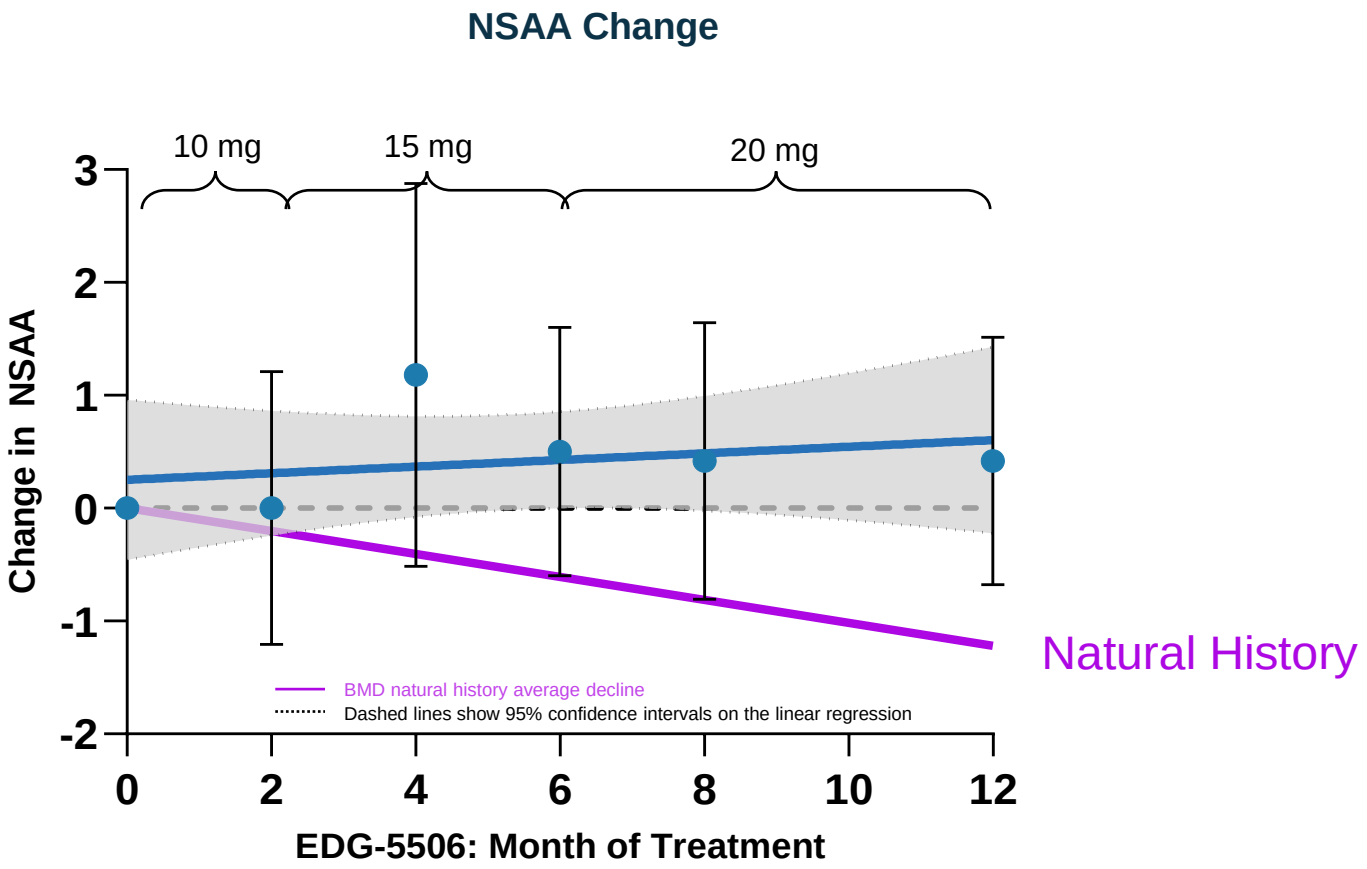


Fast Skeletal Muscle Troponin I (TNNI2)



NCT 05291091
*mean % difference from baseline shown; Means ± SEM
Source: Data on file; ** p=<0.001 ; ***p<0.0001

North Star Ambulatory Assessment (NSAA) Shows Trend toward Improvement Relative to Natural History



BMD individuals with a baseline NSAA score of 10-32 exhibit an estimated yearly NSAA decline of -1.22 points

NCT05291091
Means ± SEM; Source: data on file; Dashed lines show 95% confidence intervals on the linear regression
Natural history based on data presented by Luca Bello at MDA (2022) and van de Velde NM *et. al.*, *Neurology*, 2021 Barp et al., 2017 Scientific Reports

CANYON: Phase 2 Trial in Becker

A 14-month long trial to evaluate the effect of EDG-5506 on safety, tolerability, biomarkers of muscle damage and functional measures in individuals living with BMD

Population

- Male, ages 12-50
- Genetic diagnosis of Becker
- Ability to complete physical function activities (i.e., NSAA, 100-meter timed test)

Sites will enroll across the United States, United Kingdom, and the Netherlands

Assessments and Visits

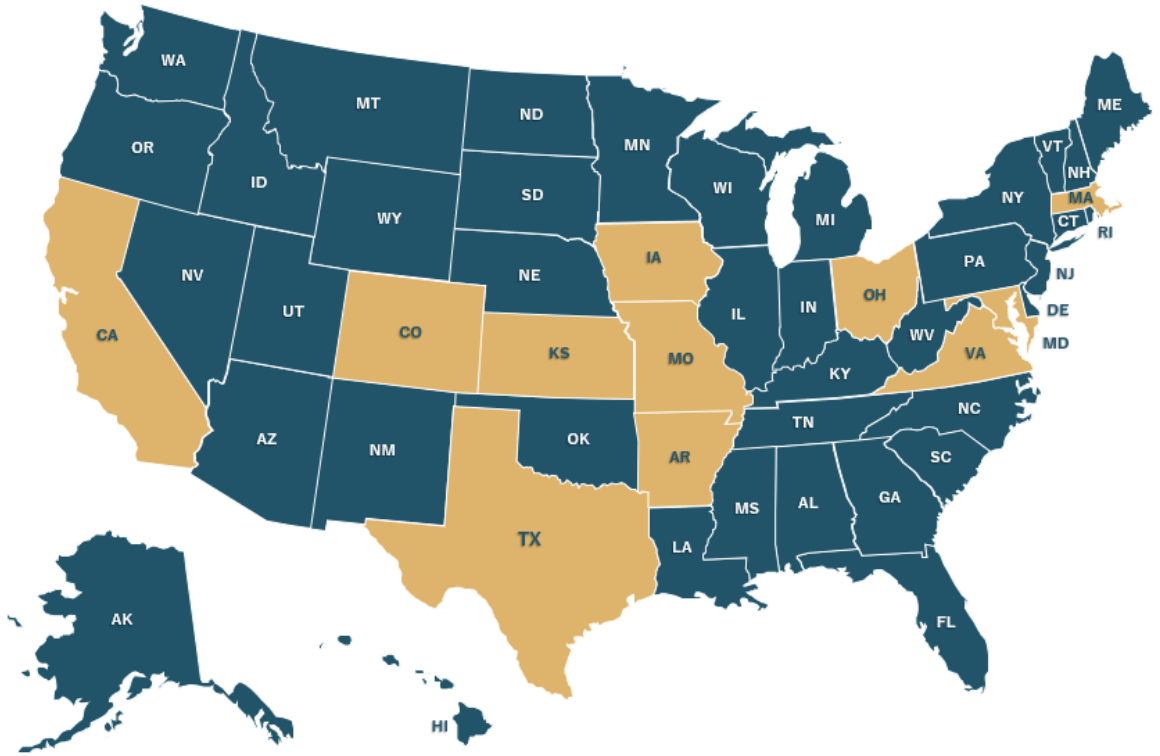
- Approximately 10 site visits required throughout 14-month trial, including screening
- Select functional assessments and blood tests, *no muscle biopsy*
- At-home elements

Sites across the US will enroll for the CANYON trial

CANYON

Sites actively recruiting

- Little Rock, Arkansas
- Sacramento, California
- Aurora, Colorado
- Iowa City, Iowa
- Kansas City, Kansas
- Baltimore, Maryland
- Worcester, Massachusetts
- St. Louis, Missouri
- Cincinnati, Ohio
- Columbus, Ohio
- Dallas, Texas
- Richmond, Virginia



Edgewise is Committed to Reducing Trial Burden for Participants

- Engages with the community to understand trial burden and barriers to support the design of patient-centric trials
- Provides support services for participants, i.e., travel liaison, pre-paid expenses, and resources to ease participation burden on families
- Expanding geographical coverage for study sites to ease travel burden for participation

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 muscle fibers
- Potential to be used alone or in combination with other therapeutic approaches for dystrophinopathies
- Designed to stop the damage where it begins

Key takeaways

- Becker muscular dystrophy (BMD) is a serious dystrophinopathy with a variable clinical course. However, once declining, individuals irreversibly lose muscle and their disease progresses

- Living with Becker poses multiple challenges. To develop treatments it is critical to listen to the community to understand their lived experience.

- In both BMD and DMD, contraction-induced injury is a key aspect of the disease process, and we believe that modulation of fast myosin can protect muscle fibers from contraction-induced injury

- EDG-5506 decreased biomarkers of muscle injury in individuals with BMD and clinical studies for BMD and DMD are underway

Edgewise THERAPEUTICS

THANK YOU!

For questions or comments please email us!

studies@edgewisetx.com

Visit us at https://edgewisetx.com/

https://www.facebook.com/Edgewisetx/

https://twitter.com/EdgewiseTx