Becker Muscular Dystrophy Natural History and ARCH, an Open Label Study in Becker: Putting the Data into Context

Symposium at the 28th International Annual Congress of the World Muscle Society
Charleston, SC
October 3, 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
Program Overview

• **Joanne M Donovan**, MD, PhD, Chair, Chief Medical Officer, Edgewise
  
  *Introduction*

• **Erik Niks**, MD, PhD, Pediatric and adult Neurologist, Leiden University Medical Center
  
  *The Natural History of Becker Muscular Dystrophy*

• **Sam Collins**, MD, PhD, Vice President, Clinical Development, Edgewise
  
  *Twelve-month Data from ARCH, an Open Label Study in Becker Muscular Dystrophy*

• **Barry Byrne**, MD, PhD, Director, Powell Gene Therapy Center, University of Florida
  
  *Putting the Data into Context*

Panel discussion to follow
Key Takeaways

• Becker muscular dystrophy is a serious dystrophinopathy. Once function begins to decline, individuals continue to irreversibly lose muscle and their disease progresses.

• Stabilizing function or even reducing the slope of decline is an important goal in Becker muscular dystrophy.
The Natural History of Becker Muscular Dystrophy

Erik Niks, MD, PhD
Pediatric and Adult Neurologist
Leiden University Medical Center
Becker Muscular Dystrophy

Natural History

Erik Niks – pediatric & adult neurologist
Disclosures

Participant in advisory boards for Edgewise, Italfarmaco, Sarepta, Epirium, Regenxbio and Janssen

Principal investigator at LUMC for clinical trials from Edgewise, Italfarmaco, Sarepta, Fibrogen, NS Pharma, Reveragen, Santhera, BioMarin, ML Bio, Janssen, ArgenX and Alexion

Grants from Pfizer, EU, DPP, PBS, AFM, NWO, SvS

No personal financial interests. Reimbursement received by LUMC.
Becker Muscular Dystrophy

14 male patients
Onset 12-25 years
Slowly progressive
Hypertrophic calves
Waisting of quadriceps

Eine neue x-chromosomale Muskeldystrophie.

Von
P. E. Becker und F. Kiener.

Mit 8 Textabbildungen.
(Eingegangen am 22. März 1955.)
Becker Muscular Dystrophy

14 male patients
Onset 12-25 years
Slowly progressive
Hypertrophic calves
Waisting of quadriceps
Clinical variation
Becker and Duchenne share the gene and protein

Analysis of deletions in DNA from patients with Becker and Duchenne muscular dystrophy

Louis M. Kunkel and co-authors*

Division of Genetics, The Children's Hospital, Boston, Massachusetts 02115, USA
Dystrophin links sarcolemma and cytoskeleton
79 exons of the DMD gene

Adapted from Duan et al. Nat Rev Dis Primers 2021
Duchenne - out of frame deletions

Adapted from Duan et al. Nat Rev Dis Primers 2021
Becker – in frame deletions

Adapted from Duan et al. Nat Rev Dis Primers 2021
Muscle biopsy

Normal

Becker

Duchenne

Beekman et al. PLoS One. 2018
Clinical symptoms

Proximal and paraspinal weakness
Acquire jumping and hopping
Ambulant beyond 16 yrs (no steroids)
Muscle pain and cramps
Muscle hypertrophy -> atrophy
Cardiomyopathy
North Star Ambulatory Assessment

17 items
Score of 0-2 per item
Unable - With assistance - Independent
Maximum of 34 points
10-meter walk/run test
Primary endpoint in DMD and BMD trials
MCID and use for external controls in DMD
BMD Natural History study - Italy

N = 69
Age 6-69
Follow-up 12 months
Mutations
  Del 45-x (28)
  Del 48    (10)
  Del x-51 (10)
  Other     (21)

NSAA at baseline 25.3 ± 10.8
Mean change at 12m -0.9 ± 1.6 (p<0.001)
BMD Natural History study - Netherlands

N = 36
Age 18-67
Annual FU - 3 years
Yearly functional assessments
MRI optional (1st and 3rd visit)
Mutations
  Del 45-47 (11)
  Involving nNOS (21)
NSAA main decline in 10-32

Schrama and Koeks et al. In preparation
Responsiveness of functional tests at 1 and 3-year FU

Standardized Response Mean (SRM)
Sample size (SS) calculation based on 50% treatment effect in 1:1 randomisation

<table>
<thead>
<tr>
<th></th>
<th>N at baseline</th>
<th>Mean (SD) at baseline</th>
<th>Mean change at 1-year follow-up (SD)</th>
<th>SRM 1 year follow-up</th>
<th>SS 1 year follow-up</th>
<th>Mean change at 3-year follow-up (SD)</th>
<th>SRM 3 year follow-up</th>
<th>SS 3 year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAA</td>
<td>32</td>
<td>18.9 (12.7)</td>
<td>-1.36 (2.45)</td>
<td>-0.55</td>
<td>209</td>
<td>-2.65 (3.87)</td>
<td>-0.69</td>
<td>136</td>
</tr>
<tr>
<td>10MWRv (m/s)</td>
<td>25</td>
<td>1.97 (1.15)</td>
<td>-0.28 (0.41)</td>
<td>-0.68</td>
<td>137</td>
<td>-0.21 (0.52)</td>
<td>-0.39</td>
<td>412</td>
</tr>
</tbody>
</table>
MRI as biomarker in BMD

Increased fat fraction
Differs between muscles
Differs within muscles
Axial and longitudinal plane

Hooijmans et al. NMR in Biomed 2020 & van de Velde et al. Neurology 2021
MRI as biomarker in BMD

Fat fraction using Dixon
N = 24 at baseline, N = 20 after 2 years
Manual delineation of 19 muscles:
• 23 slices of 10 mm with 5 mm gap
• Middle slice based on anatomical landmarks
• Values for 3 center slices and whole muscle
• Values per muscle and for 6 groups
• Functional tests: NSAA, 6MWT, TMRv
Increase in FF over 24 months

Median whole muscle FF increased between 0.2% and 2.6%
## Functional change over 24 months

### Table 1 Change in Functional Assessments Between Baseline and After 24 months

<table>
<thead>
<tr>
<th>Test</th>
<th>Median at baseline</th>
<th>Median change follow-up vs baseline (range)</th>
<th>p Value</th>
<th>SRM</th>
<th>SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAA, points</td>
<td>18 (5 to 34)</td>
<td>-2.5 (-12.0 to 1.0)</td>
<td>0.002</td>
<td>-0.81</td>
<td>98</td>
</tr>
<tr>
<td>TMRv, m/s</td>
<td>1.45 (0.26 to 4.17)</td>
<td>-0.22 (-1.4 to 0.25)</td>
<td>0.014</td>
<td>-0.68</td>
<td>138</td>
</tr>
<tr>
<td>6MWT, m</td>
<td>385 (0 to 650)</td>
<td>-12.6 (-151.9 to 33.0)</td>
<td>0.063</td>
<td>-0.46</td>
<td>310</td>
</tr>
<tr>
<td>KE, kg</td>
<td>8.56 (2.9 to 54.5)</td>
<td>-1.3 (-11.1 to 3.8)</td>
<td>0.114</td>
<td>-0.49</td>
<td>264</td>
</tr>
<tr>
<td>KF, kg</td>
<td>8.19 (2.4 to 29.7)</td>
<td>-1.4 (-7.1 to 2.8)</td>
<td>0.040</td>
<td>-0.71</td>
<td>126</td>
</tr>
</tbody>
</table>

**Abbreviations:** 6MWT = 6-minute walk test; KE = knee extension; KF = knee flexion; NSAA = North Star Ambulatory Assessment; SRM = standardized response mean; SS = sample size; TMRv = 10-meter run velocity.
Stepwise analysis

Sensitivity to detect change
(standardized response mean)

Correlation with baseline function
(NSAA, 6MWT, TMRv)

Reproducibility
Table 2  Quantitative MRI Measures in Final Step of the Flowchart

<table>
<thead>
<tr>
<th>Measure</th>
<th>SRM</th>
<th>SS</th>
<th>NSAA</th>
<th>TMRv</th>
<th>6MWT</th>
<th>Reproducibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole thigh 3CS</td>
<td>1.04</td>
<td>59</td>
<td>-0.888</td>
<td>-0.865</td>
<td>-0.832</td>
<td>ICC: 1.000, SD of the difference 0.23%</td>
</tr>
<tr>
<td>Whole thigh WM</td>
<td>1.01</td>
<td>64</td>
<td>-0.924</td>
<td>-0.891</td>
<td>-0.872</td>
<td>ICC: 1.000, SD of the difference 0.24%</td>
</tr>
<tr>
<td>Quadriceps WM</td>
<td>0.99</td>
<td>65</td>
<td>-0.878</td>
<td>-0.842</td>
<td>-0.825</td>
<td>ICC: 1.000, SD of the difference 0.35%</td>
</tr>
<tr>
<td>Quadriceps 3CS</td>
<td>1.04</td>
<td>59</td>
<td>-0.878</td>
<td>-0.842</td>
<td>-0.807</td>
<td>ICC: 1.000, SD of the difference 0.47%</td>
</tr>
<tr>
<td>Vastus lateralis 3CS</td>
<td>0.83</td>
<td>94</td>
<td>-0.866</td>
<td>-0.832</td>
<td>-0.840</td>
<td>ICC: 1.000, SD of the difference 0.47%</td>
</tr>
<tr>
<td>Vastus lateralis WM</td>
<td>0.92</td>
<td>76</td>
<td>-0.858</td>
<td>-0.818</td>
<td>-0.828</td>
<td>ICC: 1.000, SD of the difference 0.69%</td>
</tr>
<tr>
<td>Rectus femoris WM</td>
<td>0.84</td>
<td>92</td>
<td>-0.896</td>
<td>-0.877</td>
<td>-0.846</td>
<td>ICC: 1.000, SD of the difference 0.83%</td>
</tr>
<tr>
<td>Vastus intermedius 3CS</td>
<td>0.85</td>
<td>90</td>
<td>-0.874</td>
<td>-0.849</td>
<td>-0.811</td>
<td>ICC: 0.999, SD of the difference 1.55%</td>
</tr>
</tbody>
</table>

Abbreviations: 3CS = 3 center slices; 6MWT = 6-minute walk test; ICC = intraclass correlation coefficient; KE = knee extension; KF = knee flexion; NSAA = North Star Ambulatory Assessment; SRM = standardized response mean; SS = sample size; TMRv = 10-meter run velocity; WM = whole muscle.
Cognition in BMD

Cognitive and Psychological Profile of Males With Becker Muscular Dystrophy

Helen K. Young, FRACP, MMed, Belinda A. Barton, PhD, Susan Waisbren, PhD, Lourdes Portales Dale, PhD, Monique M. Ryan, FRACP, MMed, Richard I. Webster, FRACP, MMed, and Kathryn N. North, MD

Psychiatric and neurodevelopmental aspects of Becker muscular dystrophy

Madoka Mori-Yoshimura, Yukio Mizuno, Sumiko Yoshida, Naoko Ishihara, Naruhito Minami, Emiko Morimoto, Kazushi Maruo, Ikuya Nonaka, Hirofumi Komaki, Ichizo Nishino, Masayuki Sekiguchi, Noriko Sato, Shin’ichi Takeda, Yuji Takahashi

The neurocognitive profile of adults with Becker muscular dystrophy in the Netherlands

Natural history - ongoing studies

CINRG
US, Canada, UK, Italy

GRASP - Defining Endpoints in BMD
US, Europe

NorthStar Assessment for LGMD (NSAD)

MRI

ImagingNMD
US

BIND (Brain Involvement in Dystrophinopathies)
UK, Italy, Spain, Denmark, France, Netherlands
Summary

BMD and DMD are both part of a spectrum
High clinical variability and slow progression
Complex genotype-phenotype correlations
Changes in motor function > 12 months
Decline in baseline NSAA 10-32
MRI is a promising biomarker
Bridging the gap in NH data
Targeting Fast Myosin in Becker and Duchenne Muscular Dystrophy

Sam Collins, MD, PhD
Vice President, Clinical Development
The Dystroglycan Complex Helps Prevent Injury in Contracting Fibers

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

Muscle fibers from different motor units contract independently.

Resting skeletal muscle

Long muscle fibers are more dependent upon dystrophin to help support fibers.
Fast Muscle Fibers Are More Susceptible to Damage in Response to Eccentric Exercise in Unaffected Individuals

More Damage in Fast Muscle Fibers vs. Slow Muscle Fibers

- 30 mins controlled eccentric exercise
- Muscle biopsy taken immediately after exercise

Injury Biomarkers Tell the Same Story: Fast but not Slow Fiber Biomarkers are Elevated in Becker and Duchenne

- Age ranges: Control 6-73 years, Becker 6-68 years, Duchenne 2-33 years

**** p < 0.0001

132 Duchenne samples from Newcastle University Biobank, 52 Becker samples from the CINRG consortium and 52 healthy volunteers from Chen collaboration

~83% of volunteers had fast troponin levels below the LLQ of the ELISA, while only 4% of Becker and 6% of Duchenne patients had non-measurable levels of fast troponin

Reference: Barthel et. al., Muscle and Nerve, 2021
A New Strategy to Rebalance Dystrophic Muscle

Protecting muscle is predicted to preserve function
EDG-5506 Stops Fast Fiber Breakdown in Contracting *mdx* Muscles

Claflin, Su and Brooks. U Michigan

*mdx* mouse lumbrical muscle – 20, 1 second maximal isometric contractions (video sped up)
ARCH Open-Label Study Design in Becker Patients

• An open-label, single-center study of EDG-5506 to assess the safety and pharmacokinetics of EDG-5506 in adults with Becker

• Primary objective: Safety and tolerability at 12 months, now extended to 24 months

• Key inclusion criteria
  − Ambulatory males aged 18 to 55 years with a dystrophin mutation and a Becker phenotype, not on corticosteroids, who could complete 100-m timed test

• Enrollment: 12

Measures Assessed: Safety, PK, NSAA, NSAD, 100-m timed test, timed function tests
### Baseline Characteristics: Becker Participants Had Significant Functional Impairment and Decreased Muscle Mass

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Becker Participants (N=12)</th>
<th>Age Normative Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (SD)</strong></td>
<td>32.8 (8.1) years</td>
<td></td>
</tr>
<tr>
<td><strong>Functional Measures (median)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-meter walk/run</td>
<td>8.4 sec</td>
<td>&lt; 4 sec</td>
</tr>
<tr>
<td>Rise from floor</td>
<td>6/12 could perform</td>
<td>&lt; 3 sec</td>
</tr>
<tr>
<td>NSAA</td>
<td>15.5 (range 4-31)</td>
<td></td>
</tr>
<tr>
<td><strong>Serum Creatinine (mean, mg/dL)</strong></td>
<td>0.44</td>
<td>0.92 - 1.16</td>
</tr>
<tr>
<td><strong>Serum CK (mean, U/L)</strong></td>
<td>1,390</td>
<td>&lt;210</td>
</tr>
<tr>
<td><strong>DXA % Lean Mass</strong></td>
<td>54.9%</td>
<td>&gt;75%</td>
</tr>
</tbody>
</table>

Unlike clinical trials for children with Duchenne, the Becker patients in ARCH were in the functional decline phase of their disease course.
EDG-5506 Was Well Tolerated at All Doses; No Dose Reductions, No Treatment Discontinuations and No SAEs

<table>
<thead>
<tr>
<th>Treatment Emergent AE</th>
<th>10 mg EDG-5506 2 months of dosing</th>
<th>15 mg EDG-5506 4 months of dosing</th>
<th>20 mg EDG-5506 6 months of dosing</th>
<th>Total 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>2 (17%)</td>
<td>3 (25%)</td>
<td>1 (8%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>COVID-19</td>
<td>-</td>
<td>1 (8%)</td>
<td>3 (25%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>-</td>
<td>-</td>
<td>4 (33%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2 (17%)</td>
<td>1 (8%)</td>
<td>-</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (8%)</td>
<td>2 (17%)</td>
<td>2 (17%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Fall*</td>
<td>-</td>
<td>3 (25%)</td>
<td>3 (25%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Viral URI</td>
<td>1 (8%)</td>
<td>-</td>
<td>3 (25%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Influenza</td>
<td>-</td>
<td>-</td>
<td>2 (17%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>-</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>GERD</td>
<td>-</td>
<td>-</td>
<td>2 (17%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Procedural pain</td>
<td>1 (8%)</td>
<td>-</td>
<td>1 (8%)</td>
<td>2 (17%)</td>
</tr>
</tbody>
</table>

* Unassociated with other AEs and typical of falls observed in Becker patients

Source: Data on file
Muscle Damage in Muscular Dystrophies Leads to Leak of Injury Biomarkers, including CK, TNNI2 and Myoglobin

Activity-Induced Muscle Injury in Muscular Dystrophies

Contraction induced muscle damage causes excessive degeneration

Fast fibers are subsequently injured leading to release of muscle injury biomarkers into the circulation

Legend: CK, Creatine Kinase; TNNI2, Fast Skeletal Muscle Troponin I; Mb, Myoglobin

Circulating Levels of Muscle Injury Biomarkers Can be Measured to Determine Ongoing Muscle Damage in Muscular Dystrophies
EDG-5506 Led to a Sustained Decrease in Biomarkers of Muscle Damage After 12 Months of Dosing

Creatine Kinase

-37%**

Fast Skeletal Muscle Troponin I (TNNI2)

-79%***

Individuals with the Highest Baseline Values Show Greatest Biomarker Effect, Suggesting Protection Against Activity-Induced Damage

Source: Data on file; TNNI2 data projected from SOMAscan. % difference from mean baseline shown; Means ± SEM. (**p<0.001 and ***p<0.0001)
NSAA Shows Stabilization and Trend Toward Improvement – Mean +0.4 Improvement Relative to Predicted -1.2 Point Decline from NHx

Individual NSAA Responses at 12 Months – 75% Remained the Same or Improved
No Decline from Baseline On 100 Meter Time Test Velocity; No Significant Impact on Grip Strength

100-Meter Timed Test Velocity

No statistically significant change at 12 months

Maximum Grip Strength

No statistically significant change at 12 months

*last observation carried forward (all N=12, except for 2 missing values, month 4 and 8)
Source: data on file
Pain is a Significant Hallmark of Becker and Self-Reported Pain Scores Trended Better after 12 Months with EDG-5506

While the ARCH study is not placebo controlled, a positive trend in self-reported pain scores was observed after 12 months of EDG-5506 dosing.
Outcomes of the ARCH Study

- **Safety**: Well-tolerated at all doses
- **Biomarkers**: Demonstration of rapid, sustained and significant decreases in multiple biomarkers of disease progression
- **Function**: Stabilization of functional assessments with trends toward improvement
- **Pivotal Dose Identified**: Maximal biomarker response even at 10 mg dose; PK/PD supportive of 10 mg dose for pivotal cohort

**Overall, the ARCH trial identified key factors for the design of a potentially registrational trial**
Putting the Data into Context

Barry Byrne, MD, PhD
Director, UF Health Center for Advanced Therapeutics and Powell Gene Therapy Center
University of Florida
Becker and Duchenne Muscular Dystrophy are Related Dystrophinopathies

The combination of dystrophin functionality and background genetics place Becker individuals on a spectrum with Duchenne muscular dystrophy.
NSAA: A Well-Established and Validated Measure of Global Function that is Clinically Meaningful in a Real-World Context

- Composite evaluation of motor function across 17 test items with increasing difficulty

Each activity scored on whether it can be completed:
- Normally (2 points)
- With an adjustment due to weakness (1 point)
- Not at all (0 points)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Real-World Implication for Individual w/Becker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jump, Hop, Run</td>
<td>Playing sports</td>
</tr>
<tr>
<td>Stand on Heels</td>
<td>Walking on uneven ground, cycling, difficulty getting out of a chair, striding, cycling</td>
</tr>
<tr>
<td>Rise from Floor</td>
<td>Getting up after falling, playing on the floor with children</td>
</tr>
<tr>
<td>Gets to Sitting</td>
<td>Sitting up in bed, adjust to falls</td>
</tr>
<tr>
<td>Climb Box Steps</td>
<td>Independent outdoor mobility particularly easy tasks like stairs and sidewalk curbs</td>
</tr>
<tr>
<td>Stand on one Leg</td>
<td>Dressing oneself, putting on shoes/socks while standing, reaching high shelves</td>
</tr>
<tr>
<td>Stand from Chair</td>
<td>Using a toilet independently, getting out of bed, using public transportation to get around</td>
</tr>
<tr>
<td>Walk</td>
<td>Walking to mailbox to pick up mail, hiking, everyday mobility</td>
</tr>
<tr>
<td>Stand</td>
<td>Grooming, preparing meals, adapting to mobility device, transferring to chair</td>
</tr>
</tbody>
</table>
What Does a Nominal NSAA Mean to an Individual with Becker?

• Data: NSAA scores in 39 ambulatory adults enrolled in Edgewise studies
  — Grouped by baseline scores: ≥30, 20-29, 10-19, <10

• Methods:
  — At different NSAA scores, what functions are completely lost?
  — What functions require some degree of compensation because of weakness?

• Note this is a cross-sectional look at function, but from natural history studies, once decline begins, the decline in NSAA is about 1.2 points/year
Natural History: Once Declining, Decrease of ~1.2 NSAA Points/Year

NSAA Score

Group 1
Score: ≥30

Group 2
Score: 20 – 29

~5 years

~8 years

~8 years

Group 3
Score: 10 – 19

Group 4
Score: 0 – 9

~5 years

~8 years

~8 years

34 30 20 10 0
Group 1: Baseline NSAA 30 – 34
Can complete all functions

— May need to compensate for certain functions because of weakness:

![Graph showing percentage of patients compensating for loss of function in various tasks.](image-url)
Group 2: Baseline NSAA 20 – 29
Can complete most functions but need to compensate because of weakness

— Reflects progressive loss of muscle, progressive weakness
Group 3: Baseline NSAA 11 – 20
Unable to complete most functions and need to compensate for almost all functions

– Reflects progressive loss of muscle, progressive weakness
Group 4: Baseline NSAA 0 – 9
Minimal ability to complete typical ambulatory activities

– Further loss of muscle, progressive weakness, near non-ambulatory

Compensating
Loss of Function
Key Takeaways

• Becker muscular dystrophy is a serious dystrophinopathy. Once function begins to decline, individuals continue to irreversibly lose muscle and their disease progresses.

• Stabilizing function or even reducing the slope of decline is an important goal in Becker muscular dystrophy.
Next Steps

Joanne Donovan, MD, PhD
Chief Medical Officer
Edgewise Therapeutics
A Pivotal Study in Becker

A global 18-month trial to evaluate the safety and efficacy of EDG-5506 in individuals living with Becker

Population:
- Male, ages 18-50
- Genetic diagnosis of Becker
- Ambulatory with NSAA 5-32

Primary endpoint:
- NSAA

Additional endpoints:
- TFT’s, MRI, biomarkers, PROs

Visit Schedule

- Study Visits (month):
  - 0
  - 1
  - 3
  - 6
  - 9 (Call only)
  - 12
  - 15 (Call only)
  - 18

- Screening visit
- EDG-5506 10 mg PO daily
- Placebo
Questions?
It's time to get real about Becker muscular dystrophy

BECKER EDUCATION & ENGAGEMENT DAY

A day for individuals with Becker and their families

MARK YOUR CALENDAR!

Registration Link and More Information Coming Soon
Acknowledgements:

Study Participants and their families

Rare Disease Research
Atlanta GA
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Han Phan, MD

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