12-Month Topline Results from the ARCH Open Label Study of EDG-5506 in Adults with Becker Muscular Dystrophy

June 27, 2023
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Agenda

1. Introduction to Edgewise Therapeutics
   Dr. Kevin Koch

2. BMD Disease Overview
   Dr. Craig McDonald

3. Results from the 12-Months ARCH BMD Trial
   Dr. Joanne Donovan

4. EDG-5506 Opportunity in BMD
   Dr. Behrad Derakhshan

5. Closing Remarks
   Dr. Kevin Koch
Opening Remarks

Kevin Koch, CEO
Edgewise Therapeutics is a Clinical-Stage Company Focused on Advancing Innovative Treatments for Devastating Muscle Disorders

- Experienced management team with deep expertise in muscle physiology/rare diseases
- Leveraging our discovery and development capabilities to advance innovative programs
- Developing EDG-5506 to become the foundational therapy for muscular dystrophies
- Expanding our pipeline by developing EDG-7500 targeting select cardiovascular diseases

Our vision is to improve the lives of patients and families suffering from rare muscle disorders
Our Precision Medicine Platform Generated Two Portfolio Programs Addressing Multiple Indications Currently in Development

<table>
<thead>
<tr>
<th>Program</th>
<th>Indications</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDG-5506</td>
<td>Myosin ATPase</td>
<td>BMD</td>
<td>● ● ●</td>
<td>● ● ●</td>
<td>● ● ●</td>
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<tr>
<td>EDG-5506</td>
<td>Myosin ATPase</td>
<td>DMD</td>
<td>● ● ●</td>
<td>● ● ●</td>
<td>● ● ●</td>
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<tr>
<td>EDG-5506</td>
<td>Myosin ATPase</td>
<td>LGMD, McArdle</td>
<td>● ● ●</td>
<td>● ● ●</td>
<td>● ● ●</td>
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<tr>
<td>EDG-7500</td>
<td>Undisclosed</td>
<td>HCM</td>
<td>● ●</td>
<td>● ●</td>
<td>● ●</td>
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<tr>
<td>EDG-003</td>
<td>Undisclosed</td>
<td>Cardiovascular</td>
<td>● ●</td>
<td>● ●</td>
<td>● ●</td>
</tr>
</tbody>
</table>

Abbreviations: BMD, Becker muscular dystrophy; DMD, Duchenne muscular dystrophy; LGMD, limb-girdle muscular dystrophy; HCM, hypertrophic cardiomyopathy
EDG-5506
Muscular Dystrophies
EDG-5506: A First in Class Myosin Inhibitor With Potentially Disease-Modifying Properties Being Evaluated in Multiple Dystrophinopathies

- EDG-5506 is a novel investigational, orally administered, allosteric, selective, fast myofiber (type II) myosin inhibitor
- EDG-5506 is designed to limit muscle damage, protect and normalize muscle, block the loss of muscle and subsequent loss of function
- Fast Track Designation received from the FDA for Becker muscular dystrophy
- Evaluating multiple indications including, DMD, BMD, LGMD2i and McArdle disease
- COM Patents for EDG-5506 expire in 2039 (subject to extensions)
BMD Disease Overview

Dr. Craig McDonald
BMD is a Progressive Muscle Disorder Caused by Mutations of the Dystrophin Gene that Produce a Protein with Decreased Function

- BMD is a X-linked recessive genetic disorder that causes an in-frame mutation in the dystrophin gene, affecting the body’s ability to produce dystrophin

- The age of symptom onset can range from 5 to 60 years old, typically symptoms begin between ages 8 to 13

- Walking problems in BMD patients are usually noticed by the age of 15 and loss of ambulation often occurs in young adulthood

- The most common cause of death is heart failure from cardiomyopathy

“Becker may be considered milder than Duchenne, but that doesn’t mean its any less devastating” – Neuromuscular Specialist, EU

BMD Presents with Proximal Limb Weakness and Calf Hypertrophy Resulting in Loss of Function and Ambulation at an Early Age

A 12-Year-Old BMD Boy Presenting with Positive Gowers Sign

- Hypotonia noted bilaterally in upper and lower extremities, along with diffuse weakness of the proximal muscles
- To stand from a supine or sitting position (A), rolls into the prone position (B), kneels, and pushes himself upright with his hands on the knees (C) and thighs (D)

Adult BMD Patient

BMD individuals have ongoing, contraction-induced muscle damage, resulting in fibrosis, progressive loss of skeletal muscle function, severe disability, and early death

Note: NM = Neuromuscular; NMS = Neuromuscular Specialist; MDA = Muscular Dystrophy Association
Source: Bluestar interviews and analysis
* video courtesy of Luca Belli - MDA 2022
Physicians Indicate BMD Diagnosis is Often Delayed, Usually Around 7 Years of Age; Treatment Focuses on Symptom Management

Typical BMD Diagnostic Journey (US)

Presentation

Primary Care Physician, Pediatrician

Community Neurology Consult

Neurologist or NMS at COE Consult (can also be academic center)

Genetic Testing

BMD Diagnosed

Treatment / Management

Patients may also be treated in the community setting or are lost to follow-up

Overall treatment at a MDA COE or academic center

“Mostly, patients present to their PCP or pediatrician around age 7 or 8. Where there is an existing family history, it helps to cut down the diagnostic journey by a half or third” – US KOL

“Newborn screening, spurred by approval of GTx, will undoubtedly drive a much earlier diagnosis of BMD also” – US KOL

“Treatment is primarily supportive, and we follow up with patients yearly” – US KOL

Key: Majority of Patients

Minority of Patients

Physicians Indicate that Newborn Screening for Dystrophinopathies will Significantly Improve the Time to Diagnosis

Abbreviations: NM = Neuromuscular; NMS = Neuromuscular Specialist; MDA = Muscular Dystrophy Association

Source: Bluestar interviews and analysis
BMD is Estimated to Affect ~5,000 Individuals in the US, >5,000 in the EU4/UK and ~1,200 in Japan

BMD Epidemiology by Geography

<table>
<thead>
<tr>
<th>Geography</th>
<th>BMD Prevalence</th>
<th>Total BMD Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>3.6/100,000 males</td>
<td>~5,000</td>
</tr>
<tr>
<td>UK</td>
<td>1.6–3.6/100,000</td>
<td>1,000 to 2,400</td>
</tr>
<tr>
<td>Germany</td>
<td>1.6/100,000*</td>
<td>~1,300</td>
</tr>
<tr>
<td>Spain</td>
<td>0.78/100,000</td>
<td>~370</td>
</tr>
<tr>
<td>Italy</td>
<td>1.3–2.4/100,000</td>
<td>800 to 1,400</td>
</tr>
<tr>
<td>France</td>
<td>1.6/100,000*</td>
<td>~1,000</td>
</tr>
<tr>
<td>Japan</td>
<td>1.9/100,000</td>
<td>~1,200</td>
</tr>
</tbody>
</table>

• A 2022 systematic review and meta-analysis of DMD and BMD epidemiological studies states that the global prevalence of BMD is 1.6 per 100,000 people

• There are ~5,000 prevalent BMD patients in the US

• There are 4,500-6,500 prevalent BMD patients in the EU4/UK based on country-specific and global estimates

• The large geographic disparity in prevalence suggests that there is a high rate of underdiagnosis

>12,000 BMD Patients in the US, EU4/UK and Japan

*Global prevalence was used due to lack of country specific data
In BMD, Much Like in DMD, Diminished Function Develops as a Result of Muscle Loss and Fat Replacement

- Average fat fraction in BMD individuals similar to DMD
- Greater fat accumulation in select muscles compared to DMD for a given functional status

Source: Muscle & Nerve. 2021;1–9; Sneha Taylor, MD and Joseph Pater, MD, Consultant 360 Volume 12 - Issue 9 - September 2013
NSAA: A Well-Established and Validated Measure of Global Function in DMD and BMD 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)

### Measure Real-World Implication for BMD Patient

<table>
<thead>
<tr>
<th>Measure</th>
<th>Implication</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>

“As far as how BMD impacts my day most, it would be from the very beginning – the moment I wake up. I have to have help from my wife to get up, go to the bathroom, get dressed, and get in my wheelchair. And so, the way it impacts my day is every day right from the very beginning.”

– Individual Living with BMD
BMD Can Have a Variable Clinical Course; However, Once Declining, Individuals Have a Relentless Course of Disease Progression

Even Moderate Dysfunction Predicts Rapid Deterioration

- ~30% Individuals with near maximal NSAA have muscle weakness but have not reached the threshold that leads to rapid decline
- ~70% Individuals with NSAA <32 have lost muscle mass and have more fat infiltration; function is progressively lost

The Predictable Decline in Function in the Majority of BMD Patients Facilitates a Highly Focused Clinical Trial

Source: Edgewise analysis; Barp et al., 2017 Scientific Reports
* Luca Bello presentation MDA 2022
Longitudinally, NSAA Decreases an Average of 1.2 Points Annually in BMD Patients Who Have Progressive Disease

The Padova BMD Natural History Study, the most comprehensive study of its kind to date, demonstrates that **NSAA decline is consistent in BMD patients who are already progressing**

- BMD individuals with a baseline NSAA score of 10-32 exhibit an estimated yearly NSAA decline of **-1.22 points**
- The NSAA observations from the Padova group are further validated by a separate Natural History Study from Erik Niks and colleagues who observed a **-2.5 points decline over 2 years**

### Baseline NSAA Score

<table>
<thead>
<tr>
<th>Baseline NSAA Score</th>
<th>Estimated Yearly Change</th>
<th>Standard Error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>33-34</td>
<td>-0.03</td>
<td>0.01</td>
<td>NS</td>
</tr>
<tr>
<td>10-32</td>
<td>-1.22</td>
<td>0.07</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Source: Data on file; Data presented by Luca Bello at MDA (2022); van de Velde NM et. al., Neurology, 2021
To Contextualize the NSAA Scores in BMD, We Looked at Baseline NSAAAs in BMD Adults Enrolled in Edgewise’s Studies

• We asked:
  1. At different NSAA scores, what functions are completely lost?
  2. What functions require some degree of compensation because of weakness?

• While this is a cross-sectional look at function, we know from natural history that patients decline ~1.2 points/year or about 10 points over 8 years
The Majority of BMD Patients Have Progressive Disease and are Either Compensating or Have Complete Loss of Function by NSAA

Group 1
Score: ≥30
Decreasing Function
Can Complete All Functions
Years to Progression
~8

Group 2
Score: 20-29
But Weakness Evident
~5

Group 3
Score: 10-19
Most Cannot Complete Many Functions
~8

Group 4
Score: 0-9
Minimal Ability To Complete Typical Ambulatory Activities

Source: Data on file; Barp et al., Scientific Reports, 2017
Patients Highlight the Impact that Loss of Ambulation Has on Their Daily Living, Often Requiring Significant Planning and Effort

“First thing I did was started walking with a cane... And then gradually –probably 6 years ago– for long distances or if we went somewhere really hilly, I started using a mobility scooter to get around. And then where I worked it was a pretty big building, so I started using that at work... and then recently, I also sometimes use an electric wheelchair.”
– BMD Patient

“There’s a lot of things you gotta consider once you have to start to use mobility devices. You have to consider where you are going, if its accessible, a lot of things you didn’t have to consider before. So that’s probably been the biggest hurdle for me recently... It’s just one of those things you have to just learn to be okay with because sometimes the world is just not built for people that are disabled.”
– BMD Patient

Source: VOZ BMD Patient Research
Topline 12-month Results from the ARCH Open Label BMD Study

Joanne Donovan MD PhD, CMO
ARCH Open-Label Study Design in BMD Patients

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

- Primary objective: Safety and tolerability at 12 months

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

- Enrollment: 12
ARCH Baseline Characteristics: BMD Participants Had Significant Functional Impairment and Decreased Muscle Mass

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BMD Participants (N=12)</th>
<th>Age Normative Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>32.8 (8.1) years</td>
<td></td>
</tr>
<tr>
<td>Functional Measures (median)</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>Serum Creatinine (mean, mg/dL)</td>
<td>0.44</td>
<td>0.92 - 1.16</td>
</tr>
<tr>
<td>Serum CK (mean, U/L)</td>
<td>1,390</td>
<td>&lt;210</td>
</tr>
<tr>
<td>DXA % Lean Mass</td>
<td>54.9%</td>
<td>&gt;75%</td>
</tr>
</tbody>
</table>

Unlike clinical trials for children with DMD, all the BMD patients in ARCH are in the functional decline phase of their disease course.
EDG-5506 was well tolerated at all doses; no dose reductions or adjustments, no treatment discontinuations and no SAEs.

### Number of Participants Reporting an AE

<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>1 (8%)</td>
<td></td>
<td>3 (25%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td></td>
<td>4 (33%)</td>
<td></td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2 (17%)</td>
<td>1 (8%)</td>
<td></td>
<td>3 (25%)</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>3 (25%)</td>
<td></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>2 (17%)</td>
<td></td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
<td></td>
<td>2 (17%)</td>
</tr>
<tr>
<td>GERD</td>
<td></td>
<td>2 (17%)</td>
<td></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 BMD patients*
Muscle Damage in Muscular Dystrophies Leads to Leak of Injury Biomarkers, including CK, TNNI2 and Myoglobin, into the Circulation

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

Circulating Levels of Muscle Injury Biomarkers Can be Measured to Determine Ongoing Muscle Damage in Muscular Dystrophies

Legend: CK, Creatine Kinase; TNNI2, Fast Skeletal Muscle Troponin I; Mb, Myoglobin
EDG-5506 Led to a Sustained Decrease in Biomarkers of Muscle Damage After 12 Months of Dosing

Creatine Kinase

Fast Skeletal Muscle Troponin I (TNNI2)

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)
Biomarkers of Muscle Damage Show Near Maximal Decrease at 2 Months of 10 mg Daily Dosing

Rapid, Significant and Sustained Decreases in Biomarkers of Muscle Damage

Means ± SEM; Source: Data on file
* Fast skeletal muscle troponin I assessed by SOMAscan
NSAA Shows Stabilization and Trend Toward Improvement – Mean +0.4 Improvement Relative to a Predicted -1.2 Point Decline from NHx

Individual NSAA Responses at 12 Months – 75% Remained the Same or Improved

NSAA Change

<table>
<thead>
<tr>
<th>Change in NSAA</th>
<th>10 mg</th>
<th>15 mg</th>
<th>20 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>=0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=+0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=+1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=+2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=+3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Change in NSAA

EDG-5506: Month of Treatment

Means ± 95% CI; Source: data on file

Natural history based on data presented by Luca Bello at MDA (2022) and van de Velde NM et al., Neurology, 2021

Means ± 95% CI; Source: data on file

Natural history based on data presented by Luca Bello at MDA (2022) and van de Velde NM et al., Neurology, 2021
The Observation That After 12 Months 75% of BMD Patient’s NSAA are Either Stable or Improving, Deviates from Natural History

Most BMD patients in ARCH should be declining consistent with their predicted natural history

However, 9 of the 12 BMD patients in ARCH are either stable or improving on their NSAA

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<td>-1.22</td>
<td>0.07</td>
<td>&lt;0.0001</td>
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Source: Data on file; Data presented by Luca Bello at MDA (2022); van de Velde NM et. al., Neurology, 2021
No Decline from Baseline On the Key Secondary Endpoint Measure of 100 Meter Velocity; No Significant Impact on 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)*
Pain is a Significant Hallmark of BMD and Self-Reported Pain Scores Also 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.

“We had some folks come in and tell us that they were experiencing less cramping and generally were feeling better”
– ARCH Investigator
Observed EDG-5506 Clinical Exposures at the 10 mg Dose Cover/Exceed Target Exposures Predicted from Disease Models

- Target muscle concentrations of EDG-5506 in preclinical models of efficacy were 1,000-4,000 ng/g, with a corresponding plasma concentration of 30-90 ng/ml.

- Using muscle biopsy data from the Phase 1 MAD, this equates to approximately 15-70 ng/ml in BMD patients (60x more compound in muscle vs plasma).

Means ± SD; Source: Data on file
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
ARCH Study Continues at 10 mg Dose

- An open-label, single-center study of EDG-5506 to assess the safety and pharmacokinetics of EDG-5506 in adults with BMD
- Primary objective: Safety and tolerability at 12 months
- Key inclusion criteria
  - Ambulatory males aged 18 to 55 years with a dystrophin mutation and a BMD 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

All patients in ARCH reduced to 10 mg dose
Based on the Observations in ARCH, the CANYON Study has been Amended and Now Also Includes a Pivotal Cohort

Old CANYON Design:
- Global multi-center placebo-controlled study of EDG-5506 to assess the safety and effects on biomarkers of EDG-5506 with Becker muscular dystrophy (BMD)
- Population: Adolescent and adult BMD with NSAA 10-32, not on corticosteroids
- Primary Endpoint: CK at 12 months
- Secondary Endpoints: NSAA, 100m timed test, biomarkers of muscle damage and MRI
- Enrollment: 66

Amended CANYON Design (only adult cohorts):
- Eliminated the 20 mg dose cohorts
- Continue the 10 mg dose cohort and change the 15 mg dose cohort to 10 mg
- Primary endpoint of C1/C2 remains CK at 12 months
- Secondary endpoints for C1/C2 include NSAA, 100m timed test, biomarkers of muscle damage and MRI
- Review of the C1/C2 data (n = 32) at 12 months will inform analysis of the GRAND CANYON pivotal cohort

### Old CANYON Design:

**Adult BMD Patients**
- 10 mg PO daily
- 15 mg PO daily
- 20 mg PO daily
- Placebo

**Adolescent BMD Patients**
- 5 mg PO daily
- 12.5 mg PO daily
- Placebo

### Amended CANYON Design:

**Adult BMD Patients**
- C1/C2 Cohorts 10 mg PO daily (12 mos.)
- Placebo
- N=32

**Adolescent BMD Patients**
- Placebo

**GRAND CANYON: PIVOAL Cohort 10 mg PO daily (18 mos.)**
- N=120

- 5 mg PO daily
- 12.5 mg PO daily
- Placebo
The GRAND CANYON Pivotal Cohort, Has Been Designed as a Potentially Registrational Study with NSAA as the Primary Endpoint

- Global multi-center placebo-controlled study of EDG-5506 to assess the efficacy and safety of EDG-5506 with BMD
- Population: Adult BMD with NSAA 5-32, not on corticosteroids
- Primary endpoint: NSAA at 18 months
- Secondary Endpoints: 100 m timed test, biomarkers of muscle damage, MRI
- Enrollment: 120
- Powered at >90% for observing a difference corresponding to the natural history NSAA decline of 1.2 points/year
EDG-5506 Opportunity in BMD

Behrad Derakhshan PhD, CBO
Qual/Quant Research has Shaped Edgewise’s Understanding of the BMD Treatment Landscape and EDG-5506 Opportunity

Identified EDG-5506 Attributes that Informed Clinical Decision Making, Strategic Disease Shaping Initiatives for Optimal Product Positioning and Overall Commercial Opportunity
The Lack of an Approved Therapy Represents the Major Unmet Need and Greatest Frustration for Physicians Managing BMD

Disease Modifying Therapies
- The major unmet need in the BMD space revolves around the lack of disease modifying therapies

Strong Natural History
- Stronger natural history data is important to better predict phenotype and understand disease progression

Adequate Attention
- Physicians suggest that patients may feel that BMD is often overlooked/overshadowed by DMD

Earlier Diagnosis
- Currently the diagnostic process for BMD takes 6-18 months; KOLs indicate that once disease-modifying treatments become available the diagnostic process will be shortened

“Main unmet need is that there is no medical therapy available to preserve muscle function” – Italian KOL

“If I had the resources, I would put effort into getting more natural history data” – US KOL

“Perhaps the BMD families feel that they are not given the same importance as DMD” – UK KOL

“We could still work on the delay in diagnosis and genetic confirmation” – German KOL

Source: Edgewise Therapeutics independent quantitative and qualitative market research (Bluestar BioAdvisors); KOL qualitative interviews; Abbreviations: BMD/DMD, Becker/Duchenne Muscular Dystrophy; KOL, key opinion leader
There are Three Agents in Development for BMD; KOLs Express the Most Excitement about EDG-5506

**BMD Competitive Landscape (Global)**

<table>
<thead>
<tr>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Pivotal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PF1801</td>
<td>Vamorolone</td>
<td>EDG-5506</td>
</tr>
<tr>
<td></td>
<td>(GLP-1 receptor agonist)</td>
<td>(Anti-inflammatory</td>
<td>(Myosin inhibitor)</td>
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<tr>
<td></td>
<td></td>
<td>corticosteroid)</td>
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**KOL Commentary**

- When discussing the development pipeline, most KOLs brought up EDG-5506 unprompted, either by name or by general familiarity with the ‘myosin inhibitor’ story
- KOLs readily discussed their excitement for EDG-5506 and its unique approach to slowing disease progression

"The pipeline is mainly the myosin modulator from Edgewise" – German KOL

"I am aware of the Edgewise product. They have done a Phase 1 study and they are planning a Phase 2 study" – Italian KOL

Source: (1) Bluestar analysis (2) ClinicalTrial.gov (3) PharmaProject (4) TrialTrove (5) Company Website
Physicians Highlight EDG-5506 Has the Potential to Change BMD Disease Progression

MOA

• KOLs believe that modulating type II skeletal myosin is a unique and viable MOA for BMD, noting that the concept of “reducing contraction-induced injury” to muscle fibers is an elegant approach to preserving muscle function

“"We have damage that happens continuously in BMD patients and counteracting that damage is a major mechanism” – US KOL

Efficacy/Endpoints

• The NSAA is currently viewed as the most validated primary endpoint for a registrational trial in BMD due to its validation in DMD
• Disease stabilization as measured by NSAA is considered a clinically meaningful outcome

“Stabilizing disease in these (BMD) patients would be significant” – DK KOL

Safety/ROA

• EDG-5506’s safety/tolerability profile is particularly attractive
• KOLs are quick to point out the attractiveness of a once daily oral tablet

If Approved, Physicians Indicate That They Would Like to Prescribe EDG-5506 to All BMD Patients, Regardless of the Study Population

Source: Edgewise Therapeutics independent quantitative and qualitative market research (Bluestar BioAdvisors); KOL qualitative interviews; Abbreviations: BMD/DMD, Becker/Duchenne Muscular Dystrophy; NSAA, North Star Ambulatory Assessment; MOA, mechanism of action; KOL, key opinion leader; ROA, route of administration
With No Approved Therapies for BMD, EDG-5506 has the Potential to Benefit a Significant Number of BMD Patients

**Epidemiology**

~12,000 BMD Patients in the US, Europe and Japan combined

**Target Population**

Ambulatory patients with **NSAA of 5-32** expected to rapidly decline**

**Expanded Opportunity**

DMD gene therapies create patients **Phenotypically Similar to BMD Patients**

There is Significant Demand for a BMD Therapy

Survey Question:

“How likely would you be to reach out to patients who have been lost to follow-up if Product X (EDG-5506) was approved?”

80% of physicians surveyed will reach out to their BMD patients previously lost to follow-up post-approval of EDG-5506

Combined EDG-5506 Addressable Pool of ~8,500 BMD Patients with High Willingness to Treat Due to Significant Unmet Need; DMD Patients Treated with Gene Therapies Represent Additional Upside

Source: Edgewise Therapeutics independent quantitative and qualitative market research (Bluestar BioAdvisors); KOL qualitative interviews; Romiti PA et al., Pediatrics, 2015; Emery AE, Neuromuscul. Disord., 1991; MD STARnet Data and Statistics; Duchenne muscular dystrophy. National Center for Advancing Translational Sciences; Duan D et al., Nat. Rev. Dis. Primers, 2021

* Evaluate Pharma: Duchenne Muscular Dystrophy Indication overview (2022)

** Luca Bello: 5-year BMD natural history data presented at the 2022 MDA Meeting, van de Valde RM et al., Neurology, 2021
A Concentrated Call Point for BMD (and DMD) Patient Care, Facilitates Access to Patients with a Lean and Focused Sales Force

Most BMD Patients are Managed at a Multidisciplinary Care Center, Such as a Neuromuscular Center of Excellence (COE) Or an Academic Center

- In the U.S., KOLs estimate that <5% of patients are treated in the community
- In Europe and Japan, KOLs do not believe any patients are managed outside of a COE or academic center
- Concentration of care for BMD patients shows significant overlap with DMD care centers allowing the ability to leverage a single sales force

Source: Edgewise Therapeutics independent quantitative and qualitative market research (Bluestar BioAdvisors); KOL qualitative interviews
Strong Execution has Created Multiple Value Generating Milestones in the Next 12-18 Months

<table>
<thead>
<tr>
<th>Event</th>
<th>Timeframe</th>
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<tbody>
<tr>
<td>Initiation of GRAND CANYON Pivotal Cohort in BMD</td>
<td>2H23</td>
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<tr>
<td>Initiation of Phase 1 Trial with EDG-7500</td>
<td>2H23</td>
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<tr>
<td>DMD Phase 2 Three-Month Dose-Ranging Data</td>
<td>2H23</td>
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<tr>
<td>BMD ARCH 24 Month Data</td>
<td>1H24</td>
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<tr>
<td>Phase 2 Exercise Challenge Data in LGMD2i and McArdle</td>
<td>1H24</td>
</tr>
<tr>
<td>CANYON C1/C2 BMD Cohort Data</td>
<td>2H24</td>
</tr>
<tr>
<td>Phase 1 Data with EDG-7500</td>
<td>2H24</td>
</tr>
</tbody>
</table>
Well-Capitalized to Execute Important Value-Driving Milestones Across Both EDG-5506 and EDG-7500

$328M\textsuperscript{(1)}
Cash, Cash Equivalents and Marketable Securities
No Debt

63.3M\textsuperscript{(1)}
Common Shares Outstanding
NASDAQ: EWTX

(1) As of March 31, 2023
Thank You and Questions