Effects of EDG-5506, a Fast Myosin Modulator, on Biomarkers of Muscle Damage and Function in Adults with Becker Muscular Dystrophy (BMD)

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1. Background

Modulation of Fast Myosin Protects against Contraction-induced Muscle Damage
- Fast muscle fibers are disproportionately injured in Duchenne and Becker muscular dystrophy (DMD, BMD)
- In animal models modulation of fast myosin contraction protects against contraction induced injury while preserving function
- EDG-5506 is a selective inhibitor of fast myosin in clinical development for BMD and DMD

Dystrophin connects contractile proteins to the membrane and surrounding matrix
With dystrophin – fibers support each other
No dystrophin – fibers contract without support

1. Background (cont.)

Natural History of BMD: Longitudinal Changes in NSAA

3. Results

Baseline Characteristics: BMD Participants Had Significant Functional Impairment and Decreased Muscle Mass

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BMI Percentile</th>
<th>Age Narrative Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>175.2 cm</td>
<td>1.5</td>
</tr>
<tr>
<td>Functional Measure (median)</td>
<td>24 yrs</td>
<td>4 yrs</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>9 yrs</td>
<td>3 yrs</td>
</tr>
<tr>
<td>Height</td>
<td>165.2 cm</td>
<td></td>
</tr>
<tr>
<td>Scoliosis</td>
<td>0.64</td>
<td>1.92 - 3.95</td>
</tr>
<tr>
<td>Body Mass (mean, kg)</td>
<td>1.86</td>
<td>1.91 - 2.63</td>
</tr>
<tr>
<td>BMI</td>
<td>12.5</td>
<td>11.9 - 13.9</td>
</tr>
</tbody>
</table>

After 6 Months, EDG-5506 Led to a Sustained Decrease in Biomarkers of Muscle Damage

Biomarkers Show Near-Maximal Decrease at 10 mg Dose

EDG-5506 Was Well-Tolerated: No Dose Reductions or Adjustments, No Treatment Discontinuations Due to AE and no SAE

Additional Functional Measures Show Stability

1. Methods

An open-label, single-center study of EDG-5506 to assess the safety and pharmacokinetics (PK) of EDG-5506 in adults with Becker Muscular Dystrophy (BMD)

Primary objective: Safety and tolerability

Key inclusion criteria
- Participants who have completed Study EDG-5506-001 (Phase 1) OR
- All of the following:
  - Ambulatory males aged 18-55 years with a documented dystrophin mutation with a BMD phenotype, not on corticosteroids (who could complete 100 m timed test)

Enrollment: 12, off EDG-5506 < 3 months
Duration up to 24 months

Screening
Biomarkers, NSAA, NSAD, Treadmilk Tests
EDG-5506
10 mg/day for 2 months
EDG-5506
15 mg/day for 4 months
After 6 months all participants dose escalated to 20 mg/day EDG-5506

With EDG-5506 NSAA and NSAD Tended Toward Improvement Relative to Natural History

4. Conclusions

- EDG-5506 was well-tolerated
- Rapid and sustained decreases in multiple biomarkers of muscle injury
- Trends toward functional benefit in NSAA compared with expected decreases based on natural history data
- Results support Phase 2 trials in BMD and DMD, currently recruiting (NCT05291091 and NCT05540860)

Acknowledgements

The authors are grateful to the participants in the trial and their families

Disclaimer

EDG-5506 is an investigational drug that is not approved in any territory.

Han Phan is a consultant for Edgewise. Other authors are employees to Edgewise Therapeutics and may hold stock and/or stock options

Presented at MDA Conference, March 2023, Dallas TX