Preliminary Results from MLB-01-003: An Open Label Phase 2 Study of BBP-418 in Patients with Limb-girdle Muscular Dystrophy Type 2I

March 21, 2023
Forward-looking statements

This presentation contains forward-looking statements. Statements in this presentation may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), which are usually identified by the use of words such as “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “seeks,” “should,” “will,” and variations of such words or similar expressions. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act. These forward-looking statements, including statements relating to the clinical, therapeutic and market potential of our programs and product candidates, including our clinical development program for BBP-418 for the treatment of Limb-girdle Muscular Dystrophy Type 2I (“LGMD2I”), the potential benefits of BBP-418, including achieving a doubling of glycosylated alpha-dystroglycan (αDG) sustained over 15 months and a decrease of greater than 70% in creatine kinase (CK) at 15 months, the reliability of our novel bioassay, including the ability to measure glycosylated αDG levels from muscle biopsy samples, the intent for BBP-418 to be the first disease-modifying therapy for patients with LGMD2I with potential applicability to other α-dystroglycanopathies, and the clinical manifestations of LGMD2I and progression to loss of ambulation, respiratory decline and cardiac myopathy, the timing and success of our clinical development programs, the progress of our ongoing and planned clinical trials of BBP-418 in LGMD2I, including our plans to initiate a Phase 3 trial for BBP-418 in LGMD2I, our planned interactions with regulatory authorities, and the timing of these events, among others, reflect our current views about our plans, intentions, expectations and strategies, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations and strategies as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a number of risks, uncertainties and assumptions, including, but not limited to, initial and ongoing data from our clinical trials not being indicative of final data, the design and success of ongoing and planned clinical trials, difficulties with enrollment in our clinical trials, adverse events that may be encountered in our clinical trials, the United States Food and Drug Administration or other regulatory agencies not agreeing with our regulatory approval strategies, components of our filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted, potential adverse impacts due to the global COVID-19 pandemic such as delays in regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy, the impacts of current macroeconomic and geopolitical events, including changing conditions from the COVID-19 pandemic, hostilities in Ukraine, increasing rates of inflation and rising interest rates, on our overall business operations and expectations, as well as those risks set forth in the Risk Factors section of our Annual Report on Form 10-K for the year ended December 31, 2022 and our other filings with the U.S. Securities and Exchange Commission. Moreover, we operate in a very competitive and rapidly changing environment in which new risks emerge from time to time. These forward-looking statements are based upon the current expectations and beliefs of our management as of the date of this presentation and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Except as required by applicable law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.
To the children, families, advocates, and physicians who have been a part of this program:

Thank you

Developing new treatment options relies entirely on your guidance, dedication, and effort.
LGMD2I is a progressive neuromuscular disease with high unmet need

9k treatable patient population

Estimated US & Europe prevalence

- LGMD2I is an inherited neuromuscular disorder characterized by lower-limb weakness and loss of ambulation
- No approved disease modifying agents for LGMD2I
- Current standard of care is aimed at symptom management and includes physical therapy, steroids and pain management
- Standard of care does not prevent continuous progressive decline in LGMD2I patients

Unmet need

Source: 1Liu, et al. Genetics in Medicine. 2019. 2Includes all patients with potentially treatable mutations in FKRP, FKTN and ISPD 3Japan only.
We are developing BBP-418 as a treatment option for patients with LGMD2I based on three key principles:

**Objectives**

- **Provide first disease-modifying therapy**
  For patients with LGMD2I and potentially applicable other α-dystroglycanopathies

- **Avoid safety concerns with modulating FKRP expression**
  Avoid off-target effects

- **Convenient oral medicine**
  To reduce burden for patients

**Design principles**

- Target the condition directly at the source
- Naturally occurring compound with encouraging safety profile
- Provide an oral treatment option

BBP-418 is the only treatment option in development for LGMD2I that could incorporate all of these features.
Program context

ATTR-CM
Idea $58M

Achondroplasia and related conditions
Idea $75M

ADH1
Idea $31M

LGMD2I
Idea $38M

CAH
Idea $68M

Phase 3

Note: Costs represent total BBIO investment from inception to POC/P3 Initiation. CAH POC expected in 2H 2023
Jeffrey Rosenfeld, M.D., Ph.D.

Neurology, Neuromuscular Medicine, Loma Linda University School of Medicine
History of LGMD diagnosis and treatment

LGMD treated as a syndrome characterized by similar features

Genetic testing identifies many distinct diseases with different genetic causes

LGMD2I caused by mutations in FKRP transformed diagnosis
Holds the promise of targeted therapies

Today, there are >30 forms of LGMD*

First mutations in Calpain 3 and Myot identified*
LGMD2I a progressive neuromuscular disease with high unmet need

### Disease overview

<table>
<thead>
<tr>
<th>7k</th>
<th>Prevalence (US &amp; EU)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>L276I</td>
<td>Most common LGMD2I mutation</td>
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</tbody>
</table>

### Early childhood

Symptom onset

### Clinical manifestations

- **Loss of ambulation:** beginning as early as late teens
- **Respiratory decline:** invasive assistance potentially required by early 30s
- **Cardiac dysfunction:** up to 60%

- No approved disease modifying agents for LGMD2I
- Current standard of care is aimed at symptom management and includes physical therapy, steroids and pain management
- Standard of care does not prevent continuous progressive decline in LGMD2I patients

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¹Includes potential treatable mutations in LGMD

LGMD2I is caused by mutations in FKRP and characterized by an established genotype/phenotype association

<table>
<thead>
<tr>
<th>Birth</th>
<th>Early Childhood</th>
<th>Late Childhood</th>
<th>Adolescence to adulthood</th>
</tr>
</thead>
<tbody>
<tr>
<td>L276I Homozygotes</td>
<td>Asymptomatic</td>
<td>Age of symptom onset 18 ± 3 years old</td>
<td>Loss of ambulation: 25% by age 40</td>
</tr>
<tr>
<td></td>
<td>Asymptomatic</td>
<td>Lower limb &amp; proximal weakness</td>
<td>Respiratory decline: Non-invasive assistance required by 10% by age 40 and invasive assistance required by &lt;1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+/-calf hypertrophy, muscle pain, hyper-CKemia</td>
<td>Cardiac dysfunction: ~30%</td>
</tr>
<tr>
<td>Other FKRP genotypes</td>
<td>Asymptomatic</td>
<td>Age of symptom onset 5 ± 1 years old</td>
<td>Loss of ambulation: most by age 20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower limb &amp; proximal weakness</td>
<td>Respiratory decline: Invasive assistance required by 5% by age 30</td>
</tr>
<tr>
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<td>Cardiac dysfunction: ~60%</td>
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While current treatments for LGMD2I are purely supportive, BBP-418 has potential to be the first disease-modifying treatment available.

Executive Summary

LGMD2I pathology
Genetically defined disease caused by FKRP mutation
Dysfunctional FKRP results in hypo-glycosylated αDG

Surrogate endpoint
Developed novel, validated assay to quantify αDG
Direct measure of disease and its severity

Natural History
Glycosylated αDG levels are consistent with genotype
Patients exhibit clinical progression over 12 months

Phase 2
Improvement in surrogate endpoint and clinical measures after 15 months of BBP-418 treatment
Oral BBP-418 is under investigation as an upstream substrate supplement to drive residual activity of mutant FKRP in LGMD2I, targeting the disease at its source.

**LGMD2I Disease Mechanism**

- Functional FKRP fully glycosylates alpha-dystroglycan (αDG) which stabilizes myocytes by binding extracellular ligands to act as a “shock absorber” for muscle fibers.
- Partial loss of function mutation in FKRP results in dysfunctional, hypo-glycosylated αDG in myocytes which increases susceptibility to damage.

**BBP-418 Therapeutic Approach**

- Supply supraphysiological levels of ribitol upstream to drive residual activity of mutant FKRP enzyme and increase αDG glycosylation levels.
- Orally-administered BBP-418 (exogenous ribitol).

Mutations in FKRP prevent addition of ribitol-5-P to alpha-dystroglycan (hypo-glycosylated αDG) limiting αDG’s ability to function as a “shock absorber” for muscle fibers.
ML Bio has developed a novel, validated glycosylated αDG assay that can quantify differences associated with FKRP status and BBP-418 treatment.

**Novel Western Blot**
- Validated for use in clinic
- Quantification of αDG in TA muscle
- Sensitive, specific and robust

**Quantification**

Example: Standard curve allows for interpolation of αDG and calculation of % of normal

- 700nm channel
- 800nm channel

**Robustness: Performance of Positive control**

<table>
<thead>
<tr>
<th>αDG-Glycan %CV</th>
<th>Natural History</th>
<th>Phase 2</th>
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<tbody>
<tr>
<td>~15</td>
<td></td>
<td>~18</td>
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Interpolation of healthy control (10µg healthy TA lysate) to the standard curve was used as a performance measure to assess assay robustness. %CV across all blots in each study was under 20%
We have developed a reliable method to monitor glycosylation of αDG and assess the efficacy of new therapies for LGMD2I.

Example Western blot showing clear treatment effect with BBP-418

Assay can detect levels of glycosylated αDG (yellow band) in patient samples and increases with BBP-418 treatment.

Very little glycosylated αDG is seen in untreated LGMD2I patient muscle biopsy samples at baseline (shown in duplicate).

With BBP-418 treatment, an increase in the glycosylated αDG is seen.

1Blots have been reordered to allow for side-by-side comparison of treatment effect within a patient.
We have completed two LGMD2I patient studies and are about to start our Phase 3

<table>
<thead>
<tr>
<th>Study</th>
<th>Phase</th>
<th>Description</th>
<th>Key Takeaways</th>
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</table>
| MLB-01-001  | Natural History (N=101) | - Large natural history study to define LGMD2I phenotypes  
- Validate muscle biomarker for LGMD2I to support therapeutic development | - Defined disease trajectory over ~1 year  
- Muscle biomarker reflects genotype/phenotype |
| MLB-01-003  | Phase 2 (N=14) | - Open label, dose-finding study to evaluate safety and tolerability of BBP-418 in LGMD2I                                                                                                                                 | - Encouraging safety profile in LGMD2I patients  
- Bioassay data suggest BBP-418 is improving disease at the molecular level  
- Early evidence of clinical efficacy |
| MLB-01-005  | Phase 3 (N=80–100) | - Placebo-controlled study to evaluate efficacy and safety of BBP-418 in LGMD2I                                                                                                                                 | - Evaluate clinical efficacy & long-term safety |
In the LGMD2I natural history conducted, glycosylation of αDG reflects disease severity

Reduced αDG glycosylation in other FKRP genotypes vs. L276I/L276I homozygous LGMD2I patients

Patient samples were interpolated to standard curve to determine % of normal glycosylation of αDG; lines show medians; figure includes all patients with biopsies in MLB-01-001

Other FKRP genotypes with earlier onset and loss of ambulation

L276I Homozygotes (L276I/L276I)

- Loss of ambulation: 25% by age 40
- Respiratory decline: Non-invasive assistance required by 10% by age 40 and invasive assistance required by <1%
- Cardiac dysfunction: ~30%

Other FKRP genotypes (L276I/ non-L276I) (non-L276I/ non-L276I)

- Loss of ambulation: most by age 20
- Respiratory decline: Invasive assistance required by 5% by age 30
- Cardiac dysfunction: ~60%
1. **BBP-418 is being investigated in an open label Phase 2 Study**

### Key Endpoints
- NSAD
- 10-meter walk test/100-meter timed test
- FVC
- PUL2.0
- Glycosylated αDG levels
- Serum creatine kinase

### Key inclusion criteria
- Age between 12-55 years at enrollment
- Genetically confirmed LGMD2I
- Body weight >30kg
- Able to complete 10MWT ≤12 seconds unaided (moderate disease) or unable to (severe disease)

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**Dose escalation**
- 90 days (N=14)

**Maximum dose**
- 90 days (N=14)

**Long-term extension**
- 24 months

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**After Part 1, all patients transitioned to highest dose 12g BID**

- **Cohort 1**
  - 6g QD n=4
  - 12g BID n=4

- **Cohort 2**
  - 6g BID n=4
  - 12g BID n=4

- **Cohort 3**
  - 12g BID n=6
  - 12g BID n=6
BBP-418 has been well tolerated, with only minor GI related adverse events recorded in the Phase 2 study

- 14 of 136 adverse events (AEs) in the study were recorded as possibly or probably related to BBP-418 treatment
- 14 possibly/probably related AEs include: diarrhea, dehydration, nausea, vomiting, dyspepsia, gastroenteritis, and headaches
- No discontinuations or interruptions in therapy
- 3 severe adverse events related to underlying disease recorded; all deemed unrelated to the treatment

<table>
<thead>
<tr>
<th>TEAE</th>
<th># of incidents</th>
<th>Severity</th>
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<tbody>
<tr>
<td>Diarrhea*</td>
<td>6</td>
<td>25% Grade 2, 75% Grade 1</td>
</tr>
<tr>
<td>Dehydration</td>
<td>1</td>
<td>100% Grade 1</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>100% Grade 1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>100% Grade 1</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>1</td>
<td>100% Grade 1</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>1</td>
<td>100% Grade 2</td>
</tr>
<tr>
<td>Headaches</td>
<td>1</td>
<td>100% Grade 2</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>14</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Includes diarrhea and diarrhea intermittent
BBP-418 demonstrated sustained increases in levels of glycosylated αDG and sustained decreases in CK over time

**Increase in glycosylated αDG post treatment with BBP-418 (median ± 95% CI)**

- **L276l/L276l homozygous**
  - Median (%): 16.5, 39.4, 39.7, 44.3
  - N: 8, 8, 8, 6

- **Other FKRP genotypes**
  - Median (%): 5.9, 9.5, 10.4, 25.7
  - N: 6, 5, 6, 1

- **Doubling of αDG levels with BBP-418 treatment**

**Reduction in mean serum creatine kinase (CK) post treatment with BBP-418**

- **Serum CK (U/L)**
  - Reference range: 55–170 units/L for men and 30–135 units/L for women
  - Reduction of ≥75% from baseline

- **Cohort 1 Day 1 CK draws taken after functional assessments; all other draws done prior to functional assessment**
- After Day 90, all subjects received 12 g BID (weight-adjusted)

+ 3 mo = Part 1, 90-day, +6 mo = Part 2, Month 3, + 9 mo = Part 3, Month 9

Reference range for CK is 55–170 units/L for men and 30–135 units/L for women, figure shows reference range from 30–170 units/L

Patient samples were interpolated to standard curve to determine % of normal glycosylation of αDG

Wilcoxon test was used to determine significance
Improvement in ambulatory and clinical measures observed after 15 months of treatment with BBP-418

Change from baseline in 10MWT (m/s)  
Change from baseline in 100MTT (s)  
Change from baseline in NSAD

Blue lines denote natural history data and red lines denote on-treatment data collected during the Phase 2 study. Green arrows indicate direction of improvement.

Data exclude 1 subject from month 15 timepoint due to post-COVID decline. Phase 2 data: 6 months = Part 2, Month 3, 9 months = Part 3, Month 3, 15 months = Part 3, Month 9
ML Bio Solutions is initiating a Phase 3 study of BBP-418 in LGMD2I targeting an FPI in mid Q3 2023

A Phase 3 Randomized, Placebo-controlled, Double-blind Study to Evaluate the Efficacy and Safety of BBP-418 (ribitol) in Patients with Limb Girdle Muscular Dystrophy 2I (LGMD2I)

**Key Enrollment Criteria**
- Genetically confirmed, symptomatic LGMD2I/R9
- 12 to 60 years of age

**Interim endpoints**
- Glycosylated αDG
- Clinical endpoints at 12 months

**Final analysis endpoints**
- NSAD
- Glycosylated αDG
- Serum CK
- 100-meter timed test (s)
- 10-meter walk test (m/s)
- Pulmonary function (FVC)
- PUL 2.0

We are discussing a strategy for accelerated approval with the regulatory agencies and will disclose more in the future.