European LGMDR9 Community Conference

SATURDAY 25TH MAY 2024

Overview of FORTIFY: Phase 3 study of BBP-418 by ML Bio Solutions

Professor John Vissing

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The John Walton Muscular Dystrophy Research Centre

Newcastle University

The Newcastle upon Tyne Hospitals NHS Foundation Trust

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ML Bio is developing BBP-418 as a potential treatment option for patients with Limb Girdle Muscular Dystrophy 2I (LGMD2I/R9)

May 25, 2024

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- Dr. John Vissing has the following relationships to disclose:
- Dr. Vissing is not an employee of ML Bio Solutions
  - Dr. Vissing is an investigator in ML Bio Solutions' Phase 3 FORTIFY study.
  - Dr. Vissing is or has been a consultant for:
    - ML Bio Solutions, Amicus Therapeutics, Argenx BVBA, Arvinas, Atamyo Therapeutics, Biogen, Dyne Therapeutics, Fulcrum Therapeutics, Horizon Therapeutics, Lupin, Regeneron, Roche, Sanofi Genzyme, Sarepta Therapeutics, and UCB Biopharma SPRL, and has received research grants, travel support, and/or speaker fees from Alexion, AstraZeneca Rare Disease, Edgewise Therapeutics, Fulcrum Therapeutics, Horizon Therapeutics, Sanofi Genzyme, and UCB Biopharma SPRL.

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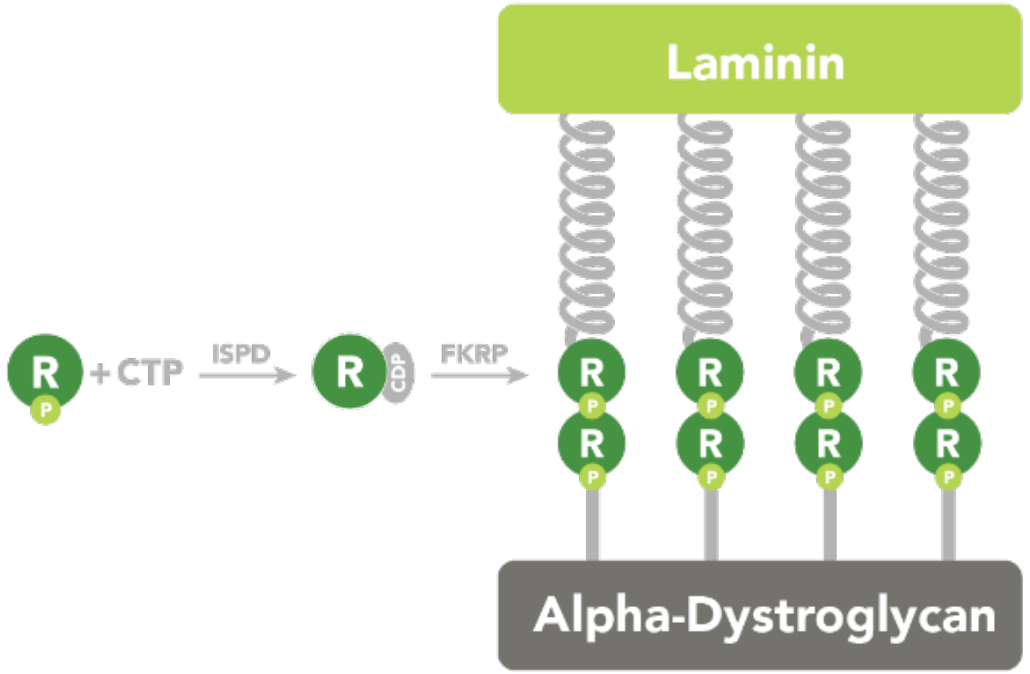
- BBP-418 is an investigational agent that is not approved for use for any indication by any regulatory authority as its efficacy and safety have not been established.

Fukutin-Related Protein (FKRP) plays a critical role in priming alpha-dystroglycan (αDG) for glycosylation

- In healthy muscles, the fukutin-related protein (**FKRP**) enzyme is responsible for an important step in a process called **glycosylation.**
- During glycosylation, sugar chains attach to the backbone of a protein called α-dystroglycan (αDG).
- Glycosylation is critical for the normal function of αDG. Once glycosylated, αDG stabilizes muscle cells by acting as a **“shock absorber”** for muscle fibers during contractions.

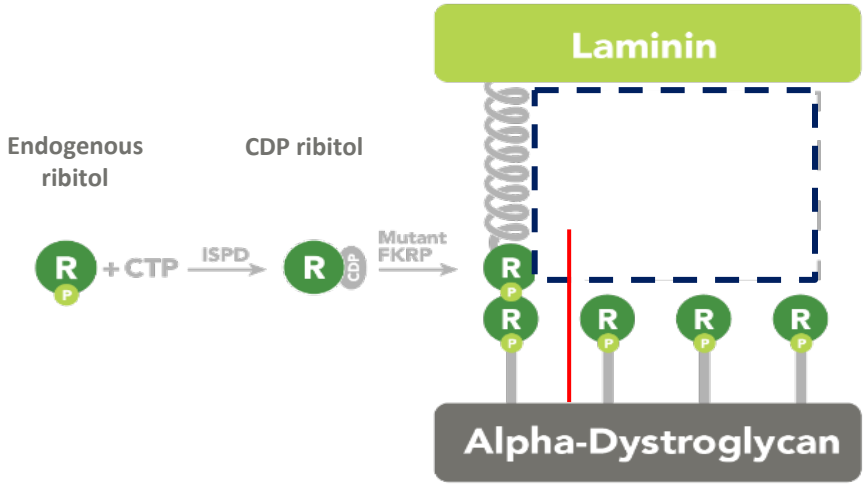


In LGMD2I/R9, the FKRP enzyme does not work properly, which leads to reduced levels of glycosylated αDG

LGMD2I/R9 Disease Mechanism

Functional FKRP 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

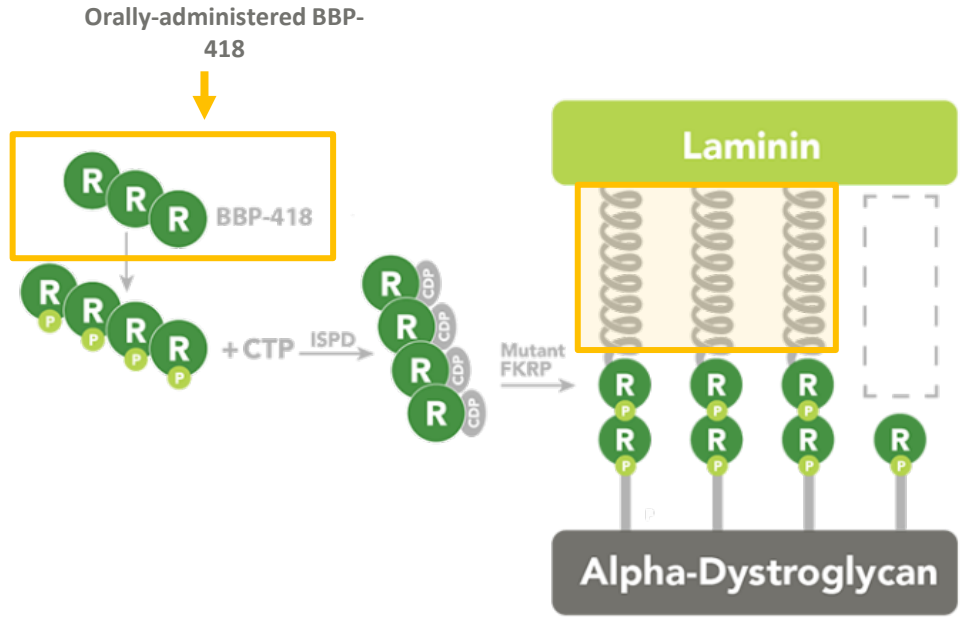


Mutations in FKRP prevent addition of ribitol-5-P to alpha-dystroglycan (hypo-glycosylated αDG) limiting αDG's ability to function as a "shock absorber" for muscle fibers

Substrate supplementation with BBP-418* has potential to help the defective FKRP enzyme work well enough to glycosylate αDG in LGMD2I/R9

Proposed BBP-418 Therapeutic Approach

Supply supraphysiological levels of synthesized pharmaceutical substrate upstream aiming to drive residual activity of mutant FKRP enzyme and increase αDG glycosylation levels



Potential partial restoration of αDG glycosylation

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ML Bio is developing BBP-418* as a potential treatment option for individuals with LGMD2I/R9 based on three key design principles

Objectives	Design principles
✓ **Provide small molecule potentially disease-modifying therapy** For individuals with LGMD2I/R9	**Targets root cause of disease (impaired glycosylation of αDG)**
✓ **Harnesses existing FKRP function** Avoid potential for overexpression of FKRP	**Pharmaceutical version of a naturally occurring compound with encouraging preliminary safety profile**
✓ **Convenient daily-dose oral medicine** To reduce burden for patients	**Provide an oral treatment option**

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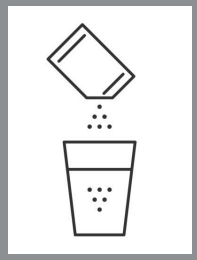
Overview of BBP-418*

BBP-418

BBP-418 is being developed as a substrate supplementation therapy, **designed to treat LGMD2I/R9 at its source***

BBP-418 is provided in the form of granules that are dissolved in water for **convenient oral dosing** twice daily



BBP-418 has been well-tolerated to date; there have been no dose limiting toxicities, discontinuations, or serious adverse events related to BBP-418 observed

Early clinical studies in a limited number of individuals with LGMD2I/R9 dosed with BBP-418 show **encouraging biomarker results** and **positive trends in functional outcomes**

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ML Bio Solutions has investigated BBP-418* in multiple studies; A multi-site, international Phase 3 study is ongoing

Study	Phase	Description	Summary & Links to More Information***
MLB-01-002,-004	Phase 1 (N= 109)	▪ Two Phase 1 studies in volunteers unaffected by LGMD2I/R9 to evaluate safety and pharmacokinetics** of BBP-418	▪ No serious adverse events or discontinuations due to adverse events related to BBP-418 in healthy volunteers ▪ Pharmacokinetics of BBP-418 with and without food defined
MLB-01-003	Phase 2 (N=14)	▪ Open label, dose-finding study to evaluate safety and tolerability of BBP-418 in LGMD2I/R9 ▪ Encouraging safety and preliminary clinical data in LGMD2I/R9 patients	• Link to Phase 2 results presented at MDA 2023 →
MLB-01-005 Fortify	Phase 3 (N=80–100)	▪ Placebo-controlled study to evaluate efficacy and safety of BBP-418 in LGMD2I/R9 ▪ Goal to evaluate clinical efficacy & long-term safety	▪ Link to Phase 3 clinicaltrials.gov website →

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**Pharmacokinetics is the study of how the body interacts with an administered substance for the duration of exposure.
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The FORTIFY Phase 3 study of BBP-418 in LGMD2I/R9 is open to enrollment

The study, known as *Fortify, will evaluate the safety and efficacy of long-term administration of BBP-418 in individuals with genetically confirmed LGMD2I/R9.

Key study details:

- 80–100 individuals with confirmed LGMD2I/R9, aged 12 to 60 years in US, UK and Australia and aged 18 to 60 years in EU
- Multi-center international study
- Double-blind randomized placebo-controlled trial
- 36-month blinded interval

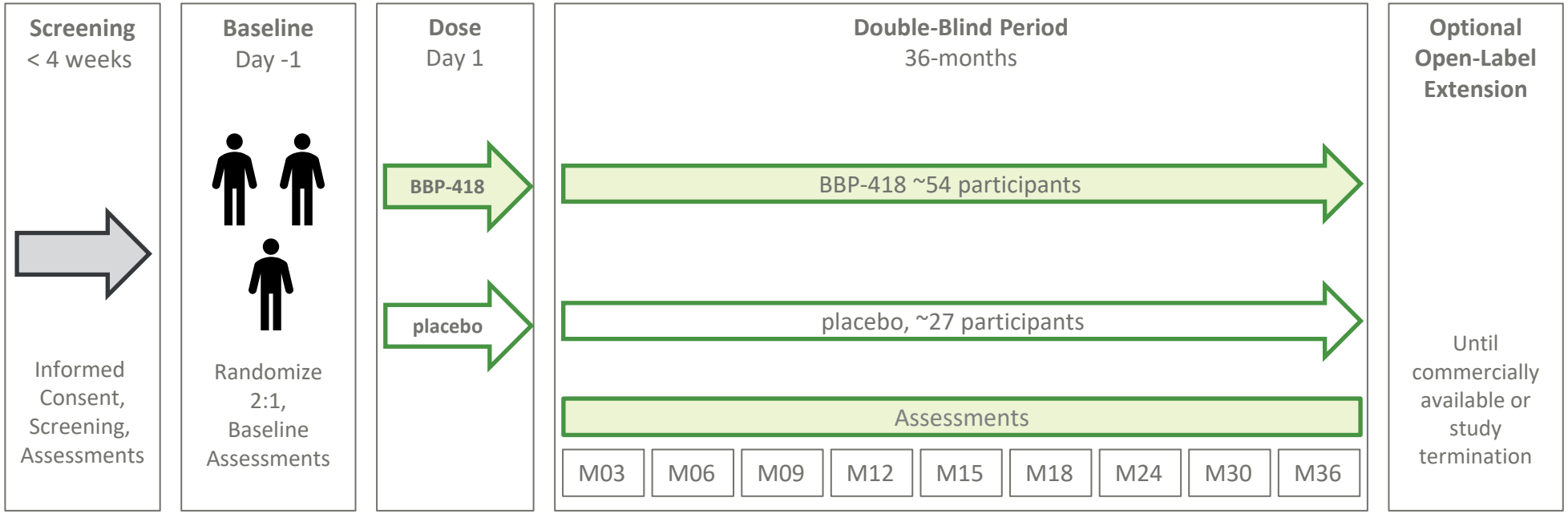
Participants may be offered the opportunity to enroll in a separate open-label extension (OLE) with access to BBP-418 upon successful completion of the Phase 3 study.

Key Endpoints:

- NSAD (primary)
- 100-meter timed test (s)
- 10-meter walk test (m/s)
- biomarkers:
  - glycosylated αDG
  - serum CK
- pulmonary function (FVC)
- PUL 2.0

*ClinicalTrials.gov Identifier: NCT05775848

Overview of the design of ML Bio's Phase 3 FORTIFY study



- During **screening**, a determination is made if participants meet the requirements of the study.
- Participants will be randomly assigned to 2 groups with 2 out of every 3 participants randomized to the investigational drug BBP-418 and 1 out of every 3 participants randomized to placebo. Doctors and participants will not know if they are receiving BBP-418 or placebo.
- **Double blind** means that neither participants nor study investigators know which participants are taking BBP-418 or placebo.
- Participants dosed with BBP-418 or placebo for 36-months with assessments, including biopsies, throughout.

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ML Bio is dedicated to individuals living with LGMD2I/R9

For more information, please visit our website:

https://mlbiosolutions.com/

Or, email us: info@mlbio solutions.com

ML Bio would like to thank all of the patients and their families who have been a part of our clinical studies or supported us in other ways. We would also like to thank our patient advocacy partners for their collaboration and support.

WITH THANKS


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