Interim analysis from the ongoing Phase 3 FORTIFY study of BBP-418 for individuals living with LGMD2I/R9 (FKRP-related) suggests benefit across functional and cardiac endpoints

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Oral presentation **21O**. Session: Clinical trial updates.
Saturday, October 3, 2026. 07:30–09:00

WMS2026 HIROSHIMA
The 31st Annual Congress of the World Muscle Society
29 September - 3 October 2026, Hiroshima, Japan

Disclosures

Katherine D. Mathews: Receives research funding from the Centers for Disease Control and Prevention, the Muscular Dystrophy Association (MDA), and the Paul D. Wellstone Muscular Dystrophy Cooperative Research Center grant (P50NS053672); Advisory board member for the Facioscapulohumeral Muscular Dystrophy (FSHD) Society and the Muscular Dystrophy Association (MDA); has served on advisory boards for AskBio, BridgeBio Pharma, Inc., Edgewise Therapeutics, ML Bio Solutions Inc., and Sarepta Therapeutics; and on safety monitoring boards for Dyne Therapeutics and Sarepta. Receives or has recently received clinical trial funding from AMO, AskBio, Biohaven, BridgeBio Pharma, Inc., Capricor Therapeutics, Inc., FibroGen (now Kyntra Bio), Italfarmaco, ML Bio Solutions Inc., Novartis, Pfizer, PTC Therapeutics, Reata, Sarepta Therapeutics, and Scholar Rock

Tahseen Mozaffar: Advisory roles with AbbVie, Alexion, Amicus Therapeutics, AnnJi, argenx, Arvinas, Audentes, Cabaletta Bio, Maze Therapeutics, Momenta, Ra Pharmaceuticals, Sanofi Genzyme, Sarepta Therapeutics, Spark Therapeutics, and UCB; speakers' bureau for Sanofi-Genzyme. Medical advisory boards: Myositis Association, Neuromuscular Disease Foundation, Myasthenia Gravis Foundation of California, Myasthenia Gravis Foundation of America. Research funding from the Muscular Dystrophy Association, the Myositis Association, the NIH, and from Alexion, Amicus Therapeutics, AnnJi, argenx, Audentes, Bristol Myers Squibb, Cabaletta, Cartesian Therapeutics, Grifols, Momenta, Ra Pharmaceuticals, Sanofi Genzyme, Spark Therapeutics, UCB, and Valerion. Serves on data safety monitoring boards for Acceleron, Applied Therapeutics, the NIH, and Sarepta Therapeutics

Volker Straub: Received speaker honoraria from Italfarmaco, Pfizer, Roche, and Sarepta Therapeutics, consultancy fees for scientific advice and meeting contributions from Astellas Gene Therapies, Asklepios BioPharmaceutical/Bayer, Cure Rare Disease, Edgewise Therapeutics, Entrada Therapeutics, Genethon, Ipsen Biopharmaceuticals, Kinea Bio, KOLON Therapeutics, ML Bio Solutions Inc., NHS Pharma, Pfizer, Roche, Sanofi, Sarepta Therapeutics, Solid Biosciences, and Uniphar Pharma, and research funding from Sanofi and Sarepta Therapeutics

Robert D. Henderson: No conflicts of interest to disclose

Douglas Sproule, Ada Lee, Amy Rainey, David Paul, Damon Bass, Tricia Blankenbiller, Uma Sinha: Employees of BridgeBio Pharma, Inc. and ML Bio Solutions Inc. at the time of this analysis and may hold stock in the company

John Vissing: Consultant on advisory boards or speaker honoraria from Amgen, Amicus, argenx BVBA, AskBio, Atamyo, Avidity Biosciences, Benitec Biopharma, Biogen, BridgeBio Pharma, Inc., Dyne Therapeutics, Edgewise Therapeutics, Entrada Therapeutics, Fulcrum Therapeutics, Hansa Biopharma, Italfarmaco, Johnson & Johnson, Lundbeck, Lupin Atlantis Holdings SA, ML Bio Solutions Inc., Novartis, Regeneron, Roche, Sanofi Genzyme, Santhera, Sarepta Therapeutics, Solid Biosciences, and UCB Biopharma SPRL

Acknowledgements: The authors would like to thank Bo Chao and Michael Yi for their contributions to this analysis

The FORTIFY clinical trial (NCT05775848) was funded by BridgeBio Pharma, Inc.

Medical writing support was provided by Ashfield MedComms, an Inizio company, and was funded by BridgeBio Pharma, Inc.

LGMD2I/R9 (FKRP-related) is a type of muscular dystrophy that results in progressive muscle weakness, including cardiac and respiratory dysfunction

Physical manifestations of LGMD2I/R9[1–7]

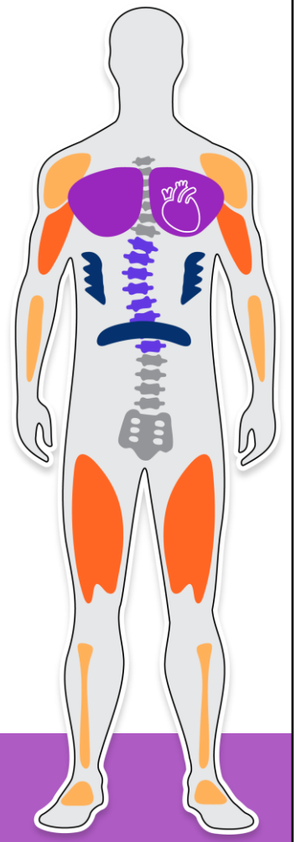
Proximal muscle weakness[2,3]

Other muscle-related symptoms[4,5]

Cardiac complications[6]

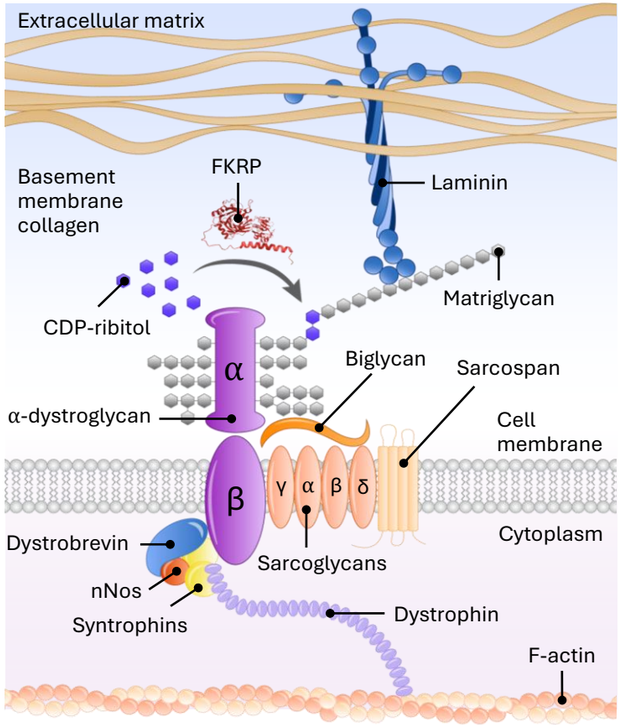
Respiratory impairment[4,7]

Skeletal deformities[4]

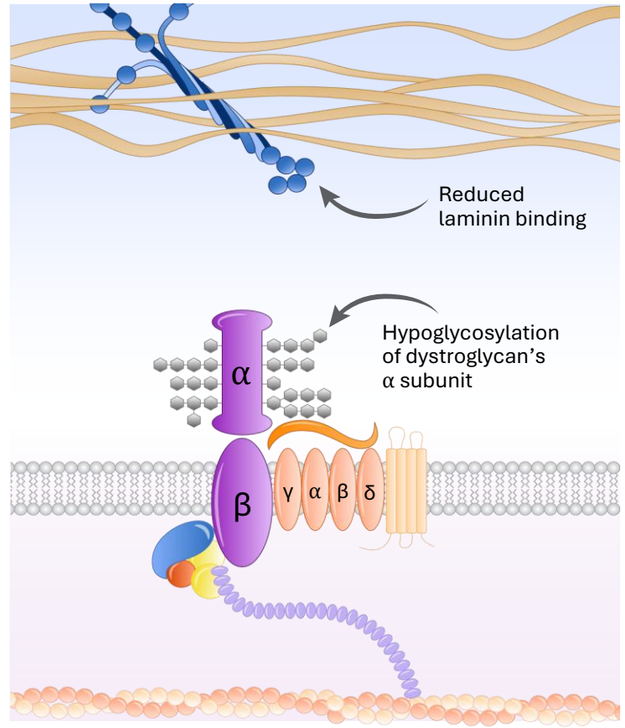


Because treatment is limited to supportive care, **patients with LGMD2I/R9 urgently need therapies** that slow or stop the progression of their disease[8,9]

Molecular Pathogenesis of LGMD2I/R9[10–12]



In **healthy muscle cells**, glycosylated αDG links the muscle cell membrane to the extracellular matrix via laminin[10]



In **affected muscle cells**, hypoglycosylation of αDG results in loss of αDG-laminin binding[10]

Images adapted from Nickolls AR, Bönnemann CG. *Dis Model Mech.* 2018. FKRP structure adapted from Kuwabara N, et al. *Nat Commun*. 2020.[10,11]

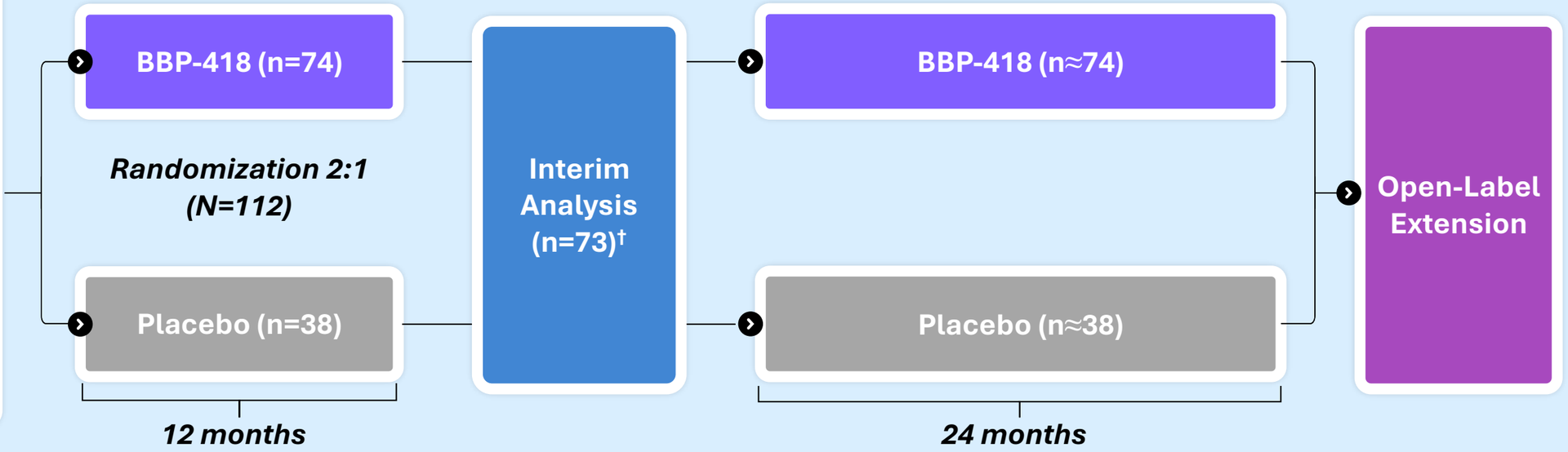
αDG=alpha-dystroglycan; CDP=cytidine diphosphate; FKRP=fukutin-related protein; LGMD2I/R9=limb-girdle muscular dystrophy type 2I/R9; nNos=neuronal nitric oxide synthase.

1. Straub V et al. *Neuromusc Dis*. 2018;28(8):702-710. doi:10.1016/j.nmd.2018.05.007 2. Audhya IF et al. *J Neuromuscul Dis*. 2022;9(4):477-492. doi:10.3233/JND-210771 3. Coffey LN et al. *Neuromuscul Disord*. 2021;31(12):1235-1240. doi:10.1016/j.nmd.2021.08.013 4. Narayanaswami P et al. *Neurology*. 2014;83(16):1453-1463. doi:10.1212/WNL.0000000000000892 5. Willis E et al. *Child Neurol Open*. 2022;9:2329048X221097518. doi:10.1177/2329048X221097518 6. Libell EM et al. *Muscle Nerve*. 2020;62(5):626-632. doi:10.1002/mus.27052 7. Lo Mauro A, Aliverti A. *Breathe (Sheff)*. 2016;12(4):318-327. doi:10.1183/20734735.012716. 8. Data on file. BridgeBio Pharma, Inc.; 2025. 9. Wicklund MP et al. *Neurol Clin Pract*. 2025;15(5):e200496. doi: 10.1212/CPJ.0000000000200496 10. Nickolls AR, Bönnemann CG. *Dis Model Mech.* 2018;11(12):dmm035931. doi:10.1242/dmm.035931 11. Kuwabara N et al. *Nat Commun*. 2020;11(1):303. doi:10.1038/s41467-019-14220-z 12. Jensen SM et al. *J Neuromuscul Dis*. 2024;11(1):59-74. doi:10.3233/JND-221629.

FORTIFY (NCT05775848) is an ongoing randomized, placebo-controlled Phase 3 study with a prespecified interim analysis[1,2]

Enrollment Criteria:

- Genetically confirmed, symptomatic LGMD2I/R9 (FKRP-related)
- Aged 12–60 years*
- Ambulatory and nonambulatory individuals
- Body weight >30 kg
- No evidence of clinically significant concomitant disease



Interim Endpoints:

- Glycosylated αDG‡ (*primary*)
- Serum creatine kinase (CK)
- Ambulatory measure:
  - 100-meter timed test (100MTT)
- Pulmonary function:
  - Forced vital capacity (FVC)

Final Analysis Endpoints:

- North Star Assessment for Limb Girdle-type Dystrophies (NSAD; *primary, 36 months*)
- Ambulatory measures:
  - 10-meter walk test (10MWT)
  - 100MTT
- Pulmonary function: FVC
- Upper limb function: Performance of Upper Limb Scale 2.0 (PUL 2.0)
- Quality of life (QoL) measures

Placebo and BBP-418 arms were stratified by age group (adult vs pediatric), ambulatory status, and genotype (L276I homozygous vs other *FKRP* genotype)

*Phase 3 trial population limited to age 18–60 years in the European Union (EU) region. †72 patients completed the month 12 visit, and 1 patient that discontinued completed an end-of-study visit that windowed into month 12. ‡Percent of control is glycosylated αDG levels relative to a control reference standard from a healthy donor.
αDG=alpha-dystroglycan; FKRP=fukutin-related protein; LGMD2I/R9= limb-girdle muscular dystrophy type 2I/R9.
1. ClinicalTrials.gov identifier: NCT05775848. Updated September 9, 2025. Accessed February 22, 2026. https://clinicaltrials.gov/study/NCT05775848/. 2. Mathews K et al. Presentation at: Muscular Dystrophy Association Conference; March 11, 2026; Orlando, USA.

Demographics in the FORTIFY Phase 3 study were mostly well balanced between BBP-418 and placebo arms

Demographics*	BBP-418 (n=74)	Placebo (n=38)
Age, mean (SD), years	37.1 (14.2)	33.3 (14.0)
12 to <18, n (%)	10 (13.5)	5 (13.2)
18 to 60, n (%)	64 (86.5)	33 (86.8)
Sex, n (%)		
Male	39 (52.7)	14 (36.8)
Female	35 (47.3)	24 (63.2)
Race, n (%)		
White	73 (98.6)	35 (92.1)
Ethnicity, n (%)		
Hispanic	3 (4.1)	2 (5.3)
Not Hispanic	71 (95.9)	36 (94.7)
Variant status, n (%)		
L276I homozygous	55 (74.3)	28 (73.7)
Other *FKRP* genotype	19 (25.7)	10 (26.3)

*The Full Analysis Set consists of randomized participants who had at least one efficacy assessment postrandomization.
FKRP=fukutin-related protein.
Mathews K et al. Presentation at: Muscular Dystrophy Association Conference; March 11, 2026; Orlando, USA. 2. Data on file. BridgeBio Pharma, Inc.; 2026.

Baseline characteristics in the FORTIFY Phase 3 study were mostly well balanced between BBP-418 and placebo arms

Baseline Characteristics[1]	BBP-418	Placebo
Glycosylated αDG (% of control)*		
Mean (SD)	22.71 (16.61)	20.66 (14.67)
Randomized patients (Full analysis set†)	n=73	n=38
Serum CK (U/L)		
Mean (SD)	2449.5 (3014.4)	2099.5 (1832.7)
NSAD ≥3 (Primary efficacy set‡)	n=67	n=36
100MTT (m/s)		
Mean (SD)	1.33 (0.82)	1.37 (0.80)
Ambulatory patients (Secondary efficacy set§)	n=62	n=32
FVC (% predicted, sitting position)		
Mean (SD)	77.95 (16.94)	77.17 (16.40)
Ambulatory patients (Secondary efficacy set§)	n=59	n=33
HS-troponin I (ng/L)[2]		
Mean (SD)	31.9 (84.08)	99.2 (445.35)
Patients with elevated HS-troponin I, n (%‖)	13 (17.8)	12 (33.3)
Randomized patients (Full analysis set†)	n=73	n=36
LVEF (%)[2]		
Mean (SD)	56.63 (7.83)	56.91 (7.99)
Patients with LVEF <50%, n (%‖)	12 (17.4)	6 (16.7)
Randomized patients (Full analysis set†)	n=69	n=36

*Percent of control describes glycosylated αDG levels relative to a control reference standard from a healthy donor. †The Full Analysis Set consists of randomized participants who had at least one efficacy assessment postrandomization. ‡The primary efficacy set consists of randomized participants who provided a total score of ≥3 on the NSAD at baseline. §The secondary efficacy set consisted of randomized participants with nonzero scores at screening (or if a score was not available at screening, then it was nonzero at baseline) for all of the following: 10MWT (or if 10MWT was not available, then NSAD Item #29a [velocity]), PUL 2.0, and FVC (% predicted, sitting) (or if FVC was not available, then the investigator reported that spirometry was performed). ‖Percentages are based on the number of participants with available baseline assessments. 10MWT=10-meter walk test; 100MTT=100-meter timed test; αDG=alpha-dystroglycan; CK=creatine kinase; FVC=forced vital capacity; HS-troponin I=high-sensitivity troponin I; LVEF=left ventricular ejection fraction; m/s=meter/second; NSAD=North Star Assessment for Limb Girdle-type Dystrophies; PUL 2.0=Performance of Upper Limb Scale 2.0; U/L=units/liter. 1. Mathews K et al. Presentation at: Muscular Dystrophy Association Conference; March 11, 2026; Orlando, USA. 2. Data on file. BridgeBio Pharma, Inc.; 2026.

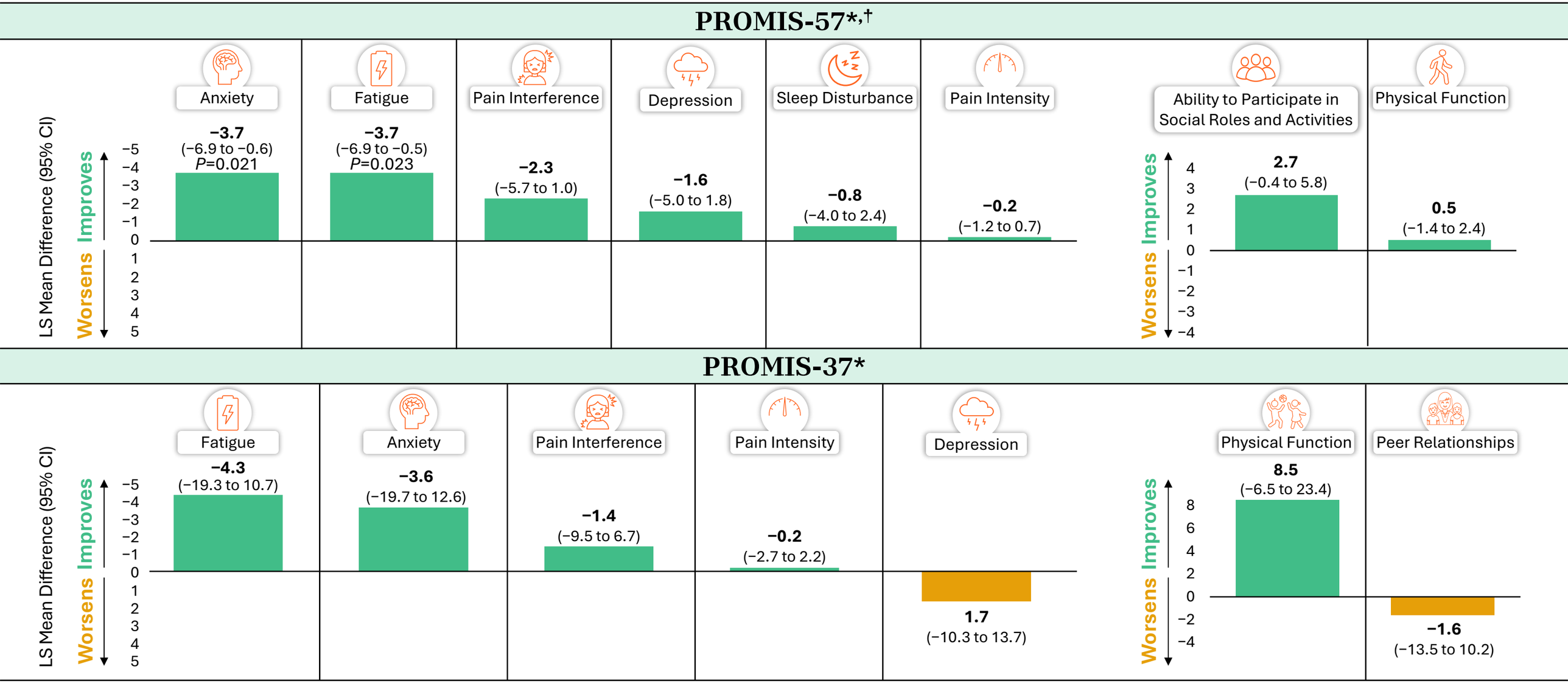
The Phase 3 interim analysis results show consistent and favorable effects of BBP-418 versus placebo on clinical and biomarker endpoints

Endpoints	LS Mean change from Baseline BBP-418	LS Mean change from Baseline Placebo	*P*-value
Interim analysis key endpoints (α-controlled)			
Glycosylated αDG at 3 months, % of control*	+17.12	−0.04	<0.0001
Glycosylated αDG at 12 months, % of control*	+23.60	+0.82	<0.0001
Serum CK at 12 months, U/L	−1869	+186	<0.0001
100MTT at 12 months, m/s	+0.14	−0.12	<0.0001
FVC (% predicted, sitting) at 12 months	+2.97	−1.92	0.0071
Final analysis key endpoints at 12 months (non-α-controlled)			
NSAD, points	+1.3	−1.3	0.0001†
10MWT, m/s	+0.13	−0.1	<0.0001†
PUL 2.0, points	+0.8	+1.1	0.6779

*Percent of control describes glycosylated αDG levels relative to a control reference standard from a healthy donor. †Nominally statistically significant based on exploratory analysis; analysis not part of α-controlled hierarchy at interim analysis.
10MWT=10-meter walk test; 100MTT=100-meter timed test; αDG=alpha-dystroglycan; CK=creatine kinase; FVC=forced vital capacity; m/s=meter/second; NSAD=North Star Assessment for Limb Girdle-type Dystrophies; PUL 2.0=Performance of Upper Limb Scale 2.0; U/L=units/liter.
Mathews K et al. Presentation at: Muscular Dystrophy Association Conference; March 11, 2026; Orlando, USA.

Interim analysis data cutoff: June 27, 2025

Exploratory analyses showed improvements in pre-defined PROMIS® domains with BBP-418 versus placebo at 12 months, with clinically meaningful benefits in anxiety and fatigue



*Exploratory analysis, not an α-controlled endpoint at 12-months data readout (PROMIS 57: aged ≥18 years, n=44 for BBP-418, and n=19 for placebo; PROMIS-37 aged <18 years, n=6 for BBP-418, and n=4 for placebo). †Physical function, fatigue, and anxiety were predefined as domains of interest on the PROMIS-57 at 12 months in the interim analysis. LS=least-squares; PROMIS®=Patient-Reported Outcomes Measurement Information System; PROMIS-37=PROMIS 37-item profile; PROMIS-57=PROMIS 57-item profile. Mathews K et al. Poster PP01.108. Presented at: 19th International Congress on Neuromuscular Diseases; July 7-11, 2026; Florence, Italy.

Interim analysis data cutoff: June 27, 2025

Exploratory analyses at Month 12 showed that BBP-418 reduced HS-troponin I and preserved LVEF versus placebo

HS-troponin I

BBP-418 was associated with a greater reduction in HS-troponin I from baseline than placebo at Month 12

LS mean difference

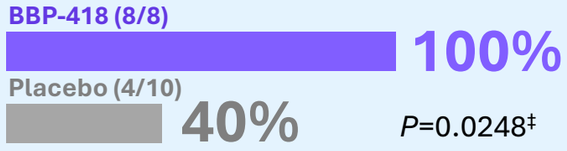
−17.8 ng/L

(95% CI: –35.1 to –0.5)

P=0.0443*

Month 12 analysis (all participants with observed values):
BBP-418, n=49; placebo, n=20

Proportion of patients with elevated HS-Troponin I at baseline who achieved normal levels at Month 12†



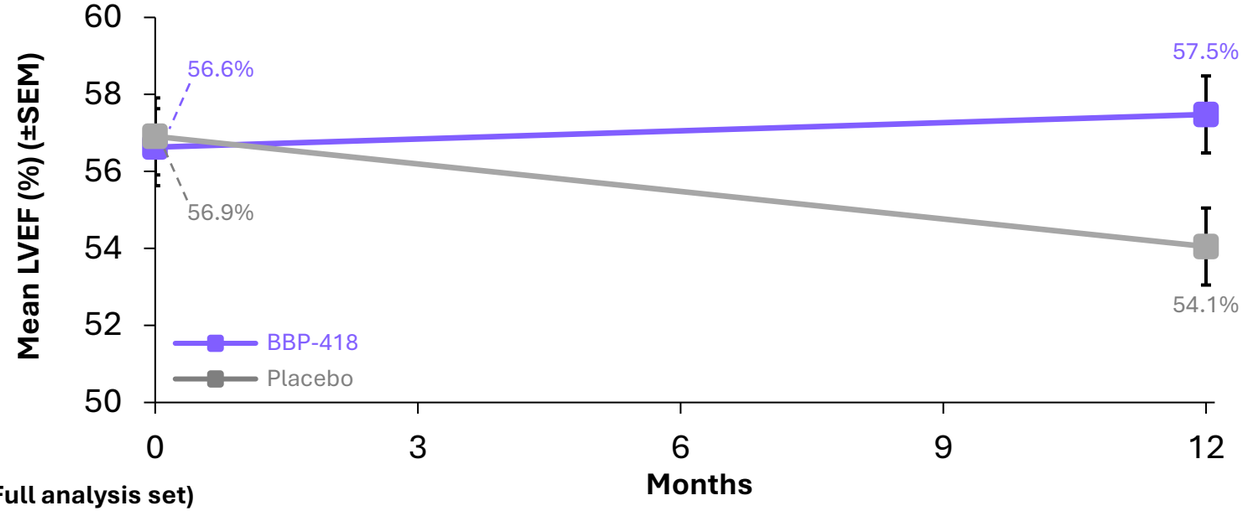
P=0.0248‡

Normal range of HS-troponin I:
Adult men: <20; Adult women: <15; for the pediatric participants in the study, the adult woman normal range was applied

At baseline, 22.9% (n=25/109) of participants had elevated HS-Troponin-I

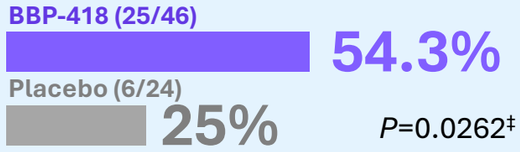
Left Ventricular Ejection Fraction

Patients receiving BBP-418 had relatively stable LVEF at Month 12



n (Full analysis set)		
BBP-418	69	48
Placebo	36	22

Proportion of patients with stable or improved LVEF by TTE at Month 12



P=0.0262‡

At baseline, 17.1% (n=18/105) of participants had LVEF <50%

Endpoints depicted are not α-controlled.
*Exploratory analysis, not an α-controlled endpoint at 12-months data readout. Comparison of BBP-418 change from baseline to placebo change from baseline is based on a linear model. This analysis is based on the full analysis set. †Analysis are summarized for changes from elevated at baseline to normal postbaseline. ‡Nominal p-value based on exploratory analysis CMH Chi-square; analysis not part of alpha-controlled hierarchy.
CMH=Cochran-Mantel-Haenszel; HS-troponin I=high-sensitivity troponin I; LS=least-squares; LVEF=left ventricular ejection fraction; TTE=transthoracic echocardiography.
Data on file. BridgeBio Pharma, Inc.; 2026.

Phase 3 interim analysis data support a favorable safety profile for BBP-418 in LGMD2I/R9[1]

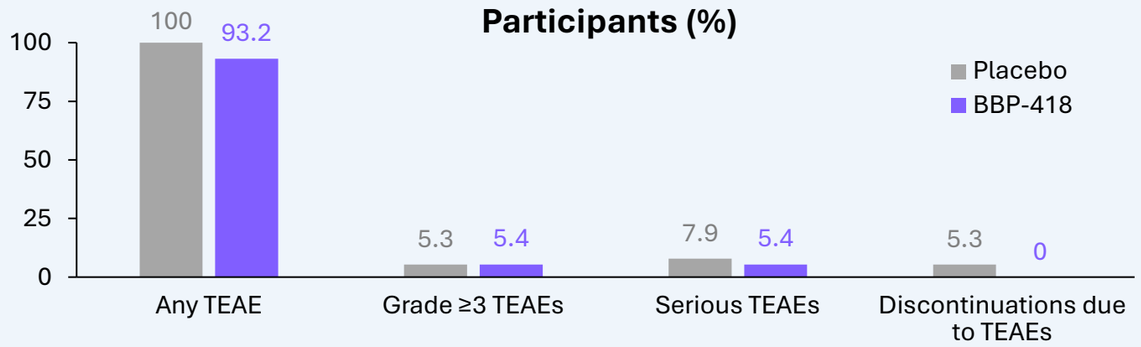
Safety Population

Placebo: n=38

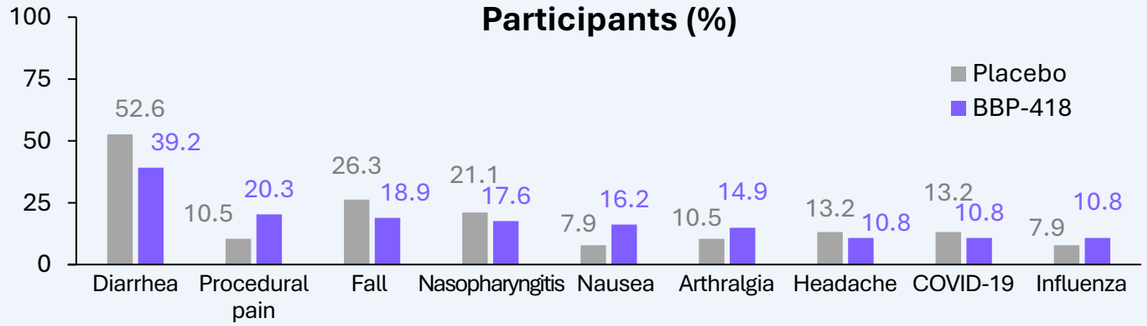
BBP-418: n=74

- Cumulative BBP-418 exposure at interim: approximately 91 patient-years
- There were no deaths or treatment related SAEs
- Phase 3 study remains ongoing with double-blind maintained

TEAEs*



Most Common TEAEs (≥10% in the BBP-418 Group)*



- Diarrhea is an identified adverse reaction to BBP-418, consistent with known polyol effects
- All diarrhea TEAEs were Grade 1 or 2; none were serious

Laboratory and Cardiac Assessments

- No laboratory pattern suggestive of hepatic, renal, cardiac, hematologic, or metabolic toxicity
- No clinically significant ECG abnormalities or ECG safety signals were observed in either treatment group
- No participant in either group had a maximum QTcF increase from baseline >60 msec

*Percentages reflect participant-level incidence percentages.
ECG=electrocardiogram; LGMD2I/R9=limb-girdle muscular dystrophy type 2I/R9; QTc=corrected QT interval; QTcF=QT interval corrected using Fridericia's formula; SAE=serious adverse event; TEAE=treatment-emergent adverse event.
1. Mathews K et al. Presentation at: Muscular Dystrophy Association Conference; March 11, 2026; Orlando, USA.

Interim analysis data cutoff: June 27, 2025

Conclusions

- BBP-418 delivered statistically significant, clinically meaningful improvements across biochemical, functional, and pulmonary endpoints
- Directionally supportive gains in patient-reported outcomes with clinically meaningful improvements in fatigue and anxiety on the predefined PROMIS-57 domains at Month 12
- Exploratory cardiac analyses showed reduced HS-troponin I and preserved LVEF versus placebo, suggesting a potential positive impact beyond skeletal muscle
- BBP-418 demonstrated a favorable safety profile, with predominantly Grade 1–2 TEAEs, no deaths, and no treatment-related SAEs
- Taken together, these findings support a favorable benefit–risk profile for BBP-418 in LGMD2I/R9

HS-troponin I=high-sensitivity troponin I; LGMD2I/R9=limb-girdle muscular dystrophy type 2I/R9; LVEF=left ventricular ejection fraction; PROMIS-57=Patient-Reported Outcomes Measurement Information System 57-item profile; SAE=serious adverse event; TEAE=treatment-emergent adverse event.