

# Development of Pediatric and Adult LGMD2I/R9 Disease-Specific Physical Function Questionnaires Using PROMIS Item Banks

Divya B. Reddy, MD<sup>1</sup>, Beth Leiro<sup>1</sup>, Katherine Mathews, MD, FAAN<sup>2</sup>, and John Vissing, MD, DMSci<sup>3</sup>

1. ML Bio Solutions, a BridgeBio company, Palo Alto, CA  
 2. University of Iowa Carver College of Medicine, Iowa City, IA  
 3. Copenhagen Neuromuscular Center, Rigshospitalet, University of Copenhagen, Copenhagen, DK



## Introduction

Limb girdle muscular dystrophy type 2I, R9 FKRP-related (LGMD2I/R9) is caused by bi-allelic partial loss-of-function of the fukutin-related protein (FKRP) gene, resulting in hypoglycosylation of  $\alpha$ -dystroglycan ( $\alpha$ DG) and progressive muscle damage.

- FORTIFY (NCT05775848) is a Phase 3 multinational double-blind placebo-controlled study enrolling individuals aged 12-60 years with LGMD2I/R9.
- BBP-418 is an oral substrate intended to saturate the partially functional FKRP enzyme, driving increased glycosylation of  $\alpha$ DG, and potentially ameliorating the root cause of LGMD2I/R9.

Although physical function deficits are well documented in LGMD2I/R9, there are no disease-specific patient-reported outcomes (PROs) that assess the impact of these deficits on daily life. Our aim was to develop disease-specific physical function PROs to assess the impact of impaired physical function in individuals with LGMD2I/R9.

## Methods

Items from the Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric and Adult Physical Function Item Banks were selected to create custom Physical Function PROMIS questionnaires. The items were methodically chosen to include LGMD2I/R9 disease concepts of interest, with careful consideration to ensure that the selection of items was informed by a variety of sources and covered a broad range of physical function.

Item selection was informed by the following criteria:

**Proximal Weakness:** The impact of proximal weakness on mobility and activities of daily living (ADL) was assessed, and items relying on proximal strength were selected.

**Activity Limitations Questionnaire (ACTIVLIM):** This PRO assesses activity limitations in patients with neuromuscular disorders and items on the PROMIS item banks that overlapped with ACTIVLIM items were selected.

**Patient Experience and Patient Advocate Endorsement:** We included information from a patient survey sponsored by ML Bio to gather insights from the LGMD2I/R9 patient community about disease burden and transcripts from patient day where patients shared their experiences of living with LGMD2I/R9. In addition, a roundtable for patient advocates was convened during which all of the selected items were endorsed. The patient advocate roundtable also highlighted additional challenges in activities of daily living, indicating that further research in this area is needed to explore common ADL related difficulties more fully in the LGMD2I/R9 patient population.

**Key Opinion Leaders (KOL) Endorsement:** A round table was convened with LGMD2I/R9 physician specialists for guidance and endorsement of selected items.

## Conclusions

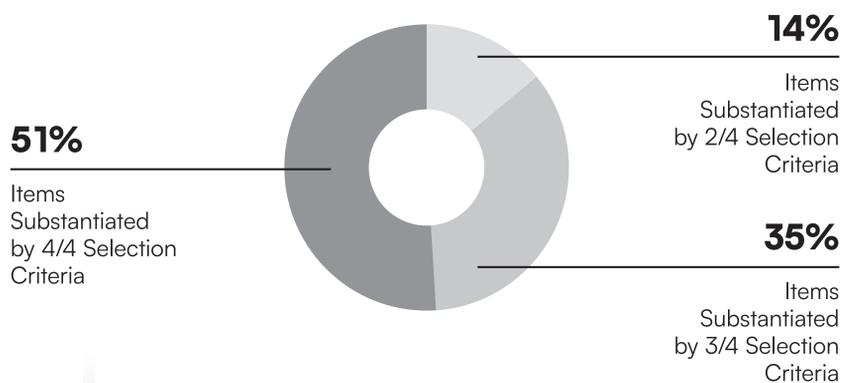
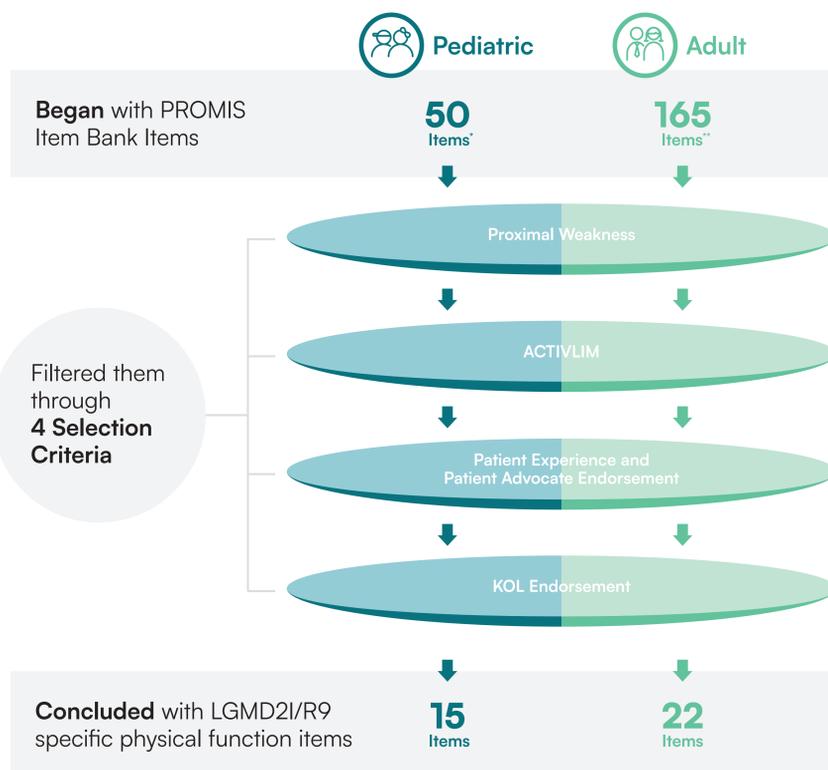
LGMD2I/R9 specific physical function questionnaires for adults and children were created using the PROMIS Item Banks. Validation studies and correlation of PRO data with standardized performance measures are planned. If validated, this PRO can be a useful addition to clinical trials, such as FORTIFY.

## Acknowledgements

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## Visualization of Process



\*PROMIS Pediatric Item Bank Mobility, PROMIS Pediatric Item Bank Upper Extremity  
 \*\*PROMIS Physical Function Item Bank

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