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December 10th, 2025

Dear Members of the Application Review Subcommittee –

My name is Kat Bryant Knudson, and I am the founder of The Speak Foundation living with Limb-Girdle Muscular Dystrophy type 2I/R9 (LGMD2I/R9). This disease impacts every aspect of life—from mobility and independence to long-term health. Like many in our community, I face the daily reality of no approved therapeutics, which makes the need for safe and effective treatment options urgent. I am a patient who has lived experience who has advocated since 2008. I cannot walk any longer and my life mission is to help others like me.

I am writing to express my strong support for the Cure Rare Disease (CRD) gene therapy initiative for LGMD 2i/R9. The approach being proposed is not only scientifically promising but directly addresses critical safety concerns in our community.

A particularly promising aspect is the use of a liver de-targeting capsid. Previous muscle-targeted gene therapies have caused serious liver side effects, *understandably raising concerns among patients and families*. In contrast, CRD's second-generation AAV capsid, AAVMYO2, has been shown to avoid liver targeting, offering a safer approach—especially for adult patients. This innovation provides hope that gene therapy can be both effective and safe.

I am also very encouraged by the combinatorial testing of ribitol with gene replacement therapy. Ribitol may soon be approved, and understanding its interaction with gene therapy—particularly regarding dosing—is crucial. Approval of ribitol will not cure LGMD2I/R9 and is not mutually exclusive with gene therapy. Importantly, even if ribitol is not approved, this project can still achieve its objectives, demonstrating flexibility and rigor in the research plan.

I also recognize that the cost of developing gene therapies is significant, and patients like myself are keenly aware of the need to maximize every dollar spent on research. The thoughtful design of this project reflects both scientific innovation and cost-consciousness, ensuring that resources are used efficiently while keeping patient safety at the forefront.

As someone living with LGMD2I/R9, I cannot overstate the importance of supporting research that prioritizes both innovation and patient safety. The Cure Rare Disease proposal addresses real patient concerns while offering a path toward meaningful treatments.

Thank you for your consideration. I am happy to provide further input or help identify additional LGMD2I/R9 patients in California who may wish to support this effort.

Sincerely,

Kathryn Bryant Knudson
Founder and President, The Speak Foundation