children's health
Children's Medical Center

UT Southwestern
Medical Center

Department of Pediatrics
Division of Pediatric Neurology

Dear CIRM board,

RE: Letter of support for CLIN2 17091

I am Professor of Pediatrics and Neurology and a clinical trialist. I have been involved in designing and directing clinical trials in pediatric neuromuscular disease for over 40 years and became Director of Clinical Research for Pediatric Neurology in 2021. I am PI for this study.

SPG50 is an autosomal recessive disease with symptom onset in infancy resulting in delayed milestones, motor impairment, cognitive delay, progressive spasticity in limbs and quadriplegia in early adolescence. There are currently no approved treatments that can change their outcome and improve their quality of life and early intervention is critical to prevent disease progressing.

We receive referrals for treatment from patients from all over the world including a newly diagnosed infant. The families impacted by this devastating disease seek our help to treat and care for their children. As a doctor who has spent decades dedicated to providing the best treatments for my patients and improving their quality of life, none is more pressing than a treatment for a rare disease that has no other viable options. Coupled by the urgent unmet medical needs and disease burden on families, this significant endeavor to make a difference is what drives us to be brave, ambitious, committed, and innovative. Not doing anything is not an option for us. We must continue to push the boundaries and expedite novel medicine to the clinic in every way we can.

I have worked in the development of this program with my colleagues from the onset both on the pre-clinical and clinical sides. The successful execution of the Phase 1/2 trial has made it possible develop a pivotal trial with a goal to seek approval for this therapy so that it can be available for all patients and not the few who have been selected for a clinical trial. As a team, we spent almost a year, meticulously designing the pivotal trial and we went back and forth with the FDA with amendments to the clinical design and selection of endpoints. The FDA have now permitted for us to proceed to a

phase 3 trial. This is a remarkable milestone, indicating the flexibility of the regulatory authorities as well as making this the first intrathecal gene therapy for rare disease to reach pivotal stage.

I appeal to the ICOI to fund this program, as I believe this is a crucial program to advancing a treatment for SPG50 disease, offering a pathway to treat the eligible children we have currently evaluated as well future children yet to be diagnosed.

Yours sincerely,

Susan Iannaccone

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