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Tuesday, January 23, 2024

RE: Subject: Endorsement of Elpida Therapeutics' Proposal (Application Number: CLIN2-15607) for a Phase 3 Clinical Trial

To the CIRM Board and Review Committee:

I am writing to convey my strongest support for Elpida Therapeutics' appeal regarding their proposal with the application number CLIN2-15607. The project outlines a phase 3 clinical trial focused on evaluating a CNS-targeted gene replacement therapy for children diagnosed with Hereditary Spastic Paraplegia Type 50 (SPG50).

This initiative stems from years of meticulous pre-clinical and clinical work, offering a unique opportunity to test the first disease-modifying therapy for SPG50, a condition with significant clinical impact and unmet need. Beyond its potential for SPG50, **the proposed study represents a pivotal opportunity for gaining insights that will undeniably advance the field of gene therapy for rare and ultra-rare diseases.**

The inclusion of the program in the Bespoke Gene Therapy Consortium (BGTC) of the Foundation of the NIH, where the SPG50 program is notably recognized as the most advanced in CNS-targeted programs, serves as a testament to its promising potential.

Our team, in collaboration with others, has been actively involved in describing SPG50 and conducting a longitudinal study since 2017 (NCT04712812) to delineate its natural history. Having personally assessed ~100 children and young adults with SPG50, along with ~250 individuals with related diseases in the AP-4-HSP spectrum, I consider myself an expert in this condition and our team a resource to the community. For us, the urgency for disease-modifying therapies becomes apparent every week when we meet with families with SPG50 from around the world.

The data derived from our natural history study not only supported Elpida's IND application for their gene therapy but also played a pivotal role in shaping the presented phase 3 study design. The study's distinctive multi-center open-label approach with a prospective matched control arm has gained endorsement from regulatory agencies.

The proposed study design and opportunity to test an AAV9-based gene replacement vector for a prototypical type of hereditary spastic paraplegia are noteworthy in the field of ultra-rare neurological diseases. Our approach aligns with the goal of developing and rigorously testing platform technologies—building on the coordinated preclinical pipeline and clinical trial readiness program we have meticulously built and de-risked over several years. This collaborative strategy strongly resonates with the objectives of CIRM and the BGTC.

Drawing on our center's extensive experience in conducting clinical research and trials for hereditary spastic paraplegia and other motor disorders, we are fully prepared to support Elpida's trial with our resources, including the aforementioned natural history study, biorepository, clinical expertise, and trial design.

Thank you for considering our endorsement of Elpida’s proposal. We are dedicated to collaborating with you to advance the field and instill hope in families affected by SPG50.

Sincerely,

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