UNIVERSITY OF IOWA HEALTH CARE

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Dear CIRM board,

RE: Letter of support for CLIN2-19061

My name is Michael Shy, and I am a Professor of Neurology and hold the Carver College of Medicine Endowed Chair in Inherited Neuropathies. I have dedicated 30 years to designing and leading clinical trials in pediatric neuromuscular and neurodegenerative diseases, with a focus on advancing therapeutic options for ultra-rare disorders with profound unmet medical need.

CMT4J is a devastating, autosomal-recessive neuropathy caused by pathogenic variants in FIG4, leading to loss of FIG4 function and dysfunctional endolysosomal trafficking. Clinical onset typically occurs in early childhood and is characterized by rapidly progressive motor decline, muscle weakness, distal and proximal denervation, respiratory compromise, and, ultimately, loss of ambulation and severe disability. For children with CMT4J, disease progression is not only relentless but often accelerates during key developmental windows. There are currently no approved treatments capable of altering the natural history or preventing neurological decline.

Our center receives referrals from families across the world, including newly diagnosed infants and children who are facing rapid functional deterioration. These families come to us searching for expertise, hope, and a path forward. After decades of working with children affected by rare neurological diseases, few conditions present as clear and urgent a therapeutic need as CMT4J. For these patients, doing nothing is simply not an option.

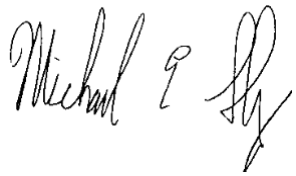
I have worked closely with the team developing the ELP-02 AAV9/FIG4 gene therapy program from its inception across both the preclinical and clinical domains. The preclinical science supporting FIG4 replacement, including survival, motor, and pathological rescue in the CMT4J mouse model has been compelling and consistent. The progress made toward a clinical-ready vector, toxicology package, and regulatory engagement has been thorough and disciplined. The team has demonstrated scientific rigor, urgency, and deep commitment to ensuring the highest standards of safety.

The goal of CLIN2-19061 is to launch a first-in-human clinical trial to treat CMT4J with AAV9-mediated FIG4 gene replacement. This trial represents the only realistic path to modifying the course of this disease and preventing irreversible neurological decline. The translational path is well-justified, the therapeutic rationale is strong, and the program has reached a stage where funding is the critical rate-limiting step to advancing into the clinic.

Given the severity of CMT4J, the rapidity of disease progression, and the absence of any disease-modifying therapy, I strongly endorse this program. I urge CIRM to support CLIN2-19061 so that we may bring this urgently needed therapy to the children who are already under our care, as well as those who will be diagnosed in the years ahead. Funding this effort has the potential to transform what is currently a devastating, progressive, and life-limiting disease into one for which meaningful treatment is finally within reach.

Thank you for your consideration and for your continued commitment to advancing therapies for rare and neglected diseases.

Your sincerely



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