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Subject: Letter of Support for **TRAN1-16907**
Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome

Dear Members of the Application Review Subcommittee,

I am Florence Lai, a clinical and research neurologist at Massachusetts General Hospital on Boston. When my 2 ½ -year-old grandson Matthew was diagnosed with Sanfilippo B, a relentless fatal brain disease in childhood which currently has no cure, my initial shock quickly turned to a flurry of networking. This led me to the pioneering work of Dr. Brian Bigger in the UK who had a successful clinical trial of lentiviral gene therapy in Sanfilippo A, a very close variant to Sanfilippo B. Dr. Donald Kohn at UCLA (also an expert on lentivirus gene therapy) agreed to tackle Sanfilippo B in the U.S. culminating in this exquisitely detailed and factual grant proposal led by Katelyn Masiuk, MD, PhD and joined by Drs. Kohn and Bigger.

Sanfilippo B has been termed "childhood Alzheimer disease" with death in the teen years after a rapid decline in all functions usually starting before age 6. As a researcher in Alzheimer disease, I fully understand the devastating implications, and do not wish this same fate for children with Sanfilippo B. With the ticking time bomb of neurodegeneration in their children, families are now invigorated with hope in the high feasibility for a **CURE** using this proposed stem cell strategy.

Despite the irrefutable evidence for success in a Sanfilippo B animal model as well as curative results in Sanfilippo A children using the same proposed lentiviral stem cell approach, this grant received a surprising and unexpected borderline score for funding. This is believed to be based on reviewers' incorrect information such as the 1:1,000,000 incidence. The **actual incidence is 1:24,581** based on newborn screening of >70,000 infants* and on par with genetic disorders like Spinal Muscular Atrophy which already has a cure. The PI's separate letter to the CIRM board details other inaccuracies that negatively impacted scoring. Successful treatment of Sanfilippo B children would have great impact: not only in saving many lives, but also saving millions of healthcare dollars per patient.

The close collaboration of funding agencies, academia and drug development companies is crucial to bring life-saving gene therapies to affected children. We rely on government agencies, like CIRM, to initiate this essential process. I urge CIRM to start this critical time-sensitive process by funding this project to cure Sanfilippo B in children like Matthew. Thank you.

Sincerely,
Florence Lai
Florence Lai, M.D.

*Chien Y-H et al. Newborn screening for Morquio disease and other lysosomal storage diseases: results from the 8-plex assay for 70,000 newborns. Orphanet Journal of Rare Diseases (2020) 15:38 https://doi.org/10.1186/s13023-020-1322-z.