Navega Therapeutics

3210 Merryfield Row
San Diego, CA 92121

May 20, 2024

Re: Application Review Subcommittee meeting for CIRM TRAN1-16022

Dear Independent Citizens Oversight Committee,

We thank CIRM and the Grants Working Group for their favorable reviews and recommendation for funding of our proposal, TRAN1-16022, *Development of an AAV Epigenetic Gene Therapy for Gain-of-Function SCN9A Disorders and Chronic Pain.*

Background

My name is Ana Maria Moreno, founder and CEO of Navega Therapeutics. I founded Navega while pursuing a PhD in Bioengineering at the University of California, San Diego. My PhD was focused on developing epigenetic gene therapy platforms via CRISPR-dCas9 and zinc fingers. Inspired by the pressing national opioid epidemic and the urgent need for non-opioid pain management solutions, I focused on targeting Nav1.7—a critical sodium channel in pain signal transmission—culminated in a breakthrough publication in Science Translational Medicine in 2021.

Following my PhD, I transitioned from academia to industry, founding Navega with support from SBIR funding and in-licensing IP from UCSD. Navega was incubated at JLABS, Johnson and Johnson's incubator, where we continued to develop and refine our gene therapy platforms. Since inception, we have been driven by the vast unmet need for effective and non-addictive pain treatments—a field surprisingly underfunded despite over 50 million Americans suffering from chronic pain. Below, I highlight some of our responses to the reviewers and recent advancements, that further bolster our readiness for this TRAN grant.

Response to Reviewer Comments

Clarifying the Scope of the Impact on the Mutation:

We initially target patients with an orphan disease due to gain-of-function Nav1.7 mutations, including those with Erythromelalgia (2:100,000 prevalence) and small-fiber neuropathy (3:100,000 prevalence). We plan to expand this to include patients with small-fiber neuropathy without Nav1.7 mutations (56:100,000 prevalence) followed by those suffering from trigeminal neuralgia. Our pivotal clinical trials will include a basket trial with cohorts of patients both with and without the mutation, enabling us to expand to a larger patient population following a PhIb/IIa clinical trial.

Feasibility and Planning:

Regarding comments about our ambitious timelines, since our application submission, we have been accepted as part of the first Charles River Laboratories through their Gene and Cell Therapy Accelerator cohort. This partnership not only provides preferred manufacturing slots but also reduces costs by 60%, allowing us more flexibility and assurance in our timeline, which we have extended by 30% beyond what CRL projected. Additionally, since submitting our application, we have conducted a pilot NHP study and tested our final gene therapy product, NT-Z001, observing no adverse events or toxicity. We have also demonstrated strong target engagement in our humanized mouse models, human DRG, patient-derived iPSCs, further supporting the feasibility of our approach.

Commitment to DEI:

As a female Mexican entrepreneur, I deeply understand the need for diversity, equity, and inclusion, which are embedded in Navega's culture and critical to our approach to preclinical and clinical trial design. Women, particularly from minority backgrounds, face significant disparities in pain treatment and assessment. Our team is committed to addressing these inequalities and has engaged with diverse patient groups and medical professionals across multiple regions (both in the USA and abroad) to ensure broad and inclusive research practices and trial designs.

We are committed to advancing this promising therapy into clinical trials and look forward to continuing our work with the support of CIRM, which will ultimately aid in addressing the significant global burden of chronic pain.

Sincerely,

Ana Moreno, PhD

Principal Investigator

Co-Founder and CEO, Navega Therapeutics