

## DEVIN K. BINDER, M.D., PH.D.

Board-certified and Fellowship-trained Neurosurgeon Brain & Elective Spine Treatment (B.E.S.T.) Center 9940 Talbert Avenue, Suite 201 Fountain Valley, CA 92708 (949) 829-2378 (-BEST) (phone) (714) 769-6121 (fax) www.bestcenteroc.com info@bestcenteroc.com

May 17, 2024

Re: Grant Number: TRAN-16022

To Whom It May Concern:

I would like to write a letter of support for the work of Dr. Ana Moreno at Navega Therapeutics. Her research and clinical trial efforts are unparalleled in the treatment of chronic, debilitating neuropathic pain. As you may know, neuropathic pain is notoriously difficult to treat - the majority of patients are under-treated due to lack of therapeutic options. The few that respond partially only do so in a palliative sense where the sensation is generally, imprecisely suppressed via medication or electrical stimulation; notably, the pathology tends to persist and often habituates to these therapies. Dr. Moreno's treatment is uniquely positioned to offer a paradigm shift in the treatment of neuropathic pain conditions; as you may know, it seeks to genetically modify the expression of a sodium channel (NaV1.7) involved in nociceptive signaling which addresses one of the root causes of severe, refractory neuropathic pain. Of note, this treatment is particularly important for erythromelalgia which is a strikingly debilitating condition correlating with NaV1.7 over-expression clinically manifested by severe ulceration of the lower extremities due to sympathetic nerve dysfunction, hypersensitive C fibers and skin perfusion abnormalities with ensuing severe thermoregulatory and nutritive deficiencies. We have a patient who has suffered from this condition from a very young age and is now in her late 40's with inexorable complications rendering our advanced palliative therapies (lumbar sympathetic blocks, surgical sympathectomies and intrathecal pump) much less effective. Dr. Moreno's therapy has incalculable benefits in addressing this pain in a minimally invasive way with long-lasting analgesia that keeps her collateral tissue intact. This is, as of yet, unheard of in the chronic pain literature and can offer long-lasting, durable relief for the first time in history for this condition. I also have patients with Complex Regional Pain Syndrome, Charcot-Marie-Tooth disease, familial dysautonomia, diabetic neuropathy and interstitial cystitis as well as spinal tumor surgery-related neuropathic pain that can respond in a profound way to epigenetic ion-channel suppression. The vast majority of patients with these and similar conditions have few options - for the first time in decades, we have a targeted treatment that would improve the quality of life for patients endlessly enduring among the worst known chronic pain diseases.

It is with this perspective that we unequivocally support and stand behind Dr. Moreno's work which is intellectually sound, undoubtedly practicable and extraordinarily unmatched in its precision and consistency. We implore that she be granted funding to pursue this endeavor and provide our ailing patients the respite that they rightfully deserve.

Sincerely yours,

Devin K. Binder, M.D., Ph.D. Board-certified and Fellowship-trained Neurosurgeon Brain and Elective Spine Treatment (B.E.S.T.) Center www.bestcenteroc.com info@bestcenteroc.com