# Congress of the United States
## Washington, DC 20515

April 18, 2023

The Honorable Robert Califf, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20933

Kathleen Donohue, M.D.
Director
Division of Rare Diseases and Medical Genetics
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Dear Commissioner Califf and Director Donohue:

We write to express our deep concerns regarding policies enacted by the Food and Drug Administration's (FDA) Division of Rare Disease and Medical Genetics (DRDMG). The mission statement of DRDMG is "to facilitate, support and accelerate the development of drug and biologic products for the benefit of patients with rare disorders." We fully support the goals of this division and seek to support these efforts; however, we believe that certain requirements may hinder patients' abilities to receive life-saving treatments.

Placebo requirements are necessary in most trials, however, in the case of certain fatal heterogeneous degenerative diseases—such as CLN3 Batten Disease, Pompe Disease, Fabry Disease, and muscular dystrophies—with limited patient populations and no available treatments, the use of placebos can discourage patient involvement. We have heard from parents of children with CLN3 Batten Disease and other rare diseases that would be willing to participate in clinical trials but are hesitant to remove their children from drugs that are significantly slowing down the progression of this disease. Rational and flexible clinical trial designs can accommodate the absence of a placebo, especially in cases where a trial is repurposing a drug already approved for adults and pediatrics in other conditions; for instance, Zavesca/Miglustat is being used to slow the progression of CLN3 Batten Disease in certain patient populations.

Taxpayer dollars are used at the National Institute of Health to fund natural history studies. These studies are invaluable to researchers to understand the disease course over time and help develop clinical care guidelines and, ultimately, lead to treatments and cures. The data acquired from these studies should be used as a baseline for what untreated disease progression looks like and should alleviate the need for a placebo within this fatal heterogeneous degenerative disease community. Our constituents who have had their children participate in these natural history studies and have made great sacrifices deserve to have this factored into a clinical study in place of a placebo.

We urge the FDA to reconsider clinical trial designs within the population of certain fatal heterogeneous degenerative diseases so that patients do not have to choose between medication that is slowing the progress of their disease and participating in FDA trials. We look forward to your response and to working together to ensure that the most vulnerable patient population has the ability to participate in clinical trials, without the risk of a placebo that would cause irreversible harm.

Sincerely,

RANDY K. WEBER
United States Representative

DAN CRENSHAW
United States Representative

BRIAN BABIN, D.D.S.
United States Representative