NNPDF Submission re FDA Docket # FDA-2021-N-1297

April 2022

To the FDA:

We write to you as the national patient and family support organization for the Niemann-Pick community, dedicated to supporting and empowering patients and families affected by Niemann-Pick disease, through education, collaboration and research.

In our discussions with the FDA in recent months, and the past few years, we have shared several recurrent themes of paramount importance to the Niemann-Pick, type C (NPC) community. Our expert clinicians and NPC families have strongly conveyed:

- The opinion and experience of our expert clinicians and families confirm that the NPC CSS measures areas of change that are truly **reliable and meaningful** in both clinical trials and practice settings over time.
- Our patients and families have a great sense of urgency about the unmet clinical need.
- Our NPC community is willing to accept the risk of uncertain efficacy of a potential therapy, knowing that to do nothing will lead to neurologic decline and death.
- Our patients and families have an informed tolerance of side effects and treatment risks, again knowing that the downward spiral of this neurodegenerative disease is certain without intervention.

We have expressed our concern that in the longer-term quest for a biomarker or surrogate endpoint, we are not addressing the immediate needs of our patients who currently have no approved treatments for this relentless, degenerative disease. We encourage the FDA to work in partnership with NPC experts, industry, and the patient community to ensure the viability of trials and clinical development, to apply patient and caregiver perspectives when evaluating the risk-benefit of experimental therapies, and to recognize the utility of our NPC-CSS and not disregard its meaningfulness as an international tool.

We further encourage the FDA to continue working with our community to accelerate clinical development for patients with Niemann-Pick type C.

Respectfully,

Joslyn Crowe

Joslyn Crowe, Executive Director