December 15, 2025

To: Martin A. Makary, M.D., M.P.H., FDA Commissioner
Cc: Vinay Prasad M.D., M.P.H., Chief Medical Officer and Director, CBER; Amy Comstock Rick, J.D., Associate Director for Rare Disease Strategy and Director Rare Disease Hub, CDER; Jim Traficant, FDA Chief of Staff, Office of the Commissioner

Commissioner Makary,

I am Terri Klein, mother of a daughter with a rare disorder and President and CEO of the National MPS Society. I am writing to you with the honor and responsibility each of these roles hold, representing the thousands of families who face these devastating diseases, often with limited or no treatment options.

This community of parents, physicians, and advocates excitedly and anxiously await the PDUFA target date of February 8th for the gene therapy clemidsogene lanparvovec (also known as RGX-121), a one-time treatment for mucopolysaccharidosis type II (MPS II), or Hunter syndrome. They are holding on to the promise of hope by placing their faith in the FDA acting on its commitment to **accelerate** innovative new medicines and use flexible regulatory pathways for rare diseases.

Hunter syndrome is an ultra-rare disease with an extraordinarily high unmet need. It is life-threatening, severely debilitating and progressive, ultimately leading to a vegetative state and early death. It remains one of the only rare pediatric diseases where we can treat the body, but we still cannot protect the brain—and that unmet need is costing our children their future. We can no longer accept a world where children lose their ability to speak, learn, and connect simply because no therapy exists to safeguard their cognition. With clemidsogene lanparvovec under review, we no longer have to.

Today, we have reached a critical juncture: after 20 years of inadequate treatment, science has finally reached the point where we can change the neurological course of disease *and* we have regulatory pathways in place to act at the first sign of efficacy. Additionally, for the first time, a growing number of newborns are being screened for MPS II in the United States, making early intervention and access to meaningful medicines even more urgent. Families and clinicians deserve to have treatment options.

I have been pleased to see your public support of greater flexibility for new medicines treating conditions with high unmet medical need. **Clemidsogene lanparvovec is exactly the type of therapy Subpart E and accelerated approval were enacted to support.** These pathways were

created to prevent scenarios where rare disease children die or decline while waiting for perfect data. We are living in that scenario right now, and we have the opportunity to change this now.

The FDA has stated a greater tolerance for uncertainty is necessary for rare and ultra-rare diseases like Hunter syndrome. As your team reviews the very encouraging safety, surrogate endpoint, and neurodevelopmental data supporting the BLA submission for clemidsogene lanparvovec, families cannot afford the 'certainty' that comes at the cost of irreversible neurologic loss and loss of life. The price of waiting for perfect, large trials or more data in this ultra-rare disease is lost speech, lost mobility, lost cognition, and lost time. These outcomes cannot be recovered.

For Hunter syndrome patients and their families, the chance, with a one-time treatment, to improve or maintain communication, cognition, behavior, sleep, ability to eat, transition, and longer independence would be life-changing.

With your support, boys living with Hunter Syndrome can have access to a treatment that would dramatically alter their lives for the better, and I implore you to act with urgency and approve clemidsogene lanparvovec on behalf of the children whose hope and health are in your hands.

Thank you for your time, consideration, and commitment to our children.

Regards,

Terri Klein

President & CEO
National MPS Society