Congress of the United States
Washington, DC 20515

July 1, 2025

The Honorable Dr. Marty Makary
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Makary:

As Chairs of the Congressional Mitochondrial Disease Caucus, representing our constituents in MA-02 PA-01, who are impacted by Mitochondrial Disease, we write to express our concern regarding the prolonged delays and the recent decision by the Food and Drug Administration (FDA) to reject the New Drug Application for elamipretide, a potential treatment for Barth Syndrome—an ultra-rare mitochondrial disorder marked by severe muscle weakness and life-threatening cardiac dysfunction. This decision was made despite a 10–6 vote by the FDA's Advisory Committee in favor of approval. Instead, the FDA has outlined a protracted and uncertain path forward for potential approval.

This decision, made despite over a decade of rigorous development, compelling clinical data, and robust support from patients, caregivers, and the scientific community, raises urgent questions about the FDA's current framework for evaluating therapies targeting ultra-rare diseases. In rare disease communities delays in access to potentially life-saving treatments can result in irreversible consequences or loss of life.

The elamipretide case is emblematic of a larger, systemic challenge: the need for a regulatory paradigm that is both scientifically rigorous and appropriately calibrated to the realities of rare diseases. We urge the agency to explore and adopt reforms that would make the FDA's review processes more responsive to these conditions. Specifically, we encourage the FDA to consider:

- Alternative evidentiary models for ultra-rare diseases where traditional randomized controlled trials may be infeasible;
- Enhanced reliance on real-world evidence and post-approval monitoring for safety and efficacy;
- A reexamination of the accelerated approval and rare disease pathways to ensure they are functioning as intended;
- Greater transparency in the agency's decision-making processes, especially for rare disease applications.

As we consider potential legislation to address the agency's regulation of rare disease therapies, we encourage you to share with us any internal review of FDA processes you may have undertaken, particularly if those reviews include a focus on flexibility, transparency, and patient-centeredness. If there are barriers to approving rare disease therapies, please share those as well. The FDA's feedback and our possible legislative proposals to address areas of concern are essential to restoring hope to families affected by mitochondrial and other rare diseases—and to ensure that future therapies are not derailed by a system that was not built to accommodate their unique challenges.

Thank you for your continued leadership and your commitment to public health, as well as giving our correspondence your full and fair consideration, consistent with applicable statutes and regulations. We look forward to working with you to make meaningful progress for the rare disease community.

Sincerely,

Brian K. Fitzpatrick
Member of Congress

James P. McGovern
Member of Congress