Congress of the United States

Washington, DC 20515

July 25, 2025

The Honorable Martin A Makary M.D., M.P.H.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

Dear Commissioner Makary,

We write to respectfully express concern and request clarity regarding the regulatory path for elamipretide, an investigational therapy intended to treat Barth syndrome. As Members of Congress representing families affected by this devastating and ultra-rare condition, we seek to better understand FDA's recent actions surrounding this therapy and the path forward for patient access.

Elamipretide represents the first and only treatment to reach this stage of development for Barth syndrome—a genetic mitochondrial disorder with no approved therapies and a dramatically shortened life expectancy. The stakes for these patients and their families are high. We appreciate the FDA's engagement on this issue to date, including the use of the Advisory Committee (AdComm) process, and recognize the important role that regulatory review plays in protecting patients. At the same time, the recent Complete Response Letter (CRL) has raised several questions that we hope the agency can address.

Specifically, we are seeking additional information on the following:

- **The apparent disconnect between the AdComm process and the CRL**, particularly in light of the agency's own statement that the review would be conducted through the Advisory Committee. Historically, therapies reviewed through this process—especially first-in-class rare disease treatments—are granted approval following a positive AdComm vote in the vast majority of cases.
- **The rationale for denying traditional approval for elamipretide**, despite this being the first therapy to reach this stage for Barth syndrome and despite what we understand to be an acknowledgment that additional efficacy or safety data are not required on a pre-approval basis.
- **The decision to now offer the Accelerated Approval pathway**, which had previously been ruled out by the agency when offered by the sponsor as a potential path forward. We are eager to understand what has changed and what specific steps the sponsor would be expected to take under this new approach. Given the size of the patient population, we are concerned that additional data requirements may create an unrealistic burden and delay access for years.

Additionally, we hope the agency can clarify how patient perspectives were incorporated into its decision-making process. We are aware that patients and families provided moving testimony during the AdComm meeting and have engaged with FDA through patient-focused initiatives, such as the "Tolerance of Risk Without Known Benefit" session. Yet these perspectives appear to be largely absent from the public summary of the agency's decision, therefore it is not clear how, if at all, these perspectives factored into the agency's decision-making process. In the context of a life-threatening rare disease with no alternatives, we believe the lived experience of patients must be a central part of the benefit-risk assessment.

We also seek the agency's insight into how future access might be impacted by an Accelerated Approval designation. For example, we are aware that some major insurers—including Blue Cross Blue Shield—do not currently cover drugs approved under this pathway. While not within FDA's purview, this is a real-world access

issue that is top of mind for patients, and one we hope the agency can help us better understand and navigate in coordination with other stakeholders.

Finally, we would welcome any information on how the FDA is approaching labeling decisions for elamipretide, including the potential for broader labeling that allows infants and newly diagnosed individuals to access treatment when it may be most effective.

We are grateful for the FDA's continued engagement on behalf of individuals living with rare diseases and for the agency's stated commitment to accelerating safe and effective treatments. We hope to work in partnership to ensure timely, transparent decision-making and to ensure that families impacted by Barth syndrome are not left behind.

Thank you for your attention to this matter. We look forward to your response.

Sincerely,

Kat Cammack
Member of Congress

Neal P. Dunn, M.D.
Member of Congress

Gus M. Bilirakis
Member of Congress

Vern Buchanan
Member of Congress

Laurel M. Lee
Member of Congress

Cory Mills
Member of Congress

Daniel Webster
Member of Congress