



Janet Woodcock, MD, Acting Commissioner
Patrizia Cavazzoni, MD, Director, Center for Drug Evaluation
and Research (CDER)
Robert Temple, MD, Deputy Director, Center for Drug Evaluation
and Research (CDER)
Peter Stein, MD, Director, Office of New Drugs, CDER
Hylton Joffe, MD, Director, Office of Cardiology, Hematology,
Endocrinology and Nephrology, CDER
Lisa Yanoff, MD, Deputy Director, Office of Cardiology, Hematology,
Endocrinology and Nephrology, CDER
Norman Stockbridge, MD, PhD, Director, Division of Cardiology
and Nephrology, CDER
U.S. Food and Drug Administration
Silver Spring, MD 20993

October 21, 2021

Dear Drs. Woodcock, Cavazzoni, Temple, Stein, Joffe, Yanoff and Stockbridge,

We at the Barth Syndrome Foundation (BSF) heard the devastating news yesterday that the FDA has refused to file Stealth BioTherapeutics' NDA for elamipretide in the treatment of Barth syndrome. Honestly, we are simultaneously both extremely disappointed and also stunned at how profoundly difficult the drug approval process is for ultra-rare diseases. We, as the relevant patient group, have been heavily engaged in Stealth's process all along the way, and we are very familiar with the data that have resulted. We have held multiple meetings with you and offered our patients' perspective, particularly about our increased tolerance for uncertainty of benefit. It is mind boggling to us that the FDA is not even willing to review this application and give it a fair hearing. We have never insisted that you approve the drug, because we firmly believe in the importance of determining safety and efficacy. Instead, we have asked simply that you give us – and the process for an ultra-rare disease with no other treatment options – the respect of fully reviewing the data.

From our perspective, this drug is safe and the totality of evidence is overwhelmingly positive. The results are compelling, and the patients who participated in the trial are completely convinced that their lives have been altered for the distinct good in very significant ways by this treatment. What's more, objective cardiac data have shown that their hearts have been remodeled and have defied the disease's natural history of cardiac worsening. These data

clearly cannot be the result simply of hope bias. Furthermore, we know the data package for elamipretide is stronger than that on which a number of other approvals have been based.

We are incredulous, and this FDA decision is incomprehensible to us. We will encourage Stealth to request a Type A meeting and to “file over protest.” We feel that you are committing a serious Type 2 error and that children and young people’s lives will be lost as a result.

Ironically, yesterday morning our Barth Syndrome Foundation Executive Director, Emily Milligan, served as a panelist in the EveryLife Foundation 13th Annual Rare Disease Scientific Workshop: Current and Future Barriers to the Utilization of Accelerated Approval Pathway for Novel Rare Disease Therapies. The session was called “How the Accelerated Approval Pathway Transformed Fatal Diseases into Treatable, Chronic Conditions - and Opportunities for Rare,” and I strongly urge you to view both the introduction of the subject given by Isabelle Lousada, Founder and CEO of Amyloidosis Research Consortium, (beginning at 4:11 of the video) and Emily’s highly relevant 10-minute presentation (starting at 10:28 of the video) as the first speaker. It can be found at: https://www.youtube.com/watch?v=7YBUocPO1_A

We really look forward to working with you to figure out a path forward to approved treatments for our devastating ultra-rare disease – both with this drug and with other treatments in the future.

Sincerely,

Kate McCurdy
BSF Board Chair and Mother of Son with Barth Syndrome (Deceased)