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April 2, 2024

Kate McCurdy, Chair, Barth Syndrome Foundation

Dear Kate:

In 2014, you and members of the Barth syndrome community asked us to study elamipretide for the treatment of Barth syndrome. Ten years later, I am incredibly pleased to share the news that the FDA has accepted the filing and agreed to review our new drug application. I firmly believe that FDA heard your voices from your petitions and many meetings. We believe this is an important first step to obtain the fair, equitable, appropriate, and transparent review requested by the Barth syndrome community.

We are grateful to the patients, families and physicians who participated in the studies that supported this new drug application, and wanted to share three important details below:

- First, the application was accepted on the basis of positive data from the SPIBA-001 study which compared data collected from patients on long term open-label elamipretide therapy in the TAZPOWER trial to data from patients in an external long term natural history study conducted by Johns Hopkins with your community's support and foresight. We are deeply grateful for the courage and perseverance of the TAZPOWER participants, and offer kudos to your community for supporting the natural history data collection – these two efforts, together, made the SPIBA-001 study possible.
- Second, the FDA will hold an advisory committee to help inform its review of our application. We are very pleased by this news. The primary role of an FDA advisory committee is to provide independent expert advice to the Agency and help it to make sound decisions based upon reasonable application of scientific principles. Advisory committees are extremely important for ultra-rare diseases like Barth syndrome, which are not well-understood by the broader scientific or medical community. This advisory committee will likely include one or more experts in the care and treatment of Barth syndrome and even a representative of the patient community. Importantly, this demonstrates that FDA heard and responded to your call for a *transparent review* process, because FDA encourages participation from all public stakeholders during advisory committee meetings. The meeting will include an open public hearing session, during which patients, family members, caregivers, and medical and scientific professionals can share relevant information or views.
- Finally, and troublingly, FDA has denied priority review designation for our application. This means that FDA's review process will be longer than expected, culminating in a decision early next year rather than this fall as anticipated. This is unfortunate and inexplicable: under the Agency's guidance, the FDA is to grant a priority review for products intended to treat a serious disease which, if approved, would represent a significant improvement over the current standard of care. As the Barth community knows too well, there are no approved therapies for Barth syndrome, and any approved therapy would be a significant improvement over the standard of care. We are deeply concerned that the FDA's decision reflects its continued skepticism regarding the seriousness of Barth syndrome, the urgency of the unmet medical need, and the relevance of the data we have generated. This may raise questions as to whether the review will be *fair and equitable*.

We will ask FDA to reconsider this decision, and will evaluate any other options available to correct what appears to be a clear error.

Congratulations again on this important milestone for your community, which we understand you will be eager to announce to patients and their families. Since you have been the driving force behind our efforts

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– it was your inspiration, your unflagging support, and your voices that carried us through these past 10 years and opened doors and hearts at the FDA – we encourage you to be the first to announce this tremendous triumph of the patient voice. We will follow with our own congratulations and plans for next steps as a company.

Warm regards,

Reenie McCarthy

Reenie McCarthy
Chief Executive Officer