Stealth BIOTHERAPEUTICS | Leading Mitochondrial Medicine

September 17, 2020

Dear Barth Syndrome Community:

Our team at Stealth BioTherapeutics is aware of the petition circulated by the Barth Syndrome Foundation (BSF) regarding provision of access to elamipretide for people with Barth syndrome. On behalf of all of us at Stealth, I am reaching out to express our continued support of the Barth community and our continued commitment to progressing access to therapy. I assure you that we understand the urgency of ensuring access to safe therapies to address the severe unmet medical needs affecting many of you and your loved ones.

We remind ourselves daily that our mission is to improve the lives of patients suffering from mitochondrial diseases like Barth syndrome. We have truly valued our long partnership with BSF and your community, from the time BSF first approached us to consider a trial in Barth syndrome in 2014, through our collaborative efforts conducting preclinical experiments with BSF Scientific and Medical Advisory Board members and through designing our TAZPOWER trial to incorporate endpoints that had been well-characterized in Barth pursuant to a robust longitudinal natural history study spearheaded by the team at Johns Hopkins in collaboration with BSF. We relied upon your efforts to educate one another about the TAZPOWER trial – which was the first trial ever conducted in Barth syndrome. With your support, we were finally able to enroll 12 brave young men after about a year of concerted outreach between 2016 and 2018. You have since supported our efforts to characterize the cardiac natural history of the disease, progressing our understanding that the improvements we've observed in stroke volume stand in contrast to an expected decline in the natural course of the disease. You've also helped to educate the FDA about your disease, from hosting a Patient Focused Drug Development meeting which we were honored to attend, to accompanying us to multiple meetings with the FDA over the past two years, first in the Division of Neurology Products, later in the Division of Gastroenterology and Inborn Errors of Metabolism Products, and finally in the newly constituted Division of Rare Disease and Medical Genetics Products.

Recognizing that patients are among the foremost experts in their own disease, we strive to incorporate the patient voice into our development efforts. To that end, your efforts also helped facilitate our incorporation of the patient voice into the clinical trial process, both through development of our patient reported outcome measure and completion of our patient and caregiver perception of change video protocol, which furthered our understanding of the real world impact of elamipretide therapy on the day to day functioning and quality of life of trial participants. These efforts also brought the disease, and your community, into our corporate consciousness in a meaningful way. We follow your posts and your progress, and we share in the heartache of each black bar placed across the BSF logo for each loss your community suffers. We know there have been far too many.

We share the perspective put forth in your petition that the results of the TAZPOWER study and its open label extension are adequate to support a New Drug Application (NDA) so that FDA can approve elamipretide in the United States. However, as we have shared publicly, FDA has recommended instead that we first conduct another clinical trial in Barth syndrome. In normal times, such a trial would take

several years to initiate and execute. The ongoing pandemic, which makes patient travel for clinic visits unadvisable, is likely to result in further delays and complications. We therefore think the potential for near-term access to elamipretide for your community is limited, barring reaching agreement with the FDA regarding a path to accelerated approval.

We believe that we have a responsibility to patient communities, particularly those such as yours who participate in our development efforts. To that end, we recently implemented an intermediate expanded access protocol that enables us to provide access to elamipretide therapy to patients suffering from rare diseases for which we do not have ongoing development initiatives. However, given FDA has not agreed that we have completed clinical development efforts in Barth syndrome, we are unable to include Barth patients in that protocol. Thus, we have no immediate avenue through which access to therapy can be offered to patients, other than emergency access for individual patients which may be permitted on a case-by-case basis.

We understand your perspective that individuals with Barth syndrome cannot wait for additional studies before receiving access to therapy. To that end, we are willing to invest the time and corporate resources in preparing and submitting an NDA for review by the FDA. This is not a commitment we make lightly, as it will require extensive effort, corporate resources, and prioritization of this program over other opportunities, and we cannot be sure, based upon the FDA's feedback to date, that the FDA will even accept our submission for review.

If our NDA submission is accepted, we recognize that the FDA would then carefully and rigorously assess whether there is substantial evidence of effectiveness supporting the approval of elamipretide for the treatment of Barth syndrome. We have previously assured the FDA of our willingness to commit to conduct additional controlled studies on a post-marketing basis following a conditional approval based on preliminary clinical and biomarker evidence collected to date. We are certainly prepared to reiterate that commitment to the FDA in the context of our further engagement with the regulators and in an NDA submission. As we further our dialogue with FDA regarding the possibility of accelerated approval, we also reiterate our commitment to ensure that your community has a seat at the table.

Warm regards,

Reenie McCarthy
Chief Executive Officer