Stealth BioTherapeutics Releases Promising Results from TAZPOWER Open-Label Extension Study in Barth Syndrome

Barth Syndrome Foundation finds encouragement in Stealth BioTherapeutics' recent published findings from the Phase 2/3 TAZPOWER OLE study that investigational drug elamipretide may improve functional activity and quality of life in individuals with the rare, life-threatening mitochondrial disease Barth syndrome. Findings from the clinical trial were shared this week at the MDA meeting in Orlando, Fla.

ORLANDO, Fla. (PRWEB) April 17, 2019 -- Stealth BioTherapeutics, a clinical-stage biotechnology company focused on novel therapies for diseases involving mitochondrial dysfunction, announced yesterday at the 2019 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference findings from the Phase 2/3 TAZPOWER and open-label extension (OLE) clinical trial evaluating efficacy of elamipretide, an investigational product that targets the binding of cardiolipin in the mitochondria, in Barth syndrome. Continued duration of therapy with elamipretide suggests favorable reductions in a key biomarker for Barth syndrome. This finding suggests elamipretide may offer therapeutic benefit by changing the underlying biology associated with Barth syndrome, resulting in improved quality of life for at least some individuals with Barth syndrome. The TAZPOWER study was the first clinical trial to test an investigational product for a potential indication in Barth syndrome.

Stealth initiated the TAZPOWER trial in 2017 upon the request of the Barth Syndrome Foundation (BSF) and received Fast Track and Orphan Drug designation from the FDA in 2017 for the study of elamipretide in Barth syndrome, a rare, life-threatening mitochondrial disease caused by a mutation in the TAZ gene. The genetic mutation leads to decreased production of tafazzin, an enzyme required to assemble cardiolipin. As a result, affected individuals can experience multiple symptoms of varying severity and incidence including heart muscle weakness (cardiomyopathy), cardiac arrhythmias, low white blood cell count (neutropenia) which can lead to serious infection, skeletal muscle weakness, delayed growth, fatigue and varying degrees of physical disability. Half of children die in their first year of life, 85% by their fifth birthday. There are presently no approved pharmacological therapies to treat Barth syndrome.

To address the severe unmet need, Hilary Vernon MD PhD, member of the BSF Scientific Medical Advisory Board and Assistant Professor at the McKusick-Nathans Institute of Genetic Medicine at John Hopkins University, conducted TAZPOWER, a double-blind, placebo-controlled cross-over trial to assess safety, tolerability, and efficacy of elamipretide. Twelve affected individuals, ages 12 and up, were randomized to receive either a once-daily subcutaneous injection of elamipretide or a placebo for an initial 12-week treatment period, followed by a four-week wash-out period, subsequently followed by a 12-week crossover to the other treatment arm. This placebo-controlled portion of the trial was completed in late 2018, and while the trial did not statistically meet the clinical primary endpoints, data collection has continued during the OLE to assess the tolerability, durability, and safety of elamipretide. The results of the OLE were shared yesterday at MDA.

Elamipretide was reported to be well-tolerated by individuals with Barth syndrome; however, injection site reactions were experienced in both groups but with higher frequency in the elamipretide treatment group.

Stealth analyzed elamipretide’s potential therapeutic effect through its association with cardiolipin. In Barth syndrome, immature, dysfunctional cardiolipin (MLCL) is present in higher concentration as compared to

normal, mature functional cardiolipin (L4-CL). When L4-CL is decreased and MLCL increases, the body's metabolism is adversely affected, which can lead to life-threatening conditions.

An analysis of the 10 participants in the TAZPOWER OLE revealed improvements in functional and patient reported outcomes. There was an inverse correlation between the average 6MWT performance and the average MLCL:L4-CL ratio. Additionally, significant improvements in the average MLCL:L4-CL ratio ($p=0.03$) were observed. This data supports the MLCL:L4-CL ratio as potentially an important biomarker in describing disease severity and potential improvement in disease.

In addition, qualitative data demonstrated improved quality of life feedback from some study participants. Examples include one participant having reported going swimming and hiking at Boy Scout camp while taking elamipretide, which he had not previously been able to do. Several boys and men reported an increase in appetite, a problem for many individuals with Barth syndrome. Another participant reported being able to walk his dog without stopping to rest and subsequently requiring less time to recover.

Hilary Vernon offered, "It has been a real privilege for me to lead the TAZPOWER study, and to have the opportunity to observe the physical and biochemical responses in our study participants."

Emily Milligan, Executive Director of BSF, also finds these improvements meaningful, "Persistent extreme fatigue is compromising to quality of life. Our community voiced this resoundingly at our Patient-Focused Drug Development (PFDD) meeting with the U.S. Food and Drug Administration (FDA). Elamipretide may offer improvements in one's functional ability to do more and live better and thusly provides a potential therapeutic for our community."

Stealth intends to request a meeting with FDA in the Spring of 2019 to discuss a plan to submit a new drug application (NDA) to FDA for elamipretide in the treatment of Barth syndrome. While BSF encourages the continued investigation of durability and tolerability of elamipretide and its potential to improve the lives of individuals living with Barth syndrome, we are hopeful that the evidence substantiated in the OLE and the testimonies provided by participants and caregivers will weigh considerably on the evaluation of elamipretide as a potential therapy for Barth syndrome.

About Barth Syndrome Foundation (BSF)
Barth Syndrome Foundation (barthsyndrome.org) is the only global network of families, healthcare providers, and researchers solely driven by the mission to save lives through education, advances in treatment and finding a cure for Barth syndrome. BSF has funded nearly $4.9M USD since 2002 and catalyzed over $21M USD in funding from other agencies to advance global scientific discoveries to end the suffering and loss of life from Barth syndrome. Additionally, BSF provides a lifeline to families and individuals living with Barth syndrome around the world, offering 24/7 individualized support, educational conferences, a robust patient registry and collaborations with specialist healthcare providers to define standards of care, treatment and rapid diagnosis.

Barth syndrome is a rare, life-threatening, genetic mitochondrial disorder primarily affecting boys. Affected individuals may suffer from heart failure, muscle weakness, and infection (caused by neutropenia). Additional characteristics of the syndrome commonly include growth delay, impaired lipid metabolism, fatigue and cardiolipin deficiency. In some individuals affected by Barth syndrome, the symptoms can be very severe, sometimes resulting in heart transplant, potentially lethal infections, and even death.

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