**TAZPOWER Analysis: Elamipretide Significantly Improves Disease Symptomatology versus Natural History Controls in Bar Syndrome**

Hilary J. Vernon1, Ryan Manuel1, John J. Jones2, Jim Carr2, Brittany Hornby1, William Reid Thompson2

1Department of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD; 2Stealth BioTherapeutics, Inc, Newton, MA; 3Department of Physical Therapy, Kennedy Krieger, Baltimore MD; 4Department of Pediatric Cardiology, Tausig Heart Center, Johns Hopkins University School of Medicine, Baltimore, MD

**INTRODUCTION**

Bar syndrome (BTHS) is a rare, X-linked disease caused by defects in TAZ, the talazekine encoding gene, required for the final remodeling step to mature cardiomyocytes, critical for mitochondrial function.

The inability to produce mature cardiomyocytes leads to clinical manifestations of BTHS, including cardiac and skeletal myopathy, neutropenia, and growth abnormalities.

Elamipretide is a water-soluble, aromatic-cationic mitochondria-targeting tetrapeptide that readily penetrates and transiently localizes to the inner mitochondrial membrane where it associates with cardiomyocytes to improve mitochondrial morphology and function in several organs (including the heart, kidney, neurons and skeletal muscle), and reduce pathogenic ROS production.

The efficacy and safety of elamipretide were studied in TAZPOWER, which was the first clinical trial to evaluate a therapeutic agent in patients with BTHS.

**OBJECTIVE**

A NHC cohort with matched propensity scoring was used to assess the effects of elamipretide in the context of the natural history of BTHS through functional and assessments and cardiac parameters.

**METHODS**

TAZPOWER was a 28-week, randomized, double-blind, placebo-controlled trial followed by an OLE.

**RESULTS**

The current analysis includes 8 patients from the TAZPOWER OLE and 19 untreated NHCs.

Key Inclusion Criteria

- Patients ≥12 years of age were required to have genetically confirmed BTHS, to be ambulatory but impaired as assessed by the 6MWT, and on stable medications.

Key Exclusion Criteria

- Patients were excluded if they had been hospitalized within 30 days, had uncontrolled hypertension or malnutrition, or implantation of a cardioverter defibrillator within 3 months or expected implantation during the study.

Natural History Comparison

- At OLE Week 72, elamipretide patients (n=19) showed greater mean improvements from baseline versus propensity matched NHCs (n=19).

- Subjects treated with elamipretide in TAZPOWER showed a significant increase from baseline in the mean distance walked based on the 6MWT, mean muscle strength by HHD, and 5XSST compared with NHCs at OLE Week 76.

- While not statistically significant, subjects treated with elamipretide in TAZPOWER showed improvement from baseline in the SWAY Balance Assessment scores at Week 72 compared with untreated NHCs.

- Statistically significant differences in MDRI were observed for subjects treated with elamipretide at OLE Week 76 compared with untreated NHCs (p=0.0001).

- Data through TAZPOWER OLE Week 72 showed sustained significant improvement in left ventricular end diastolic and end systolic (p=0.0001) volumes.

- At baseline, the mean LV and diastolic volume (SD) were lower for the TAZPOWER elamipretide patients (46.2 (8.51)) compared with the untreated NHCs at 54.41 (18.49).

- Mean post-baseline LV end-diastolic volume (SD) increased for the TAZPOWER elamipretide patients at 48.22 (8.69) mL, and decreased for the untreated NHCs at 53.5 (12.96) mL.

- The LS mean in LV end-diastolic volume observed for elamipretide TAZPOWER patients and untreated NHCs was 2.08 and -2.86, respectively, however, the LS mean difference was not significant.

**CONCLUSIONS**

TAZPOWER is the first clinical trial to evaluate the efficacy and tolerability of a potential therapeutic agent for patients in BTHS.

At baseline, ELAM-treated (n=6) and NHC BTHS patients (n=19) with similar between-group prognostic covariates (age, height, baseline 6MWT score) performed poorly on functional assessment (6MWT), with pathologic exercise symptoms of heart failure.

A treatment benefit of long-term elamipretide therapy was observed in subjects with genetically-confirmed BTHS, as shown by the statistically significant improvements from baseline in functional endpoints for subjects who were enrolled in standard treatment, compared to NHC who did not receive elamipretide treatment.

Long-term elamipretide-treated subjects showed improvements in the slope of change from baseline for left ventricular stroke volume (p=0.0001).

The authors declare that the data used in this study is compliant with ethical standards and that all participants provided informed consent.

**Figure 1. Study Design**

**Figure 2. Change from Baseline to OLE Week 76 for Elamipretide Compared with Untreated Natural History Controls**

**Figure 3. 3D LV Stroke Volume (Indexed) to Baseline BSA**

**Table 1. Baseline Prognostic Covariates: TAZPOWER Patients and Natural History Controls**
Disclosure Slide

Financial Disclosure for:

Hilary J. Vernon¹, Ryan Manuel¹, John J. Jones², Jim Carr², Brittany Hornby³, William Reid Thompson⁴

¹Department of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD; ²Stealth BioTherapeutics, Inc, Newton, MA; ³Department of Physical Therapy, Kennedy Krieger, Baltimore MD; ⁴Department of Pediatric Cardiology, Taussig Heart Center, Johns Hopkins University School of Medicine, Baltimore, MD

We have nothing to disclose
Disclosure Slide

Financial Disclosure for:

Name
Title

Xxx Company
Consultant/Consulting fee