FRIEDREICH’S ATAXIA

Friedreich’s ataxia (FA) is a rare, debilitating, life-shortening, neurodegenerative disorder caused by epigenetic silencing of the frataxin gene (FXN).

- Most patients are diagnosed in childhood, typically become wheelchair-bound within 10–15 years after diagnosis, and can survive into their mid-30s.1,4 There are approximately 22,000 patients with FA globally.1,4

Modified Friedreich’s Ataxia Scale (mFARS)

- FA progression is measured by the mFARS.
- Physician-assessed neurological exam that tracks function, upper and lower limb mobility, and gait stability.
- Validated using FAAs' 1,000 patient natural history study (FA-COMS).

Omaveloxolone is an investigational product. Safety and efficacy have not been established, nor has it been approved for use by any regulatory agency, including the US Food & Drug Administration.

MOXIE PART 2 PRIMARY EFFICACY RESULTS

- Omaveloxolone significantly improved mFARS by -2.40 points relative to placebo at Week 48 (p=0.014).
- All subsessions of mFARS and major subgroups favored Omaveloxolone.

DELABELED-START STUDY ANALYSIS METHOD

Objective:
- Comparison of the treatment difference at the end of the 48-week placebo-controlled period and the treatment difference at the end of the 72-week delayed-start period.

Study Groups:
- Omaveloxolone vs Placebo (n=34).
- Patients originally randomized to placebo in MOXIe Part 2 and initiated treatment with omaveloxolone in MOXIe Extension.

Treatment periods:
- 48-week placebo-controlled period (MOXIe Part 2) and the 72-week delayed-start period (MOXIe Extension).

Methods:
- Noninferiority test.
- Mixed model repeated measures (MMRM) fit to compare treatment difference at end of placebo-controlled period vs delayed-start period.
- Unstratified and Toeplitz covariance structures used to accommodate limited Week 72 data in MOXIe Extension.

mFARS slopes for Omaveloxolone vs placebo at Week 72 during MOXIe Extension.

MOXIE PART 2 NON-INFERIORITY RESULTS

- Difference in mFARS at end of placebo-controlled period preserved at end of delayed start.
- Non-inferiority criterion met (Upper Limit of 90% CI <0) with use of TOEPLITZ Covariance Structure.

CONCLUSION

- Delayed-start results support the positive primary endpoint findings in the pivotal MOXIe Part 2 trial.
- Maintenance of treatment effect indicates a persistent effect of Omaveloxolone on disease course in FA.
- Safety profile in MOXIe Extension similar to Part 2 and no new safety signals identified to date.

REFERENCES