Essential1: Results from a Phase 2 Trial Evaluating the Tolerability, Safety, and Efficacy of Ulixacaltamide in Adults with Essential Tremor

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Background

- Essential tremor (ET) is the most common movement disorder, with high unmet patient need.1-2
- ET is characterized by involuntary progressive tremor especially in the hands and upper limbs, contributing to patient disability.1,3
- Existing treatment options are limited, with high discontinuation rates due to poor tolerability and modest efficacy.4
- Mounting evidence indicates tremor is caused by disrupted neuronal burst firing in underlying circuitry; thought to be dependent on T-type Ca2+ channel activity.6-8
- Ulixacaltamide (PRX-944) is a novel, selective T-type Ca2+ channel blocker currently in clinical development for ET treatment.9
- Tolerability of pharmacodynamically-active doses (up to 120 mg) has been previously demonstrated,9 as well as previous evidence of tremor reduction in adults with ET.4

Methods

Essential1 Study Design

- Multi-center, randomized, double-blinded, placebo-controlled, dose-ranging trial, with optional Extension
- Participants were randomized 1:1:1 to receive 56 days of titration to 1 of 2 ulixacaltamide fixed-dose regimens (60 mg or 100 mg) or placebo, administered orally every morning.
- Safety and efficacy assessments were captured across 3 study periods: Screening/Baseline (up to 28 days); Intervention (56 days); Safety Follow-up (14 days).
- The primary efficacy endpoint was The Essential Tremor Rating Assessment Scale (TETRAS) modified Activities of Daily Living (mADL) total score, derived based on selected clinician measured TETRAS-ADL and TETRAS-Performance Subscale (TETRAS-PS) item scores.

Key Participant Inclusion and Exclusion Criteria

- Age 18-85 years
- Presence of ET ≥ 3 years duration
- Physician diagnosis of ET
- [TETRAS-PS score at Baseline ≥ 2] OR
- [Modified TETRAS ADL score at Baseline ≥ 2]
- [Global impression of ET - moderate to severe]

Participant Disposition and Baseline Characteristics

- 132 adults were randomized and treated; 116 were included eligible for V4), who were randomized to treatment, and received at least 1 dose of study drug (n = 116).

Ulixacaltamide Was Generally Well-tolerated

Nominal statistically significant improvements were observed in CGI-S and PGI-C.

- Ulixacaltamide was well tolerated, with no new safety findings.
- 3 SAEs in 2 subjects, all deemed unrelated to treatment (exacerbation of COPD in 1 patient; Discontinued

Conclusions

- Ulixacaltamide demonstrated improvement in the mADL primary efficacy endpoint relative to placebo that did not reach statistical significance, and achieved nominal statistical significance in the TETRAS-ADL secondary endpoint.
- Nominal statistically significant improvements were observed in CGI-S and PGI-C.
- Ulixacaltamide was well tolerated, with no new safety findings.
- Based on the observed efficacy and safety profile, we will engage with the FDA in an end of Phase 2 meeting in June 2023 and intend to initiate the ulixacaltamide Phase 3 program for the treatment of ET in 2H23.

References

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