Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Modulator, In Adults With Focal Epilepsy (X-TOLE)

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OBJECTIVES We conducted a 14-week, double-blind, randomized, placebo-controlled, parallel-group, dose-finding study to assess the clinical efficacy, safety, and tolerability of XEN1101, a novel potassium channel modulator, in adults with focal onset seizures (FOS).

METHODS Adults aged ≥18 years with ≥6 months of stable focal-onset seizure disorder who were on ≤3 background antiseizure medications (ASMs) and baseline mean daily event count ≥5 or ≥75% reduction were randomized 1:1:1 to XEN1101 14 mg, 20 mg, or 25 mg, or placebo, in a double-blind, 8-week blinded phase followed by a planned 6-week open-label extension (OLE). The primary endpoint was the change from baseline in frequency of total monthly seizures. Secondary endpoints included: change from baseline in frequency of focal seizures, patient-rated seizure severity, and Global Impression of Change (GIC) score. Exploratory endpoints included time to event analyses:

RESULTS 114 subjects were randomized to placebo (N=38), XEN1101 14 mg (N=38), XEN1101 20 mg (N=21), XEN1101 25 mg (N=27). XEN1101 20 mg and 25 mg were statistically significantly more efficacious than placebo with a median 60.5% and 85.1% reduction, respectively, in monthly frequency of total seizures compared to placebo (both P < 0.001). The change in monthly frequency of focal seizures was statistically significant with XEN1101 20 mg and 25 mg (both P < 0.001), with a median 62.9% and 81.2% reduction, respectively, compared to placebo. Onset and offset of changes were rapid, and effect sizes were consistent across seizure types. There were no statistically significant differences between treatment groups.

CONCLUSIONS XEN1101 showed dose-dependent, consistent, highly statistically significant and clinically meaningful reduction in total and focal seizures in a patient population who had failed 1 or more of 1-2 ASMs and were on 3 background ASMs. Based on the strong Phase 2b topline results from the X-TOLE study, Xenon intends to gather input from regulatory agencies on the potential clinical development for XEN1101.