**Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Opener, in Adults With Focal Onset Seizures (X-TOLE)**

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**XEN1101 is an oral, small-molecule, selective TRESK (KCNK3) potassium channel opener being developed for the treatment of focal onset seizures and major depression.**

**Primary endpoints** included:

- **Clinical Global Impression of Change** (21-item CGI-C; 1-7 scale; 1 = worst, 7 = best);
- **Pediatric Epilepsy Psychosocial Impact Scale** (PEPIS; 0 = none, 100 = worst possible);
- **Epilepsy Symptom Index** (ESI; 0 = none, 100 = worst possible);
- **SUNRISE** (state-units to respond in seizures within 2 weeks of taking a new drug).

**Secondary endpoints** included:

- **Phase 2b placebo-controlled, double-blind, parallel group, dose-ranging, multicenter study with an optimal 6-week double-blind treatment period** (N=114)

**XEN1101** was generally well tolerated, with a similar low SAE incidence (3.3%) as seen in placebo (2.6%) and balanced across treatment arms. Of the 114 subjects enrolled, 91 (79.7%) completed the study. Of the 23 (20.3%) withdrawn, 15 (65.2%) withdrew due to AEs.

**SAE incidence was low and balanced across groups.** There were no safety signals of concern from physical or neurologic exams or imaging studies.

**CONCLUSIONS**

- **XEN1101 demonstrated a dose-dependent and highly statistically significant reduction in COG-C/GSI-C.**
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- **XEN1101 was generally well tolerated with a similar low SAE incidence (2.6%) as seen in placebo (2.6%) and balanced across the study.**

- **The most common TEAEs leading to discontinuation across XEN1101 groups were diarrhea (2.2%), abdominal pain (2.2%), and palpitations (1.6%).**

- **There were no psychiatric adverse events of concern in CGI-C or CGI-S.**

- **Among the strong Phase 2a durability results from the X-TOLE study, Xenon intends to gather input from the E�IC and other regulatory agencies to continue planning the future clinical development of XEN1101.**