XEN1101 is a novel, small-molecule, selective K<sub>2.2/7.3</sub> potassium channel opener being developed for the treatment of focal onset seizures, primary generalized tonic-clonic seizures (PGTCS), and major depressive disorder.

- **Inclusion Criteria:**
  - History of status epilepticus, recurrent/epileptic seizures
  - Frequency of ≥3 PGTCS during the 8- to 9.5-week screening/baseline and taking 1–3 antiseizure medications (ASMs)
  - Diagnosis of PGTCS (≥2 years, ILAE 2017 classification)
  - Taking ≥5 PGTCS per month
  - Fasted for ≥2 AASMs
  - History of status epilepticus, repetitive seizures, or focal seizures
  - History of neuropsychiatric seizures: >1 year prior to visit

**Secondary endpoints:**
- Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS frequency from baseline through the DBP for XEN1101 vs placebo
- Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS frequency from baseline through the DBP for XEN1101 vs placebo
- Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS severity from baseline through the DBP for XEN1101 vs placebo
- Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS frequency from baseline through the DBP for XEN1101 vs placebo

**Primary efficacy endpoint:**
- Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS frequency from baseline through the DBP for XEN1101 vs placebo

**Primary safety endpoint:**
- Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS severity from baseline through the DBP for XEN1101 vs placebo

- **X-ACKT Study Design**
  - Up to 9.5 weeks
  - Screening/Baseline
  - ≤1 week (no titration required)
  - DBP 12 weeks
  - Follow-up: 8 weeks

- **Endpoints**
  - Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS frequency from baseline through the DBP for XEN1101 vs placebo
  - Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS severity from baseline through the DBP for XEN1101 vs placebo
  - Proportion of participants experiencing ≥50% reduction in monthly (28-day) PGTCS frequency from baseline through the DBP for XEN1101 vs placebo

**Clinical labs, ECGs and vital signs**
- Changes in clinical labs, ECGs and vital signs
- Changes in neurological and ophthalmic exams

**AE, adverse event; ASM, antiseizure medication; DBP, double-blind treatment period; ECG, electrocardiogram; ILAE, International League Against Epilepsy; MPC, median percentage change; PGTCS, primary generalized tonic-clonic seizures; PGIC, Patient Global Impression of Change; QD, once daily; TLAD, treatment-emergent adverse event.

**Further Trial Contact Details:** To inquire about becoming an investigator, please contact X-ACKT@xenon-pharma.com.

**For other general questions, please contact medicalaffairs@xenon-pharma.com.

**SUMMARY**
- X-ACKT will provide insight into the safety, tolerability, and efficacy of XEN1101 as an adjunctive therapy in the treatment of PGTCS and is designed to support FDA registration of XEN1101 for the treatment of PGTCS
- If approved, this would be the only-in-class K<sub>2.2/7.3</sub> opener ASM with once-daily administration with no titration required.