X-TOLE2 AND X-TOLE3 PHASE 3 STUDIES

**X-TOLE2** (NCT03514063) and X-TOLE3 are identical phase 3, multicenter, randomized, double-blind, placebo-controlled trials to evaluate the clinical efficacy, safety, and tolerability of XEN1101 administered as adjunctive therapy in patients with FOS. All data presented are from the double-blind treatment period (DBP).

- **XEN1101 showed a dose-dependent and highly statistically significant reduction (P<0.001 for 20 mg and 25 mg QD) in FOS frequency in all endpoints in patients who had a median of 6 antiepileptic mediations (AEMs); 50.8% of the population were on 3 background AEMs.**

- **XEN1101 was generally well tolerated with a similar low incidence of adverse events compared to placebo, except an increased incidence of pigmented dimers.**

**Table 1. X-TOLE2 and X-TOLE3 Primary and Key Secondary Objectives and Endpoints**

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Endpoints</th>
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<tr>
<td>To assess the effect of XEN1101 on patients on reducing FOS frequency</td>
<td>MPC in monthly (28 day) FOS frequency from baseline through the DBP (12 weeks/84 days)</td>
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<tr>
<td>To assess the early treatment effect of XEN1101 vs placebo on FOS frequency</td>
<td>Proportion of participants experiencing ≥50% reduction in monthly (28 day) FOS frequency from baseline through the DBP of 12 weeks</td>
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<tr>
<td>To assess the safety and tolerability of XEN1101</td>
<td>Proportion of patients experiencing at least “much improved” or “very much improved” in PGIC at week 12</td>
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**Preclinical Data**

- XEN1101 has been evaluated in phase 1 clinical studies, including a companion pharmacodynamic crossover study using transcranial magnetic stimulation. These data demonstrated that dosing XEN1101 up to 25 mg QD was generally well tolerated and reduced cortical excitability, with a strong pharmacokinetic/pharmacodynamic relationship in healthy volunteers.

**Pharmacokinetics**

- The pharmacokinetic properties of XEN1101 support once-daily (QD) oral dosing without the need for titration at initiation of dosing or tapering at termination of dosing.

**Pharmacodynamics**

- XEN1101 is being developed for the treatment of focal onset seizures (FOS), primary generalized tonic-clonic seizures, and major depressive disorder.

**REFERENCES**


**Summary**

- X-TOLE2 and X-TOLE3 will provide insight into the safety, tolerability, and efficacy of XEN1101 in FOS. These studies are designed to further evaluate the therapeutic potential of XEN1101 and support registration of XEN1101 as a novel ASM for the treatment of adults with FOS.

- XEN1101 has a novel mechanism of voltage-gated potassium channel opening and would be the only-in-class, K,7,2,7.3 opener ASM, if approved.