A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Evaluate the Safety and Efficacy of XEN1101 as an Adjunctive Therapy in the Primary Generalized Tonic-Clonic Seizures

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REFERENCES
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XEN1101
- XEN1101 is a novel, potent, selective IKNaC/1.3 (K.7.2/7.3) potassium channel opener being developed for the treatment of focal onset seizures, primary generalized tonic-clonic seizures (PGTCS), and major depressive disorder
- XEN1101 has shown antiseizure activity in maximum electroshock shock and pentyleneetetrazole preclinical models, both known to predict efficacy for primary generalized seizures1
- ICA-1056635, a K+ potassium channel opener, suppressed photosensitivity (electroencephalogram model) in patients with generalized epilepsy2
- Levetiracetam, valproic acid, lamotrigine, and brivaracetam (not approved for PGTCS) suppressed photosensitivity in patients with generalized epilepsy and demonstrated broad impact across all focal seizure subtypes, including those that progressed to generalized seizures3
- In the phase 2b X-TOLE study in patients with focal onset seizures, XEN1101 demonstrated broad impact across all focal seizure subtypes, including those that progressed to generalized seizures3
- These data support the broad-spectrum potential of XEN1101 in XEN1101 and provide the rationale for a trial of XEN1101 in patients with PGTCS
- The X-ACKT study in patients with PGTCS is designed to support US Food and Drug Administration (FDA) registration

X-ACKT STUDY
- X-ACKT (NCT05667142) is a phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the pharmacokinetics, safety, and efficacy of XEN1101 in the fed state in adults aged ≥18 years with a seizure frequency of ≥3 PGTCS over an 8- to 9.5-week screening/baseline and taking 1-3 antiseizure medications (ASMs)

Table 1. X-ACKT Primary and Key Secondary Endpoints and Objectives

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Primary</th>
<th>Endpoints</th>
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<tbody>
<tr>
<td>To assess the effect of XEN1101 vs placebo on reducing PGTCS frequency</td>
<td>MPA in monthly (28 day) PGTCS frequency from baseline through the DBP (12 weeks)</td>
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<tr>
<td>To assess the effect of XEN1101 vs placebo on reducing PGTCS frequency</td>
<td>Proportion of participants experiencing ≥50% reduction in monthly (28 day) PGTCS frequency from baseline through the DBP</td>
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<tr>
<td>To assess the safety and tolerability of XEN1101</td>
<td>Severity and frequency of adverse events</td>
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Figure 1. X-ACKT Study Design

REFERENCES
7. Medical writing support was provided by Robin Smith, PhD, of The Curry Rockefeller Group, LLC (Tarrytown, NY), and was funded by Xenon Pharmaceuticals Inc.

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DISCLOSURES
Antonio Gil-Nagel Rein: personal fees from advisory boards and a speaker from Arvelle/Angelini, Bial, Biocodex, Eisai, Grifols, GW Pharma, Pharmacia, Biocodex, Pfizer, Takeda, UCB Pharma, Lycera, and personal fees from Dharan, Avenir Pharmaceutiques, Avenir, PTC Therapeutics, and Arvelle. Antonio Gil-Nagel Rein is a co-founder and Chief Scientific Officer of Angelini, Avenir Pharmaceutiques, and Angelini. Antonio Gil-Nagel Rein has filed patent applications regarding the use of Angelini compounds in the treatment of seizures.

Elinor Ben-Menachem: consultant for Theracos, Grifols, Avenir Pharmaceuticals, and speaker for Avenir. Elinor Ben-Menachem is a co-founder and Chief Scientific Officer of Angelini, Avenir Pharmaceutiques, and Angelini. Elinor Ben-Menachem has filed patent applications regarding the use of Angelini compounds in the treatment of seizures.

W. Curt LaFrance, Jr: editorial boards of Epilepsia, Epilepsy & Behavior, Journal of Neurology, Neurosurgery and Psychiatry, and Epilepsy Foundation News. W. Curt LaFrance, Jr: has received advisory board payments from George Washington University and is a member of the board of directors for the International League Against Epilepsy. W. Curt LaFrance, Jr: has received personal fees from Angelini, Avenir, PTC Therapeutics, and Allergan.

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SUMMARY
- X-ACKT will provide insight into the safety, tolerability, and efficacy of XEN1101 as 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,7.2/7.3 opener ASM with once-daily administration without any titration required