
# Topline Results from XEN1101 “X-TOLE” Phase 2b Clinical Trial

OCTOBER 4, 2021

# Forward Looking Statement/Safe Harbor

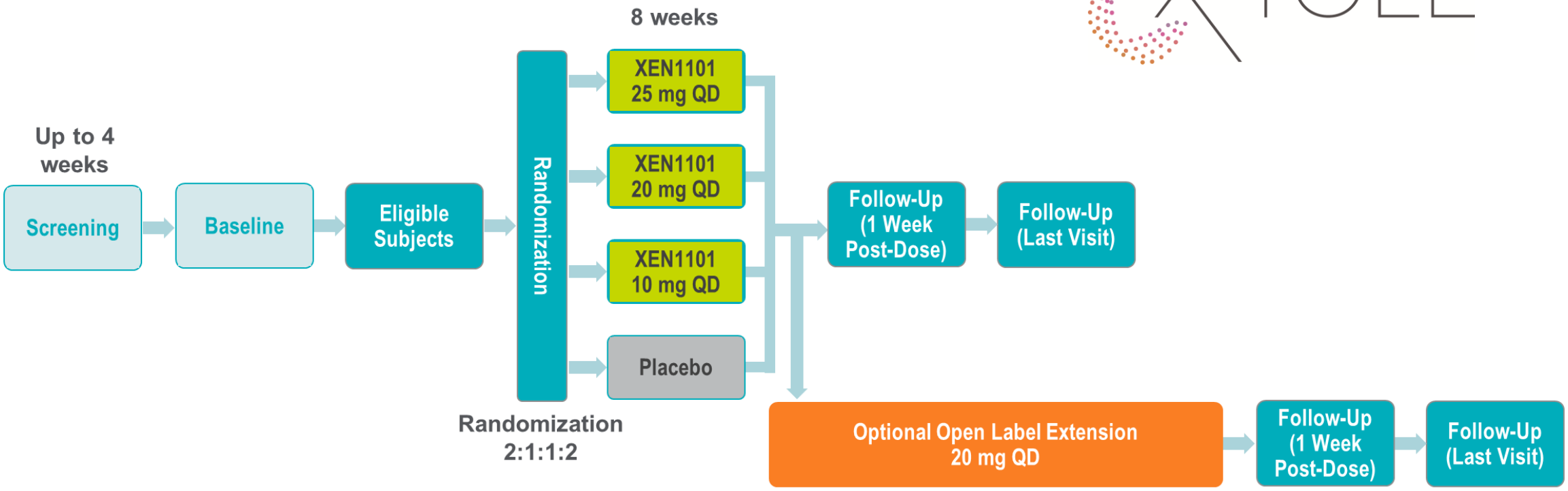
This slide presentation and the accompanying oral commentary contain forward-looking statements that involve risks, uncertainties and assumptions. If the risks or uncertainties ever materialize or the assumptions prove incorrect, our results may differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to, statements regarding research and clinical development plans and timelines; the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN1101 and other proprietary products, and those related to partnered product candidates; the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN1101 and other proprietary and partnered product candidates; the anticipated timing of IND, or IND-equivalent, submissions and the initiation of future clinical trials for XEN1101 and other proprietary products, and those related to partnered candidates; the efficacy of our clinical trial designs; the timing and results of our planned interactions with regulators regarding XEN1101; our ability to successfully develop and obtain regulatory approval of XEN1101; our ability to successfully develop and achieve milestones in the XEN1101 and other proprietary development programs; the timing and results of our interactions with regulators; anticipated enrollment in our clinical trials and the timing thereof; the progress and potential of our other ongoing development programs; the potential receipt of milestone payments and royalties from our collaborators; and the timing of potential publication or presentation of future clinical data.

These statements are based on estimates and information available to us at the time of this presentation and are not guarantees of future performance. Actual results could differ materially from our current expectations as a result of many factors, including but not limited to: the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; our assumptions regarding our planned expenditures and sufficiency of our cash to fund operations may be incorrect; our ongoing discovery and pre-clinical efforts may not yield additional product candidates; any of our or our collaborators' product candidates, including XEN1101, may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; we may not achieve additional milestones in our proprietary or partnered programs; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; regulatory agencies may be delayed in reviewing, commenting on or approving any of our or our collaborators' clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; impact of new or changing laws and regulations; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission and the securities commissions in British Columbia, Alberta and Ontario. Except as required by law, we assume no obligation and do not intend to update these forward-looking statements or to conform these statements to actual results or to changes in our expectations.

# Executive Summary

| | |
|---|---|
| **Summary of Key Findings** | • X-TOLE primary efficacy endpoint with XEN1101 demonstrated a statistically significant dose-dependent reduction from baseline in monthly focal seizure frequency when compared to placebo (monotonic dose response; p<0.001)<br>• The median percent reduction in monthly focal seizure frequency was 52.8% (2-sided p-value <0.001) in the XEN1101 25 mg group, 46.4% (2-sided p-value <0.001) in the XEN1101 20 mg group, and 33.2% (2-sided p-value = 0.035) in the XEN1101 10 mg group compared to 18.2% in the placebo group |
| **Efficacy** | • Efficacy demonstrated in X-TOLE suggests a highly CNS-active profile for XEN1101, meeting statistical significance in reduction from baseline in monthly focal seizure frequency compared to placebo and 50% reduction in monthly focal seizures versus placebo in all dosing groups<br>• XEN1101 demonstrated clear and statistically significant dose response with consistency across endpoints<br>• Statistically significant improvements in CGI-C and PGI-C were demonstrated for the 25 mg group |
| **Safety / Tolerability** | • XEN1101 was generally well-tolerated in this study with adverse events consistent with other commonly utilized ASMs<br>• The most common treatment-emergent adverse events across all XEN1101 dose groups were dizziness, somnolence, fatigue, and headache<br>• No TEAEs of pigmentary abnormalities reported during the double-blind phase of the study or in preliminary analysis during the ongoing open label extension to date with approximately 70 subjects now treated more than 12 months |
| **Commercial Outlook / Next Steps** | • The outcome of X-TOLE suggests that XEN1101 offers a clinical profile that could be highly competitive in the future adult focal seizure market<br>• XEN1101 has the potential to offer compelling efficacy that when combined with other desirable attributes such as QD dosing, no titration, and broad-spectrum activity could make XEN1101 a highly attractive agent in the future adult FOS landscape |

# XEN1101 “X-TOLE” Phase 2b Study Design



# Primary / Secondary Objectives of X-TOLE Study

## A Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Safety, Tolerability, and Efficacy of XEN1101 as Adjunctive Therapy in Focal-onset Epilepsy, with an Open-label Extension

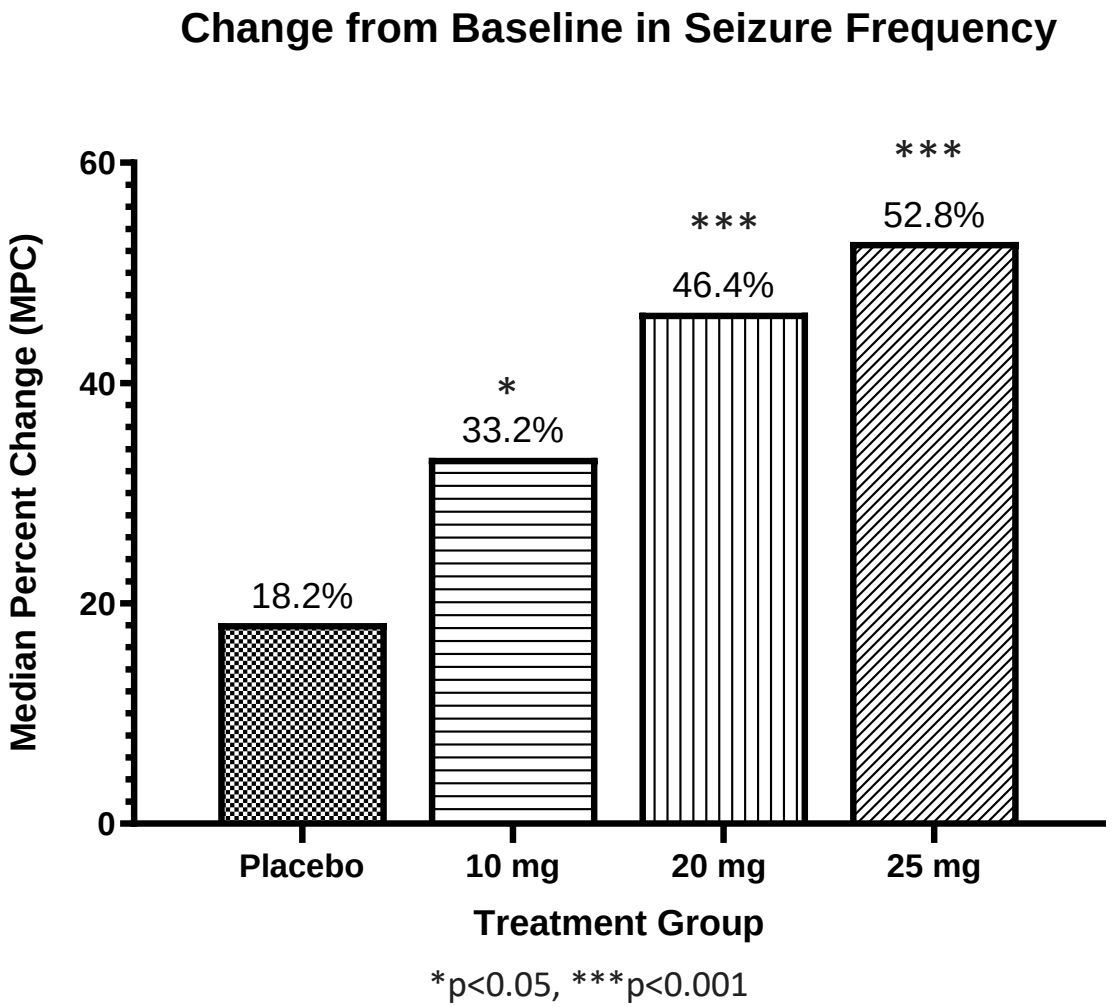
| | OBJECTIVES | ENDPOINTS |
|---|---|---|
| Primary Objectives | To assess the efficacy of XEN1101 compared to placebo on focal seizure frequency in adults with focal epilepsy taking 1 to 3 ASMs in the double-blind period (DBP) | • Median percent change (MPC) in monthly (28 days) focal seizure frequency from baseline to DBP for XEN1101 versus placebo |
| | To assess the safety and tolerability of XEN1101 in adults with focal epilepsy taking 1 to 3 ASMs in the DBP | In the DBP:<br>• Severity and frequency of associated AEs/serious adverse events (SAEs)<br>• Clinically significant changes in clinical laboratory findings<br>• Clinically significant changes in 12-lead ECG<br>• Change in suicidality risk as assessed by the C-SSRS including increase in suicidal thoughts or an attempt<br>• Clinically significant changes in vital signs including blood pressure, pulse, or weight<br>• Clinically significant changes in urological symptoms including retention as measured by the American Urological Association (AUA) Symptom Index |
| Secondary Objectives | To evaluate the 50% XEN1101 response rates in comparison to placebo in the DBP | • Responders are defined as patients experiencing ≥50% reduction in monthly (28 days) focal seizure frequency from baseline compared to DBP |
| | To evaluate trends in focal seizure frequency over time in the DBP | • Percent change from baseline in weekly focal seizure frequency for each week of the DBP |
| | To assess the effect of XEN1101 vs placebo on seizure severity and impact in adults with focal epilepsy taking 1 to 3 ASMs in the DBP | • Clinical Global Impression of Change (CGI-C) and Patient Global Impression of Change (PGI-C) scores during the DBP |

# Demographics and Baseline Characteristics (Safety Population)

| | Placebo (N=114) | XEN1101 10mg (N=46) | XEN1101 20mg (N=51) | XEN1101 25mg (N=114) | TOTAL (N=325) |
|---|---|---|---|---|---|
| **Age in years, Mean (SD)** | **42.9 (13.7)** | **40.0 (12.1)** | **41.7 (13.6)** | **38.7 (13.1)** | **40.8 (13.3)** |
| **Age at study entry category** | | | | | |
| ≥ 65, n (%) | **5 (4.4)** | **2 (4.3)** | **4 (7.8)** | **1 (0.9)** | **12 (3.7)** |
| < 65, n (%) | **109 (95.6)** | **44 (95.7)** | **47 (92.2)** | **113 (99.1)** | **313 (96.3)** |
| **Gender** | | | | | |
| Female, n (%) | **61 (53.5)** | **27 (58.7)** | **26 (51.0)** | **54 (47.4)** | **168 (51.7)** |
| Male, n (%) | **53 (46.5)** | **19 (41.3)** | **25 (49.0)** | **60 (52.6)** | **157 (48.3)** |
| **Region** | | | | | |
| Europe, n (%) | **67 (58.8)** | **31 (67.4)** | **32 (62.7)** | **68 (59.6)** | **198 (60.9)** |
| North America, n (%) | **47 (41.2)** | **15 (32.6)** | **19 (37.3)** | **46 (40.4)** | **127 (39.1)** |
| **Background ASM Use** | | | | | |
| 1, n (%) | **12 (10.5)** | **4 (8.7)** | **2 (3.9)** | **11 (9.6)** | **29 (8.9)** |
| 2, n (%) | **46 (40.4)** | **18 (39.1)** | **20 (39.2)** | **47 (41.2)** | **131 (40.3)** |
| 3, n (%) | **56 (49.1)** | **24 (52.2)** | **29 (56.9)** | **56 (49.1)** | **165 (50.8)** |
| **Number of Pre-study ASMs failed** | | | | | |
| Median [Q1, Q3] | **6.0 [3.0, 8.0]** | **5.0 [4.0, 9.0]** | **6.0 [4.0, 9.0]** | **5.5 [3.0, 9.0]** | **6.0 [4.0, 9.0]** |

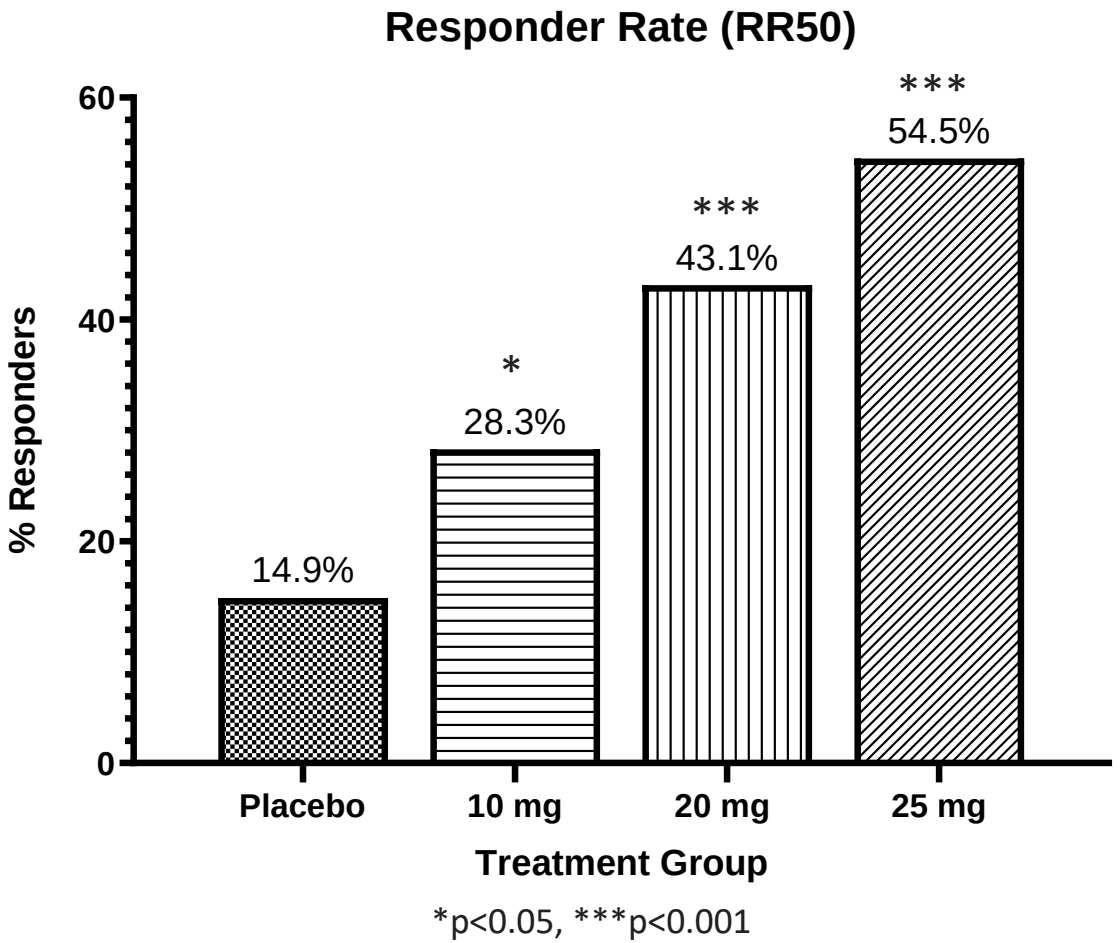
Arms well balanced and representative of a difficult to treat adult FOS patient population

# Summary of Overall Efficacy Readout




- Data suggest a highly statistically significant dose-response relationship for XEN1101 in the adjunctive treatment of focal seizures in adult patients with focal epilepsy
- Primary efficacy endpoint highly statistically significant ($p<0.001$) in 20 mg and 25 mg dose groups
- Efficacy demonstrated in difficult to treat patient population with significant burden of disease
- Efficacy data signal activity of XEN1101 in the central nervous system

# Secondary Endpoint: Responder Rates and CGI-C/PGI-C




| | XEN1101 25 mg (N=112) | Placebo (N=114) |
|---|---|---|
| CGI-C (Portion of Patients Much Improved or Very Much Improved) | 46.4% (p<0.001) | 22.8% |
| PGI-C (Portion of Patients Much Improved or Very Much Improved) | 42.9% (p=0.001) | 21.9% |

Highly significant dose dependent increase in responder analysis in all dose groups and statistically significant improvements in CGI-C/PGI-C in the 25 mg dose group

# Summary of All TEAEs* in the DBP (Safety Population)

| Subjects with n(%) | Placebo (N=114) | XEN1101 10mg (N=46) | XEN1101 20mg (N=51) | XEN1101 25mg (N=114 ) | XEN1101 Any dose (N=211) |
|---|---|---|---|---|---|
| At least one TEAE | 71 (62.3) | 31 (67.4) | 35 (68.6) | 97 (85.1) | 163 (77.3) |
| At least one serious TEAE | 3 (2.6) | 2 (4.3) | 2 (3.9) | 3 (2.6) | 7 (3.3) |
| At least one TEAE leading to permanent treatment discontinuation | 4 (3.5) | 1 (2.2) | 7 (13.7) | 18 (15.8) | 26 (12.3) |
| At least one serious TEAE leading to death | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

*TEAE: Treatment Emergent Adverse Event i.e. AEs started or worsened in Double Blind Phase including 6 weeks of follow-up

SAEs balanced across treatment groups

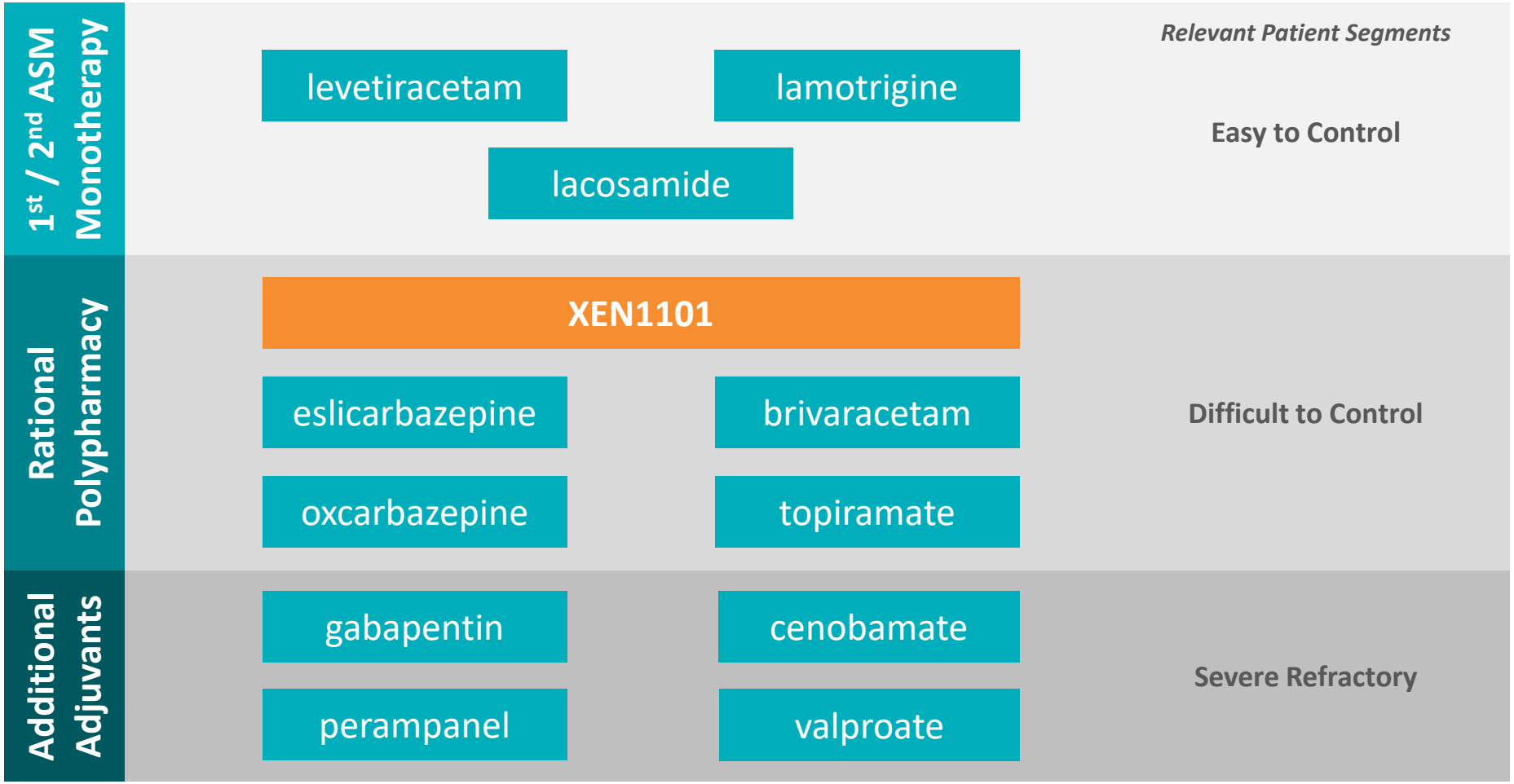
# Overall Adverse Event Profile

- XEN1101 was generally well-tolerated in this study with adverse events (AEs) consistent with other commonly prescribed ASMs
- The most common treatment emergent adverse events across all XEN1101 dose groups were dizziness (n=52, 24.6%), somnolence (n=33, 15.6%), fatigue (n=23, 10.9%), and headache (n=21, 10.0%)
- Two TEAEs of urinary retention were reported in the active treatment groups, one of which required a dose reduction, and both subjects remained on drug with no other changes or intervention
- There have been no TEAEs of pigmentary abnormalities reported during the double-blind phase of the study or in preliminary analysis during the ongoing OLE to date
- Electrocardiogram changes were evenly balanced between placebo and active treatment groups

Safety and tolerability profile in line with commonly used ASMs

# XEN1101 Clinical Positioning

**Potential Future Treatment Paradigm**




Source: Blinded Xenon Market Research

# Summary

## XEN1101 Value Proposition

### Efficacy

- Compelling efficacy data in difficult to treat adult FOS patient population
- Strong combination data supporting polypharmacy use (50.8% of patients on 3 ASMs in trial)
- May provide mood benefit beyond seizure control

### Ease of Use

- One pill, once-daily
- No titration required
- Unique and novel MOA can be leveraged in rational polypharmacy
- Forgiving PK provides coverage for missed doses

### Safety / Tolerability

- Well-tolerated with AE profile in line with other ASMs
- Evening dose results in $C_{max}$ during sleep
- No drug allergic reactions observed
- No TEAEs of pigmentary abnormalities