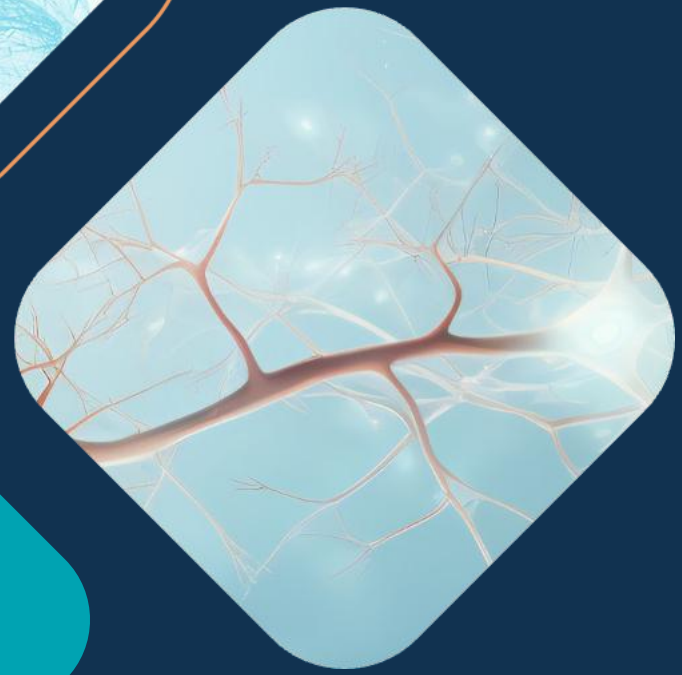


Corporate Overview

2026 J.P. MORGAN HEALTHCARE CONFERENCE
JANUARY 2026

NASDAQ: XENE
xenon-pharma.com

Xenon™

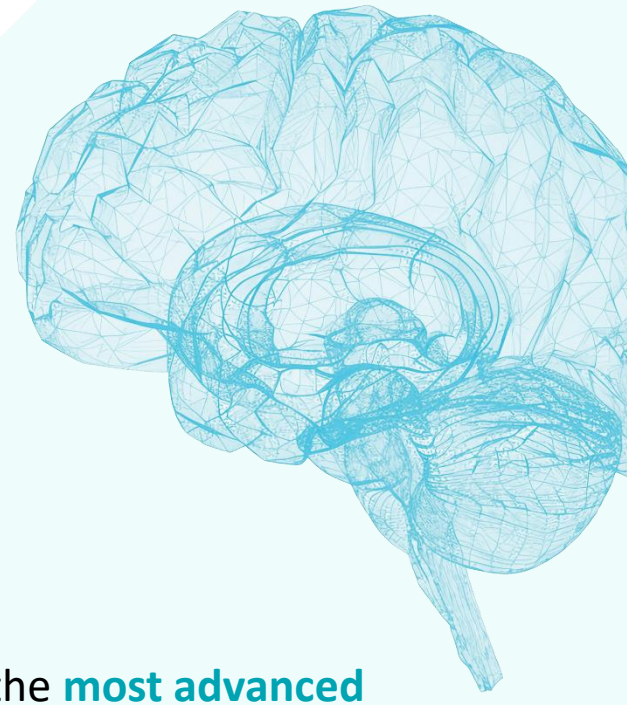
Forward Looking Statement/Safe Harbor

This slide presentation and the accompanying oral commentary contain forward-looking statements (within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995 and Canadian Securities laws) 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 and include statements regarding the timing of and potential results from clinical studies; the potential efficacy, safety profile, future development plans in current and anticipated indications, addressable market, regulatory success and commercial potential of our and our partners' product candidates; the efficacy of our clinical study designs; our ability to successfully develop and achieve milestones in our azetukalner and other pipeline and development programs, including the anticipated filing of INDs and NDAs; the timing and results of our interactions with regulators, including the timing of any NDA submission; our ability to successfully develop and obtain regulatory approval of azetukalner and our other product candidates; anticipated timing of topline data readout from our clinical studies of azetukalner; and our expectation that we will have sufficient cash to fund operations into 2027.

These forward-looking statements are based on current assumptions that involve risks, uncertainties and other factors that may cause the actual results, events, or developments to be materially different from those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: clinical studies may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; promising results from pre-clinical development activities or early clinical study results may not be replicated in later clinical studies; 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 azetukalner, 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 or completion of clinical studies; the impact of market, industry, and regulatory conditions on clinical study enrollment; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; the impact of new or changing laws and regulations; the impact of unstable economic conditions in the general domestic and global economic markets; adverse conditions from geopolitical events; as well as the other risks identified in our filings with the U.S. Securities and Exchange Commission and the securities commissions in British Columbia, Alberta, and Ontario. These forward-looking statements speak only as of the date hereof and we assume no obligation to update these forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

About Xenon Pharmaceuticals

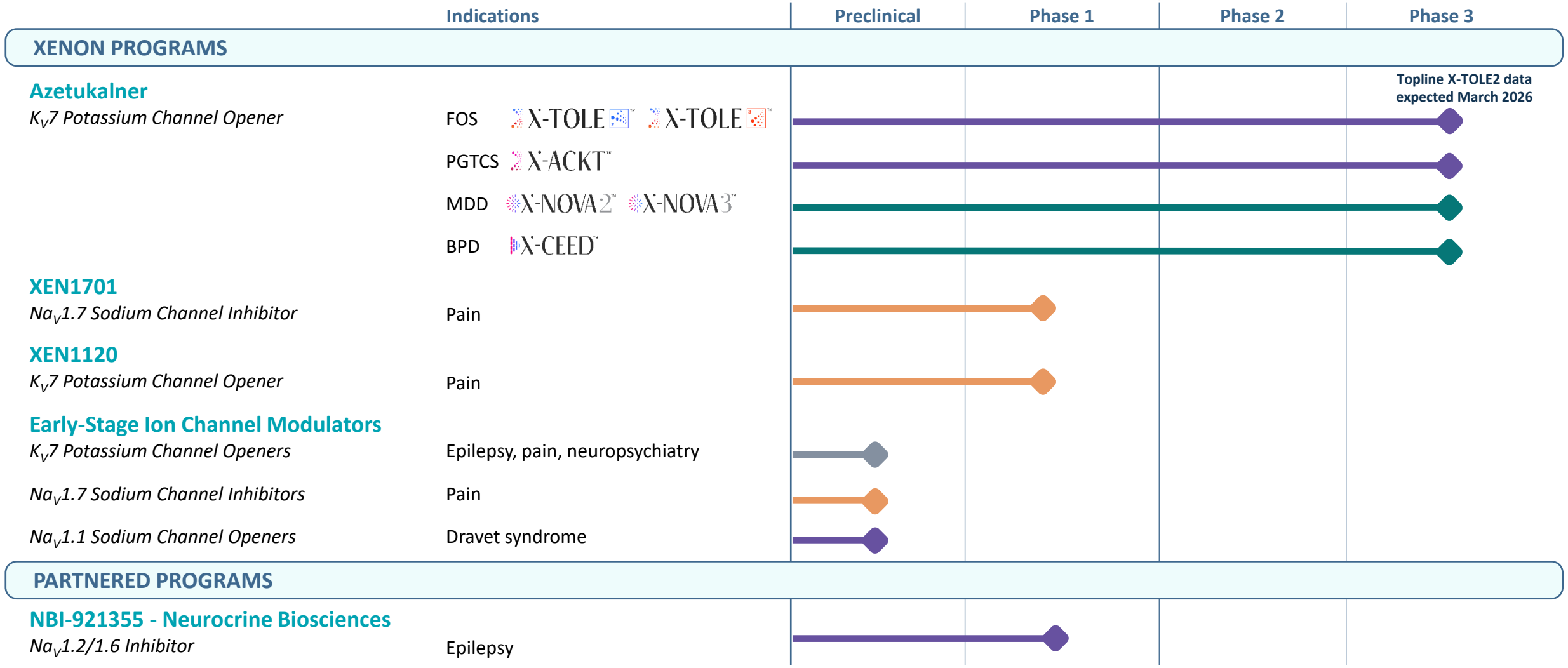
- Neuroscience-focused biopharmaceutical company and leader in small molecule, ion channel drug discovery and development
- Robust pipeline of therapeutic candidates targeting potassium and sodium channels across various indications
- Lead molecule, azetukalner, is a highly potent K_V7 channel opener in Phase 3 development in epilepsy and depression
- Strong financial position
  - $555.3 million in cash, cash equivalents and marketable securities (as of September 30, 2025) and anticipated cash runway to fund operations into 2027



AZETUKALNER (AZK) is the **most advanced** potassium channel modulator in late-stage clinical development across multiple indications and the **only K_V7 program with 800+ patient-years of efficacy & safety data**

Azetukalner is an investigational drug that has yet to be approved by the FDA

Xenon's Neuroscience-Focused Pipeline



This chart displays pipeline drug candidates currently undergoing clinical and pre-clinical testing in a variety of disease indications. The safety and efficacy of these investigational drug candidates have not been fully evaluated, and they have not yet been approved for use by any regulatory authorities.

FOS: Focal onset seizures; PGTCS: Primary generalized tonic-clonic seizures; MDD: Major depressive disorder; BPD: Bipolar depression
Purple: epilepsy; Green: depression; Orange: pain; Grey: multiple

Azetukalner's Significant Potential Across Epilepsy & Neuropsychiatry

Robust Clinical Efficacy

- Highly compelling double-blind efficacy data in FOS patients, durable long-term seizure freedom data as demonstrated in the ongoing OLE
- Clinically meaningful activity in depression and significant reductions in anhedonia observed in MDD patients

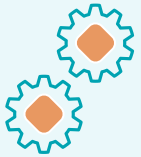
Well-Documented Safety Profile

- More than 800 patient years of data in FOS patients, with some dosed for more than 5 years
- Potentially differentiated profile in MDD patients, with no notable weight gain or sexual dysfunction observed

Ease-of-Use

- Once-daily dosing and no required titration, enabling potential for rational polypharmacy
- No meaningful DDIs or anticipated monitoring requirements

Novel Mechanism



- Highly potent $K_V7.2/7.3$ potassium channel opener with no activity on $GABA_A$

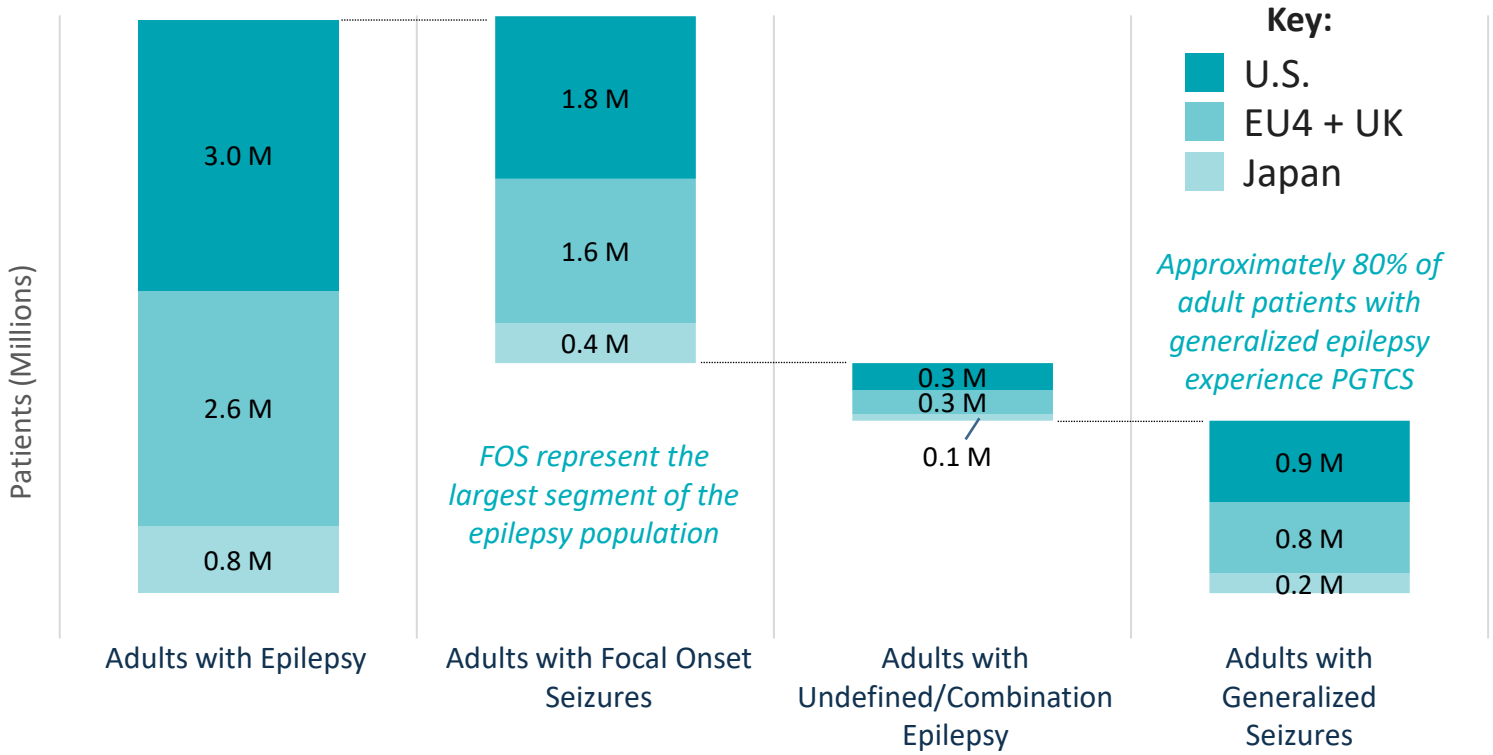
Source: 1. "Long-Term Safety and Efficacy of Azetukalner, a Novel, Potent KV7 Potassium Channel Opener, in Adults With Focal Epilepsy: ≥48-Month Interim Analysis of the Ongoing 7-Year X-TOLE Open-Label Extension." 2025 Annual Meeting of the American Epilepsy Society (AES). 2. French JA et al. JAMA Neurol.2023;80(11):1145-1154.cc

Azetukalner & Epilepsy Market Opportunity

Significant Global Epilepsy Burden

- Epilepsy is the **fourth most common neurological condition**
- Hallmark symptoms include:
  - **focal seizures** that start in one brain hemisphere (either aware or unaware)
  - **generalized seizures** the most common of which are tonic-clonic/convulsive seizures
- Despite the availability of multiple ASMs, a **substantial unmet medical need exists – up to 50% of epilepsy patients require additional treatment options**
- Rates of **comorbid depression** exist in up to 50% of epilepsy patients

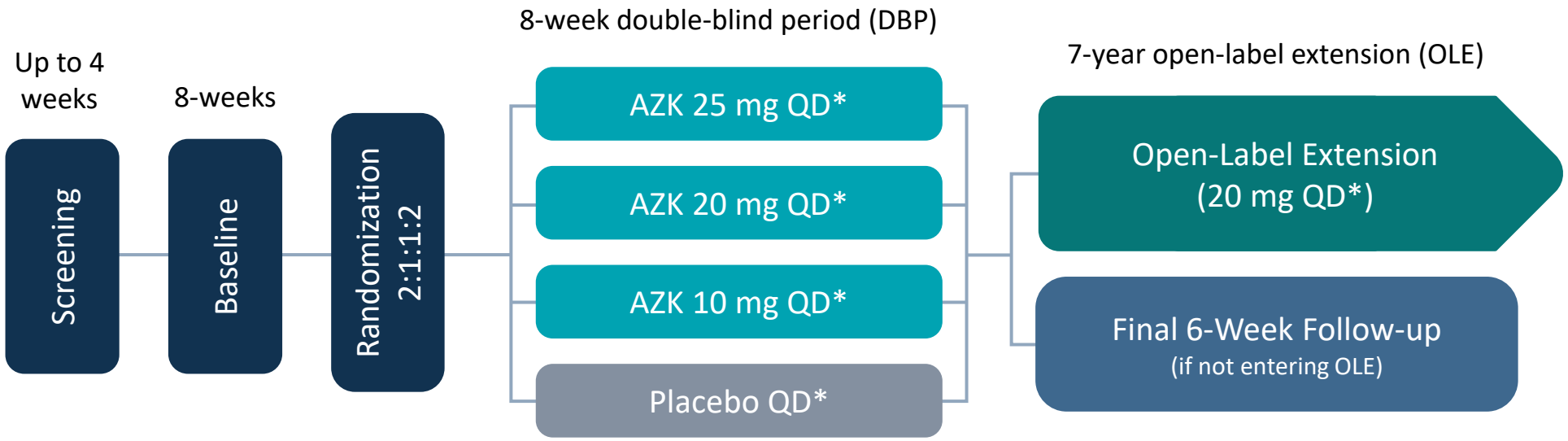
Estimated Diagnosed Adult Epilepsy Patient Population (2020)



Sources: Xenon-sponsored market research; Mula, et al, Effect of drug treatment changes and seizure outcomes on depression and suicidality in adults with drug-resistant focal epilepsy, Epilepsia, December 11, 2023

X-TOLE Phase 2b Clinical Study in Focal Onset Seizures

X-TOLE™ | Phase 2b Study and 7-year OLE

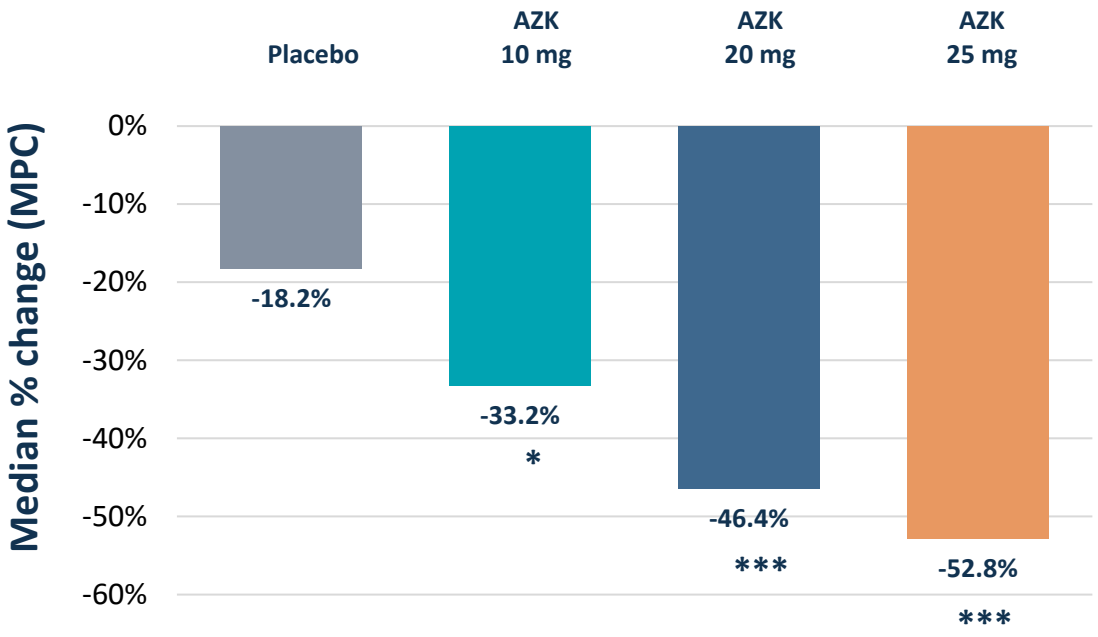


*Administered as a once-daily capsule with food with no titration period.

Topline results reported in October 2021 and subsequent analyses and OLE data presented at AES meetings

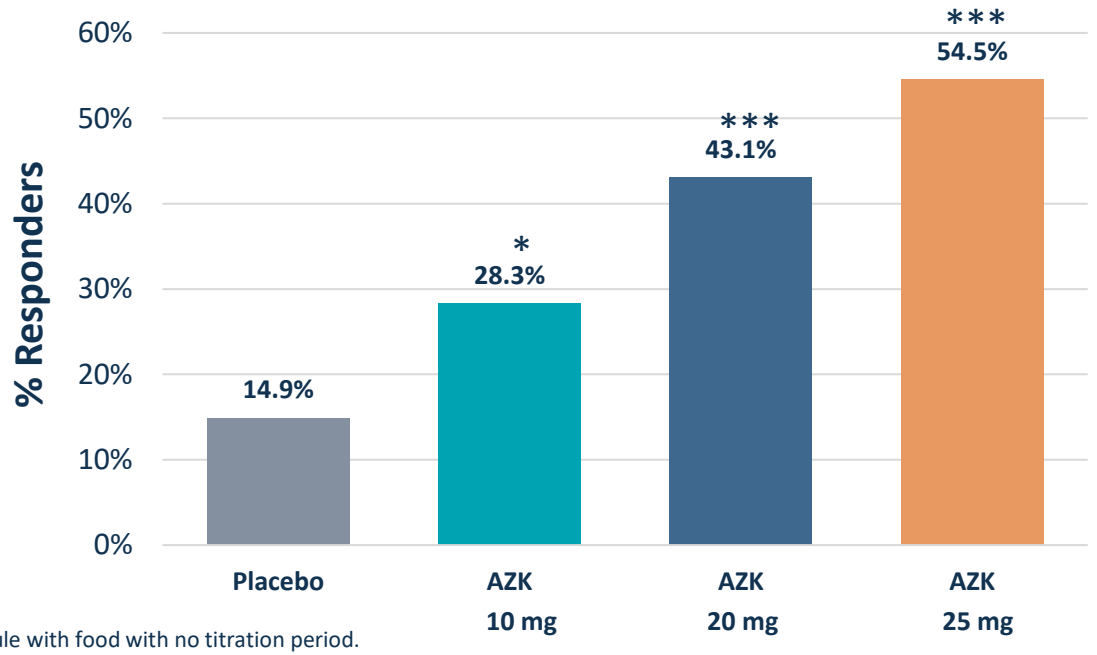
Statistically Significant and Dose Dependent Reduction in Seizures Observed in Phase 2b X-TOLE Study

Change from baseline in seizure frequency



*p<0.05, ***p<0.001

Responder rate (RR50)



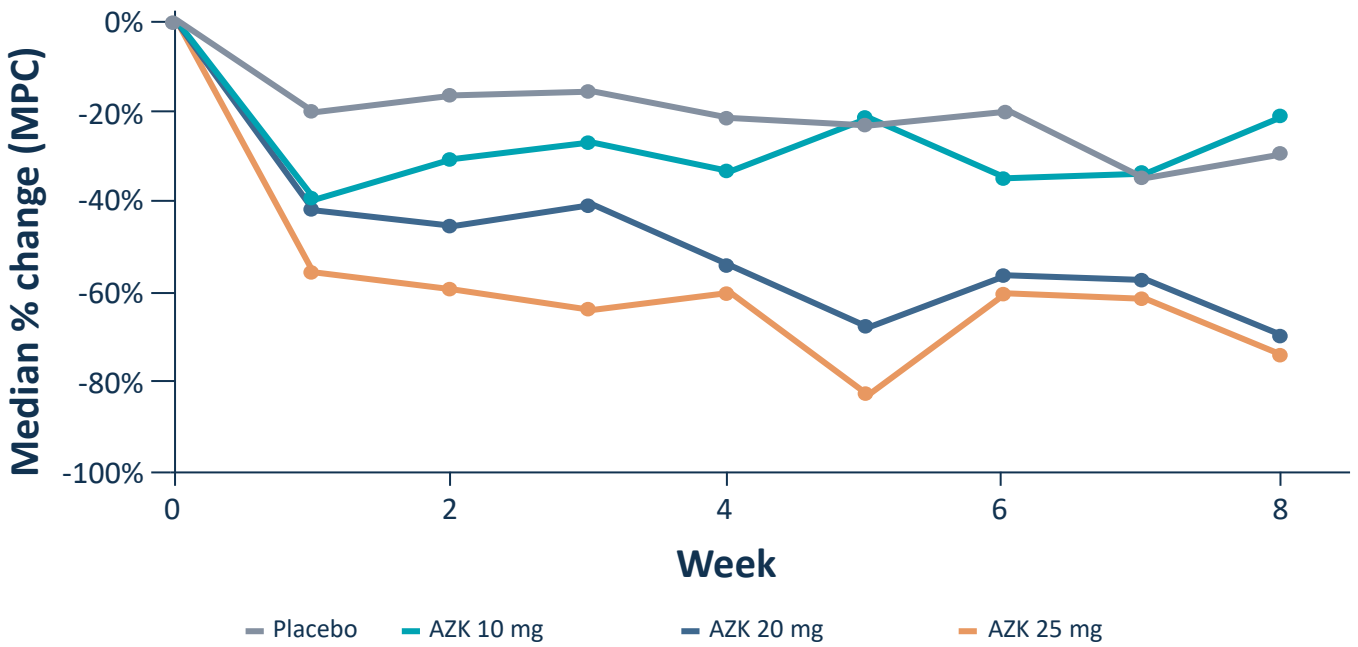
*p<0.05, ***p<0.001

Azetukalner was administered as a once-daily capsule with food with no titration period.

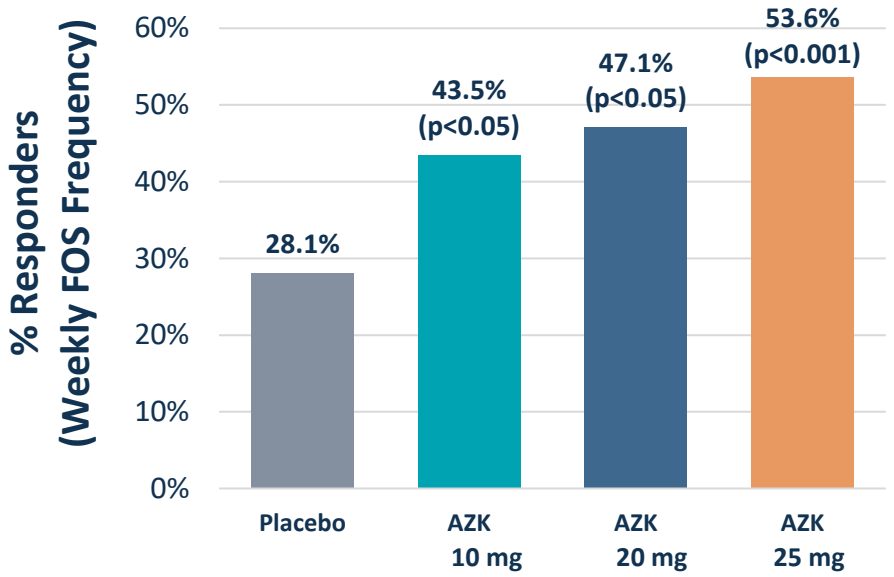
Source: "Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Modulator, in Adults with Focal Epilepsy (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).

Rapid Onset of Efficacy in Double-Blind Period (DBP)

Change from baseline in FOS frequency in DBP



Responders (RR50) based on percent change from baseline for Week 1 in weekly FOS frequency in DBP



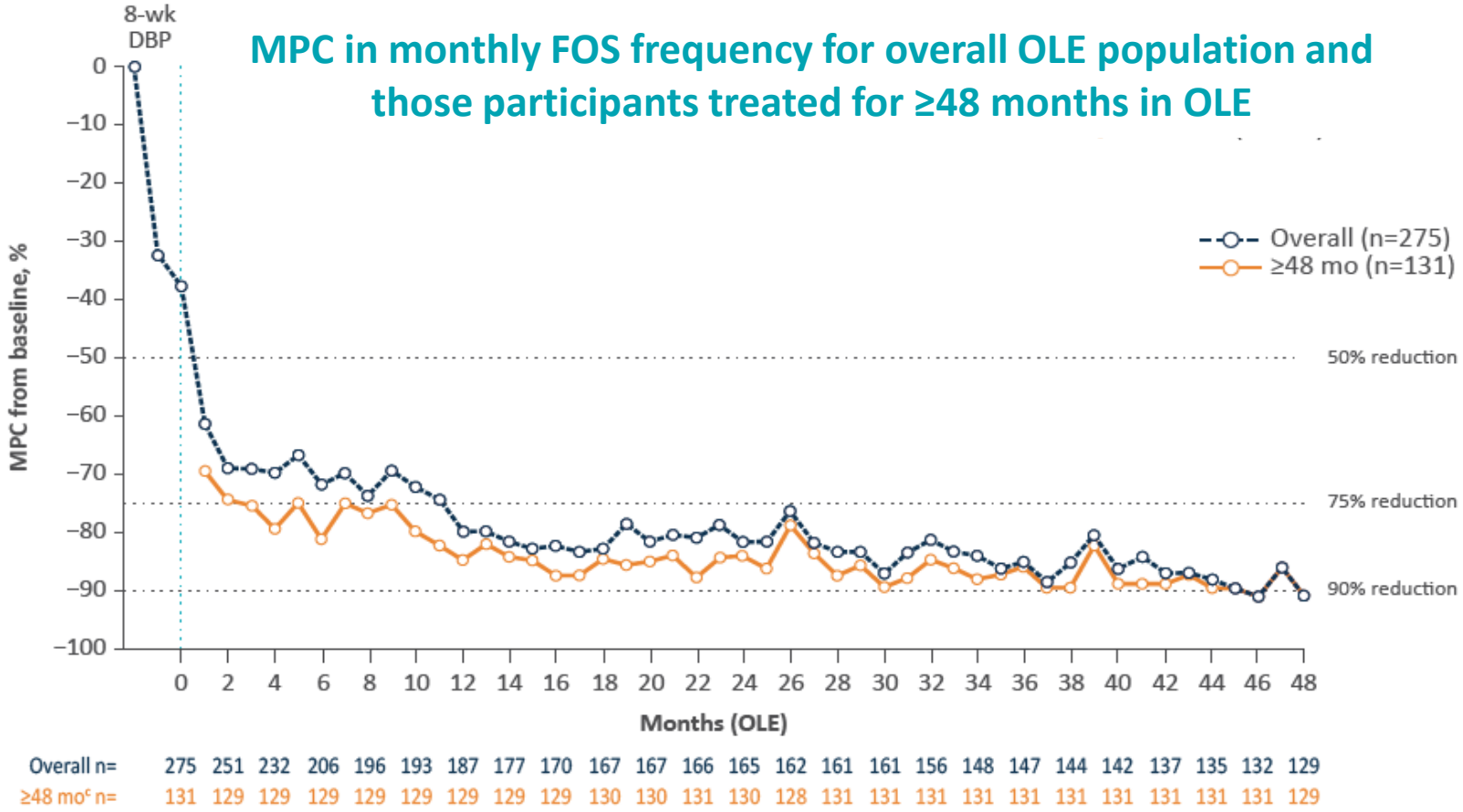
*Azetuklaner was administered as a once-daily capsule with food with no titration period.

Marked reduction in median FOS frequency at Week 1 for all doses compared with placebo

Source: "Rapid Onset of Efficacy of XEN1101, a Novel Potassium Channel Opener, in Adults with Focal Epilepsy: Results from a Phase 2b Study (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).

Robust Long-Term Efficacy Results in X-TOLE OLE

MPC in monthly FOS frequency for overall OLE population and those participants treated for ≥48 months in OLE

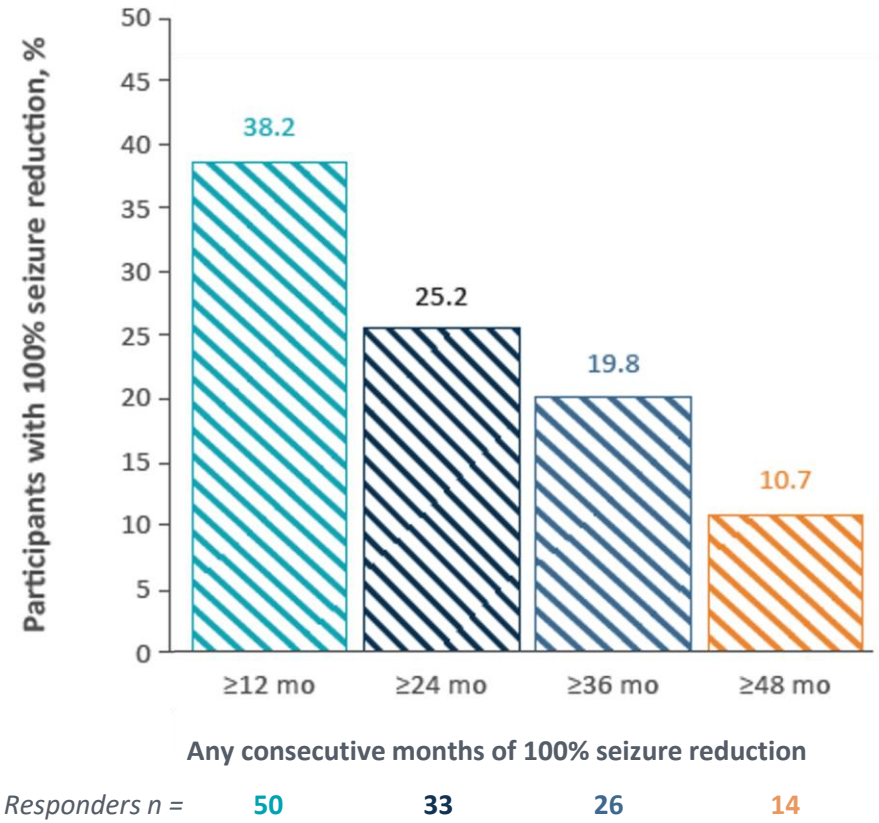


- **90.9% reduction** in monthly FOS frequency from DBP baseline at OLE month 48
- Higher monthly reductions in FOS frequency in participants receiving **1-2 ASMs at DBP baseline (n=60, 100%)** vs. those receiving 3 ASMs (n=69, 81.8%) (data not shown)

After the DBP, all participants received 20 mg azetukalner at start of OLE as a once-daily capsule with food and no titration period. Data cutoff: October 6, 2025. Monthly seizure rate was calculated for 28 days per month. Sample sizes for each month varied for the 131 participants treated for ≥48 months in the OLE due to non-compliance with daily seizure diary entries.
DBP: double-blind period; FOS: focal onset seizures; mo: month; MPC, median percent change; OLE, open-label extension.
Source: "Long-Term Safety and Efficacy of Azetukalner, a Novel, Potent KV7 Potassium Channel Opener, in Adults With Focal Epilepsy: ≥48-Month Interim Analysis of the Ongoing 7-Year X-TOLE Open-Label Extension." 2025 Annual Meeting of the American Epilepsy Society (AES).

Impressive Seizure Freedom in the X-TOLE OLE

Seizure freedom rates for any consecutive ≥12, ≥24, ≥36, and ≥48 months in OLE participants treated for ≥48 months (n=131)



Data cutoff: October 6, 2025. Monthly seizure rate was calculated for 28 days per month. OLE: open-label extension.
Source: "Long-Term Safety and Efficacy of Azetukalner, a Novel, Potent KV7 Potassium Channel Opener, in Adults With Focal Epilepsy: ≥48-Month Interim Analysis of the Ongoing 7-Year X-TOLE Open-Label Extension." 2025 Annual Meeting of the American Epilepsy Society (AES).

Safety and Tolerability Data

X-TOLE Double-Blind Period

- Azetukalner was generally well-tolerated in this study with adverse events consistent with commonly prescribed ASMs
  - The most common reported treatment emergent adverse events (TEAEs) across all azetukalner dose groups were dizziness (24.6%), somnolence (15.6%) and fatigue (10.9%), as compared to the placebo group which reported dizziness (7.0%), somnolence (7.0%) and fatigue (5.3%)
  - The most common TEAEs leading to discontinuation across all azetukalner dose groups were dizziness (4.7%), balance disorder (2.4%), dysarthria (1.9%) and gait disturbance (1.9%)
  - Serious adverse events (SAE) incidence was low and balanced across groups (3.3% across all azetukalner dose groups as compared to 2.6% in the placebo group)

X-TOLE Open-Label Extension

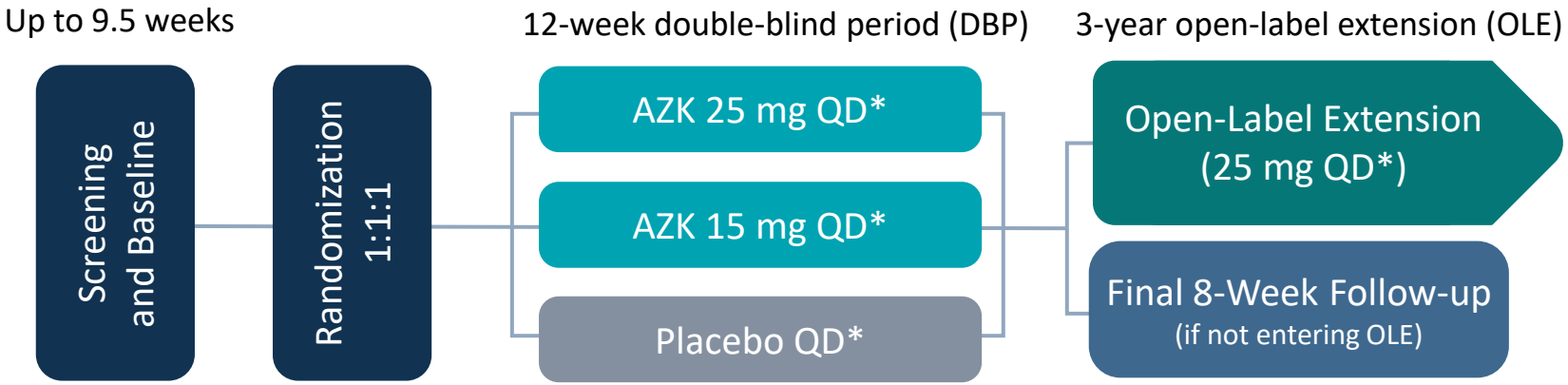
- Azetukalner was generally well tolerated in OLE, long-term safety in the OLE is comparable with the safety observed in the DBP
- As of October 6, 2025, the OLE has generated >775 patient-years of safety data exposure

Sources: “Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Modulator, in Adults with Focal Epilepsy (X-TOLE).” 2022 Annual Meeting of the American Epilepsy Society (AES).
Long-Term Safety and Efficacy of Azetukalner, a Novel, Potent KV7 Potassium Channel Opener, in Adults With Focal Epilepsy: ≥48-Month Interim Analysis of the Ongoing 7-Year X-TOLE Open-Label Extension.” 2025 Annual Meeting of the American Epilepsy Society (AES).

X-TOLE2 and X-TOLE3 Phase 3 Clinical Trials in FOS

- Phase 3 epilepsy program in focal onset seizures and primary generalized tonic-clonic seizures is underway
- Plan to submit NDA supported by efficacy data from Phase 2b study (X-TOLE) and first Phase 3 study (X-TOLE2)
- Conducting two identical multi-center, placebo-controlled Phase 3 FOS trials (target n = 360 in each study)

X-TOLE2™ | X-TOLE3™



*Administered as once-daily capsule with food with no titration period.

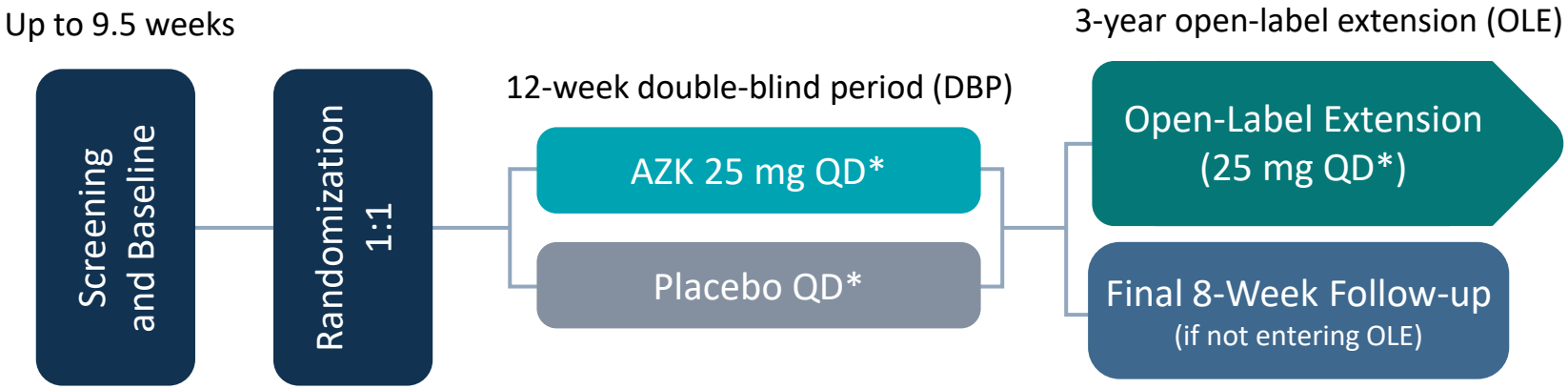
- **Primary Objective:** assess effect of azetukalner vs placebo on reducing focal onset seizure frequency
- **Secondary Objectives:** include assessing the effect of azetukalner vs placebo on RR50, early treatment effect as measured at week 1, and PGI-C

Phase 3 X-TOLE2 FOS topline data expected March 2026 followed by anticipated NDA submission H2 2026

X-ACKT Phase 3 Clinical Trial in PGTCS

- Significant unmet need remains in PGTCS despite available treatment options and an opportunity remains for a broad-spectrum agent with activity across seizure types
- Conducting a single, multi-center, placebo-controlled Phase 3 trial to support registration (n = ~160)

X-ACKT™



- **Primary Objective:** assess effect of azetukalner vs placebo on reducing frequency of primary generalized tonic-clonic seizures
- **Secondary Objectives:** include assessing the effect on azetukalner vs placebo on RR50, seizure freedom and PGI-C

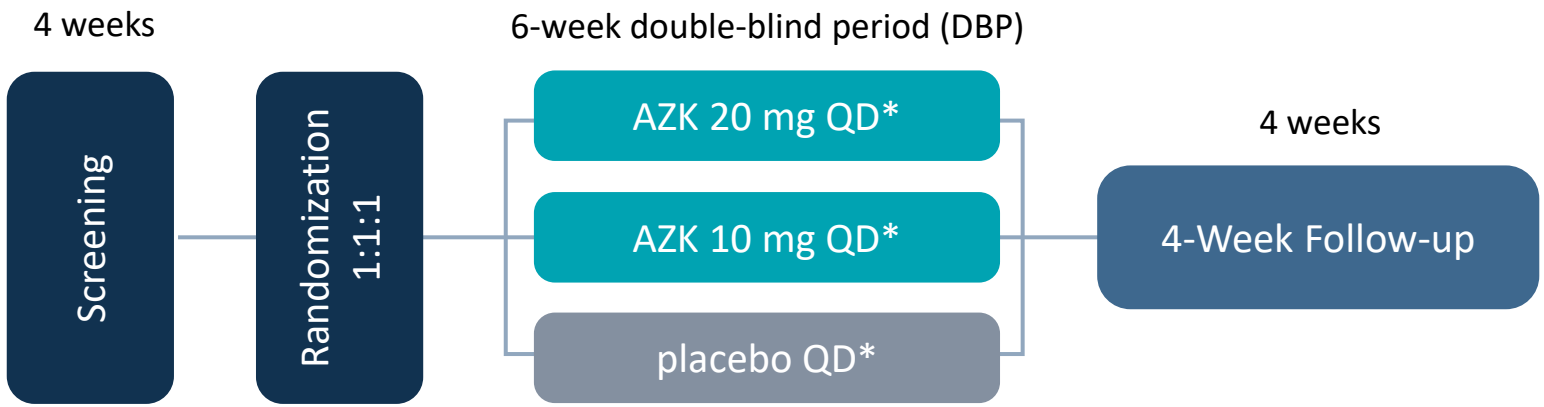
*Administered as once-daily capsule with food with no titration period. Participants aged ≥12 years and <18 years will receive either azetukalner 15mg, azetukalner 25 mg, or placebo; participants aged ≥18 years will receive either azetukalner 25 mg or placebo.

Expanding Azetukalner in Neuropsychiatry

X-NOVA Phase 2 Proof-of-Concept Clinical Study in MDD

- Conducted a Phase 2 proof-of-concept, randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety, tolerability, and efficacy of azetukalner in major depressive disorder (MDD)

X-NOVA™



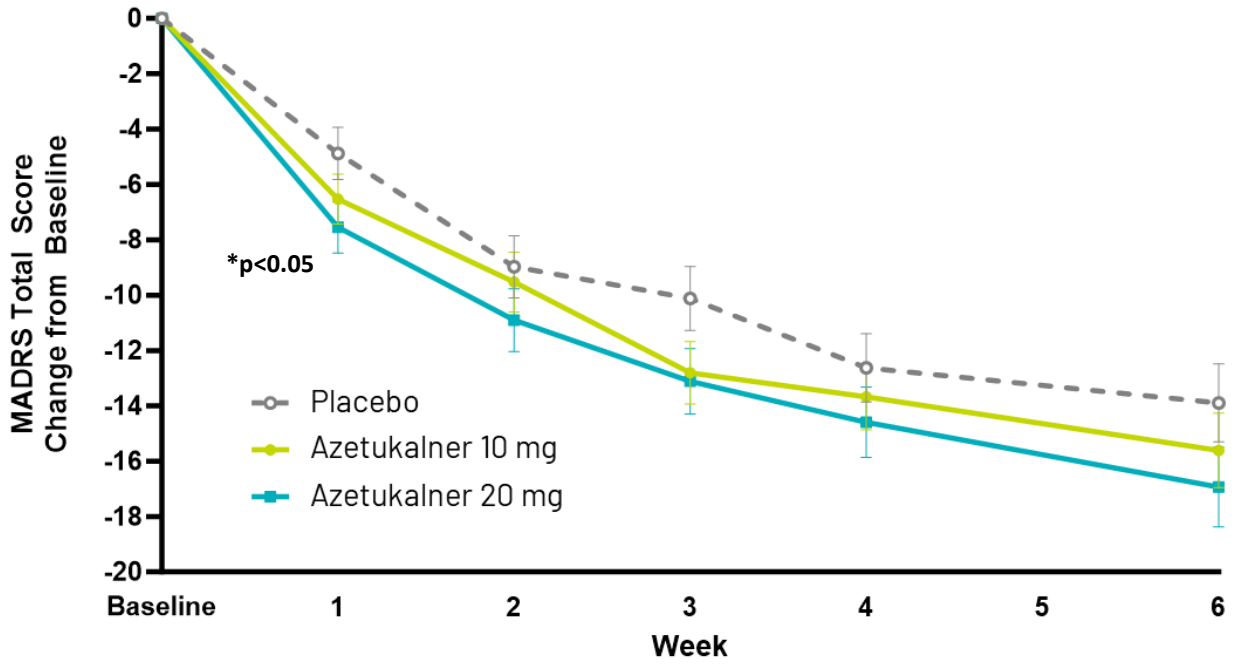
- **Primary Objective:** Montgomery-Åsberg Depression Rating Scale (MADRS) score change through week 6
- **Key Secondary Objective:** Snaith-Hamilton Pleasure Scale (SHAPS) score change through week 6

*Administered as once-daily capsule with food with no titration period.

Phase 2 topline data from X-NOVA study announced in November 2023

X-NOVA Primary Efficacy Endpoint

Change in MADRS Total Scores at Week 6 (mITT)



	placebo (N=54)	AZK 20 mg (N=53)
ΔMADRS from baseline at **Wk 6** (LS mean)	-13.90	**-16.94**
Difference vs placebo		**-3.04**
p-value		0.135

Azetukalner was administered as a once-daily capsule with food with no titration period.

A clear dose response and a clinically meaningful, but not statistically significant, 3.04 difference in MADRS at week 6 in the 20 mg group

MADRS: Montgomery-Åsberg Depression Rating Scale; LSMean (SEM) shown; mITT: modified intent to treat; population included all randomized participants who received at least 1 dose of study treatment and at least 1 post randomization MADRS score

X-NOVA Pre-Specified Endpoint Improvement in Depressive Symptoms

Change in HAM-D17 Total Score at Week 6 (mITT)

	placebo (N=54)	AZK 20 mg (N=53)
HAM-D17 total score change from baseline at **Wk 6** (LS mean)	-10.18	-13.26
Difference vs placebo		-3.08
p-value		0.042

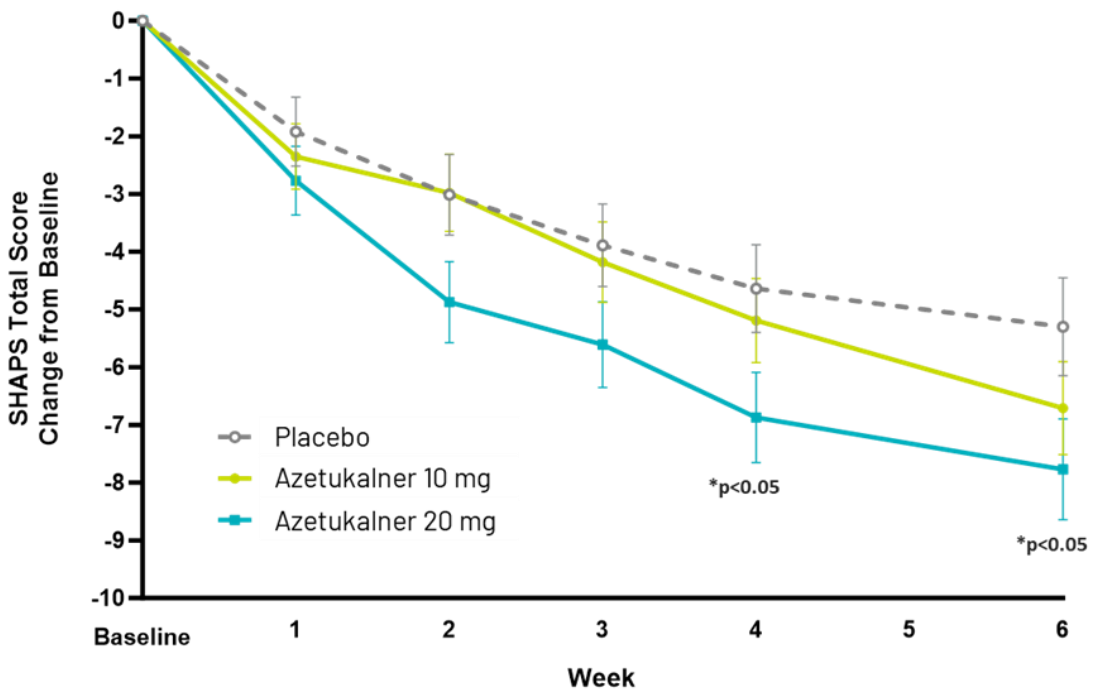
Azetukalner (XEN1101) was administered as a once-daily capsule with food with no titration period.

Improvement in depressive symptoms assessed by HAM-D17 total scores was significantly different at week 6

HAM-D17: Hamilton Depression Rating Scale was assessed at screening, baseline, and Week 6; mITT: modified intent to treat; population included all randomized participants who received at least 1 dose of study treatment and at least 1 post randomization MADRS score; p-value nominal

X-NOVA Secondary Efficacy Endpoint

Change in SHAPS Total Score at Week 6 (mITT)



	placebo (N=54)	AZK 20 mg (N=53)
SHAPS total score change from baseline at **Wk 6** (LS mean)	-5.30	-7.77
Difference vs placebo		-2.46
p-value		**0.046**

Azetukalner (XEN1101) was administered as a once-daily capsule with food with no titration period.

Anhedonia symptom improvement: significantly different change in SHAPS at week 6 in 20 mg group

SHAPS: Snaith-Hamilton Pleasure Scale; LSMean (SEM) shown; p-value nominal

X-NOVA: Safety and Tolerability Data

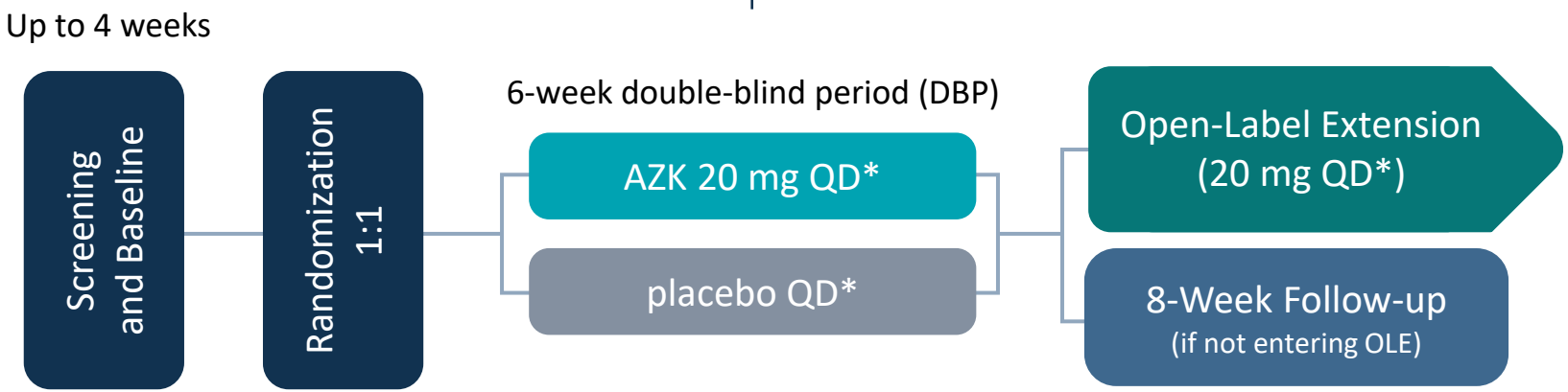
Azetukalner was generally well-tolerated with similar rates of overall adverse events reported across all treatment arms

- The most commonly reported TEAEs in the azetukalner 20 mg group included dizziness (17.9%), somnolence (10.7%), headache (8.9%), and disturbance in attention (8.9%), as compared to the placebo group, which reported dizziness (7.3%), somnolence (1.8%), headache (12.7%), and disturbance in attention (0%)
- Rates of discontinuation were similar across all treatment arms and rates of discontinuation due to TEAEs were low with three patients in the azetukalner 20 mg group (5.4%), as compared to two patients in the placebo group (3.6%)
- No SAEs were reported in the two azetukalner treatment groups, and there were two patients (3.6%) in the placebo group who experienced a treatment-emergent SAE
- Azetukalner was not associated with notable weight gain; patients did not report notable sexual dysfunction

Phase 3 Clinical Studies in Major Depressive Disorder

- Phase 3 MDD program consists of three multi-center, placebo-controlled clinical trials (N=~450 in each study)
- Plan to submit sNDA supported by efficacy data from two positive Phase 3 MDD trials

X-NOVA2™ | X-NOVA3™



*Administered as once-daily capsule with food with no titration period.

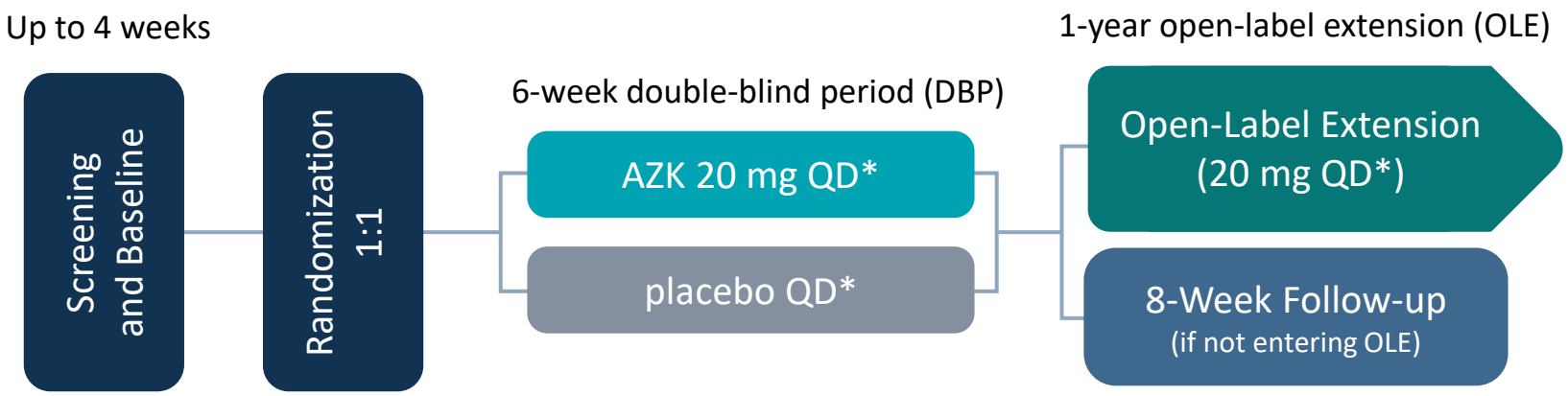
- **Primary Objective:** change from baseline in HAM-D17 score at week 6
- **Key Secondary Objectives:** include change from baseline in HAM-D17 score at week 1; change from baseline in SHAPS score at week 6; and change from baseline in CGI-S at week 6

Phase 3 X-NOVA2 and X-NOVA3 studies in MDD are ongoing; X-NOVA2 topline data expected H1 2027

Phase 3 Clinical Studies in Bipolar Depression

- Phase 3 BPD program consists of two multi-center, placebo-controlled clinical trials (n=~400 in each study) in patients with bipolar I or II depression (BPD)

X-CEED™



- **Primary Objective:** change from baseline in MADRS score at week 6
- **Key Secondary Objectives:** include change from baseline in MADRS score at week 1; change from baseline in SHAPS score at week 6; and change from baseline in CGI-S at week 6

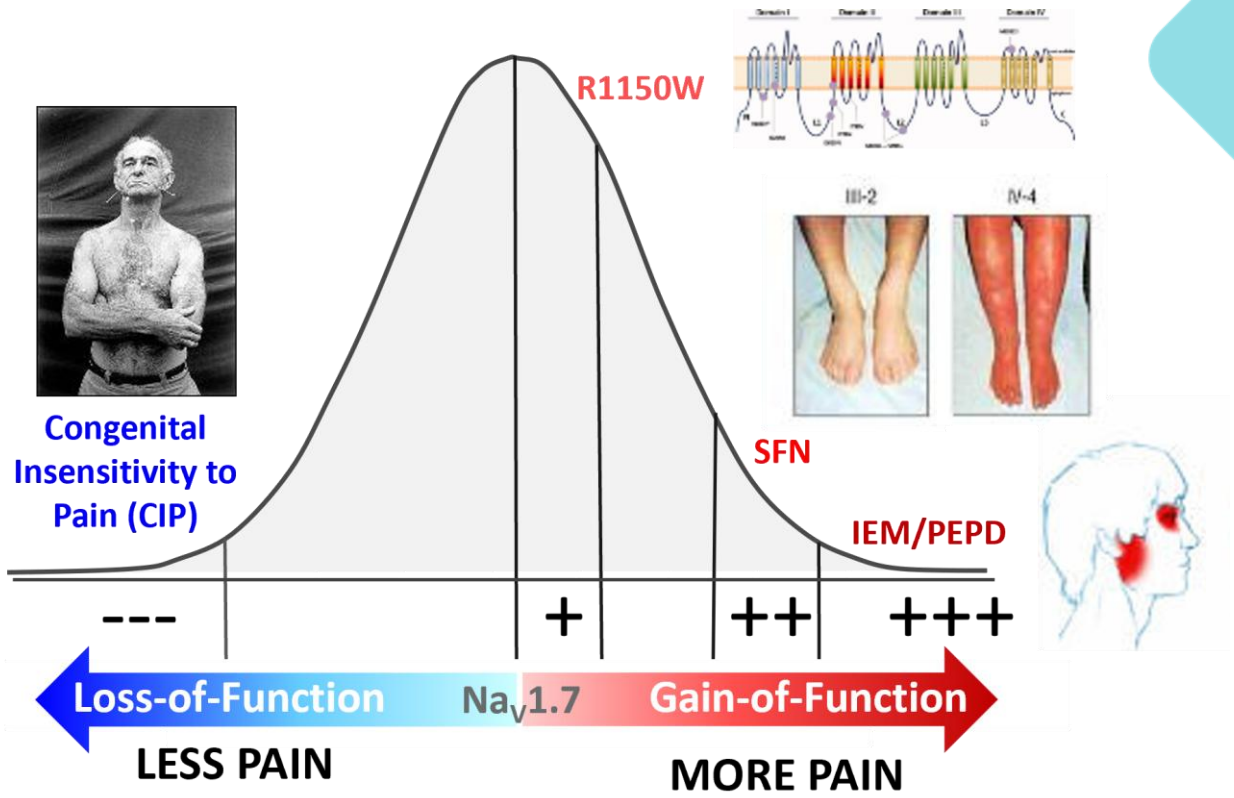
*Administered as once-daily capsule with food with no titration period.

X-CEED, first of two Phase 3 studies in BPD, is ongoing

Pain Programs

The Human Genetics of $Na_V1.7$ in Pain

- **Loss-of-function mutations in SCN9A** (the gene encoding $Na_V1.7$)can cause congenital indifference to pain (CIP) - individuals that are otherwise healthy but cannot feel pain
- **Gain-of-function mutations in SCN9A** can lead to extreme pain disorders, such as inherited erythromelalgia (IEM) or paroxysmal extreme pain disorder (PEPD), demonstrating that excessive $Na_V1.7$ activity can drive pain



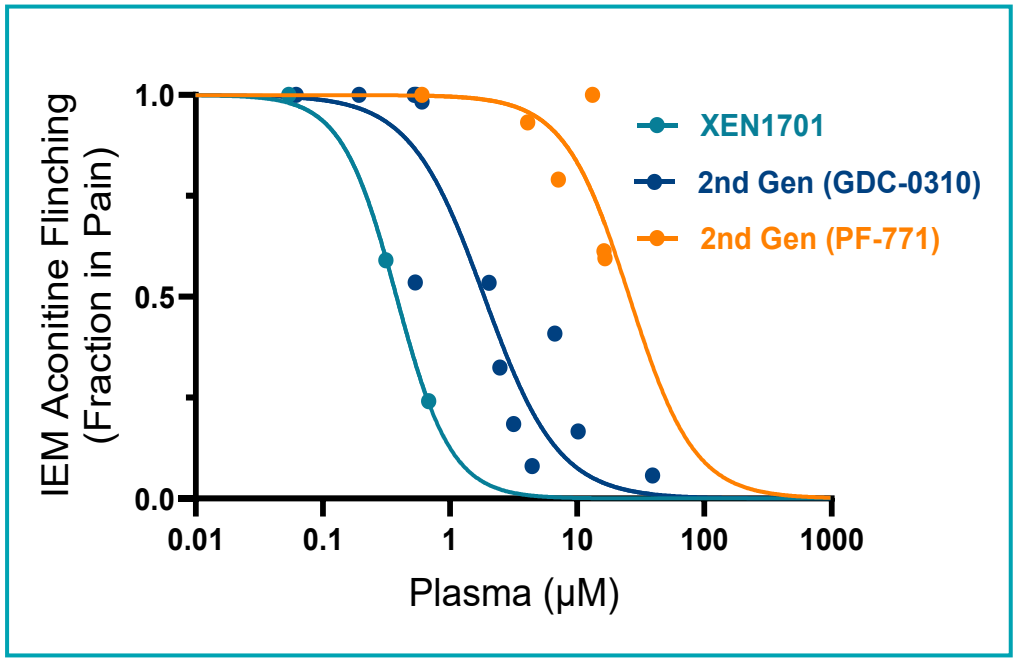
There is strong human genetic evidence to support $Na_v1.7$ as a compelling target for pain drug development

$Na_V1.7$ Pain Program

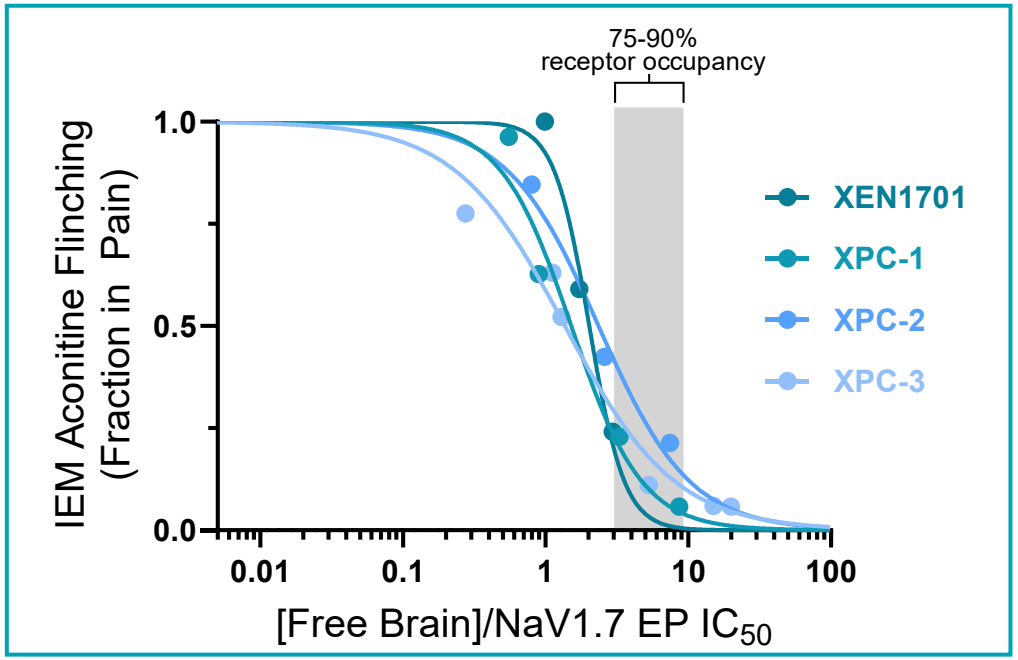
- Xenon has long history with $Na_V1.7$ science and deep ion channel drug discovery expertise and is applying this knowledge to generate a pipeline of $Na_V1.7$ molecules with differentiated profiles:
  - CNS penetrant to globally inhibit $Na_V1.7$, better mimicking patient genetics
  - Demonstrates good free fraction and tissue distribution, achieving high levels of target engagement
  - Excellent potency and selectivity to safely achieve target therapeutic levels of $Na_V1.7$ inhibition
- $Na_V1.7$ compound, XEN1701, in Phase 1 clinical study with a profile that has never been tested in clinic
- Growing early-stage pipeline of numerous other compounds and distinct chemistries advancing IND-enabling studies

XEN1701 Performance in IEM Mouse Model

XEN1701 demonstrates target engagement at low total plasma concentrations



In vivo activity correlates to free brain concentrations across Xenon's lead compounds



CNS penetrance, improved free fraction and good potency and selectivity demonstrate target engagement at low plasma exposures

$Na_V1.7$ Program Status

Advancing XEN1701, a $Na_V1.7$ channel inhibitor in development for pain

Phase 1 SAD/MAD* study underway in healthy participants

Preliminary Phase 1 data from the SAD portion of the study suggest that XEN1701 has **reached drug concentrations that are predicted to achieve receptor occupancies required for therapeutic activity** based on human genetic data

Study completion expected in 2026 to support initiating a Phase 2 proof-of-concept study in acute pain

SAD: Single Ascending Dose; MAD: Multiple Ascending Dose

Milestones

Potential Value-Creating Milestone Opportunities

Azetukalner in Epilepsy

Phase 3 studies ongoing in FOS (X-TOLE2/3) & PGTCS (X-ACKT)

X-TOLE2™ X-TOLE3™ X-ACKT™

- X-TOLE2: Topline data expected March 2026 with anticipated NDA submission in H2 2026
- X-TOLE3: Enrollment of non-Japanese participants expected to complete in 2026
- X-ACKT: Enrollment ongoing

Azetukalner in Neuropsychiatry

Phase 3 studies ongoing in MDD (X-NOVA2/3) and BPD (X-CEED)

X-NOVA2™ X-NOVA3™ X-CEED™

- X-NOVA2: Topline data expected H1 2027
- X-NOVA3 and X-CEED: Enrollment ongoing

Early-Stage Programs

Maturing pipeline, including multiple Phase 1 studies underway in pain

- XEN1701 ($Na_V1.7$) and XEN1120 (K_V7): Ph1 completion expected in 2026 to support Ph2 PoC studies in acute pain
- $Na_V1.1$ program: IND-enabling studies ongoing (Dravet syndrome)
- Neurocrine collaboration: Ph1 study ongoing for NBI-921355 ($Na_V1.2/1.6$ Inhibitor for certain types of epilepsy)

FOS: Focal onset seizures; PGTCS: Primary generalized tonic-clonic seizures; DBP: Double-blind period; MDD: Major depressive disorder; BPD: Bipolar depression; PoC: proof-of-concept

For more information

INVESTORS@XENON-PHARMA.COM