Investor Presentation

CORPORATE OVERVIEW
FEBRUARY 2026

NASDAQ: XENE
xenon-pharma.com

Xenon™

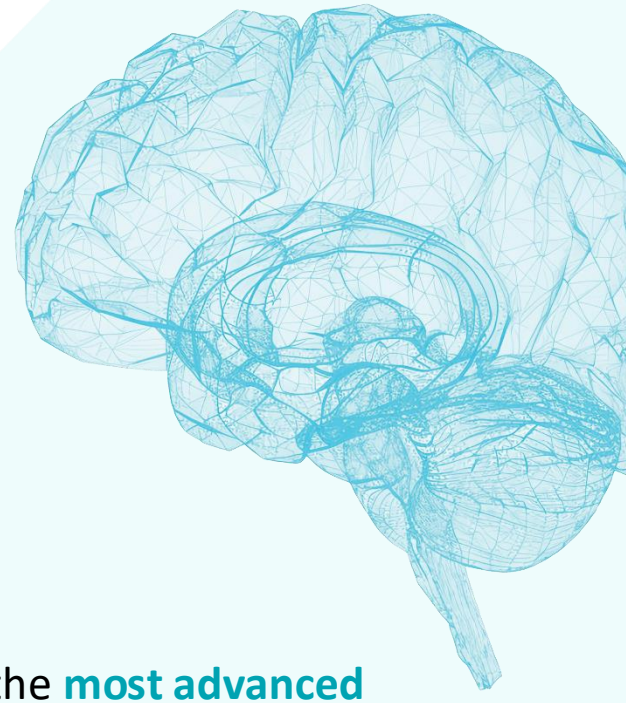
Forward Looking Statement/Safe Harbor

This slide presentation contains certain 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. These forward-looking statements are not based on historical fact, 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; and anticipated timing of topline data readout from our clinical studies of azetukalner.

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

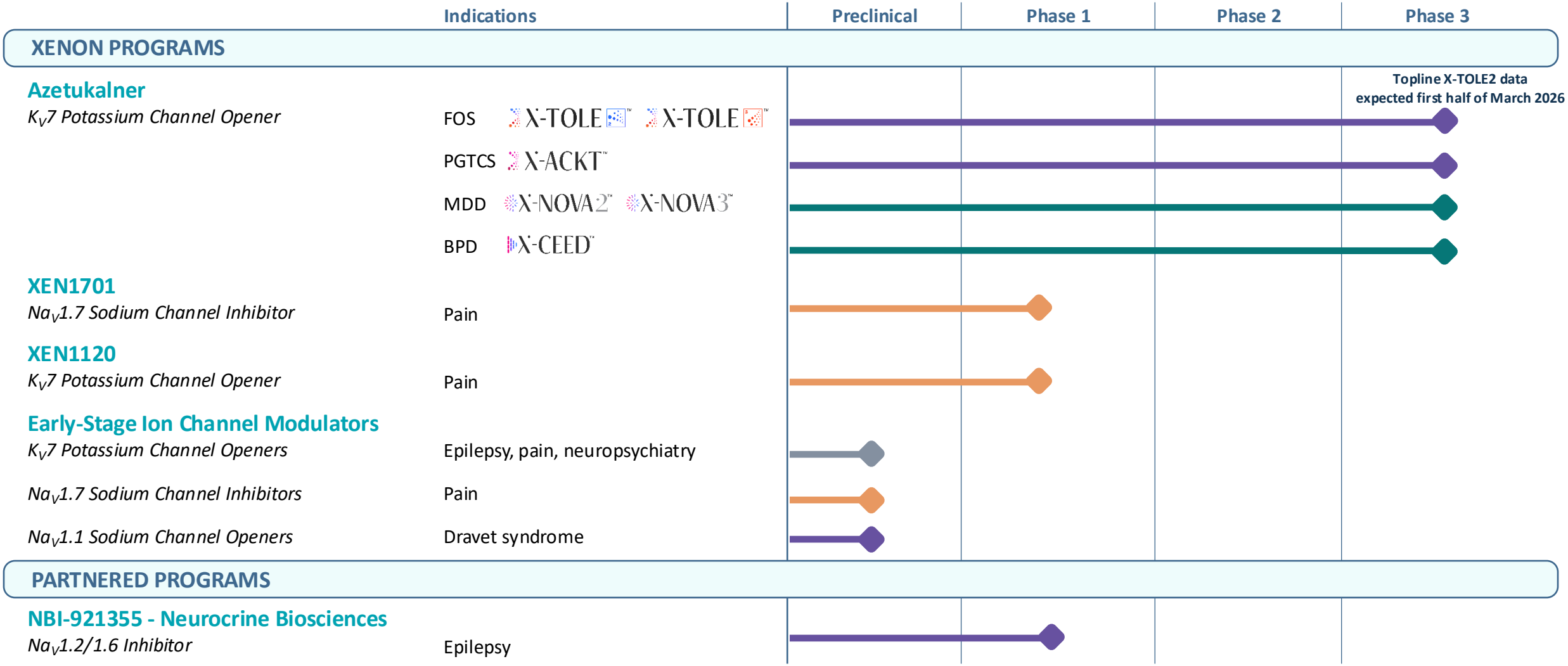
- Neuroscience-focused biopharmaceutical company and leader in small molecule, ion channel drug discovery and development
- Robust pipeline of therapeutic candidates targeting potassium and sodium channels across various indications
- Lead molecule, azetukalner, is a highly potent K_V7 channel opener in Phase 3 development in epilepsy and depression
- Strong financial position
  - Pro forma cash, cash equivalents and marketable securities of $716 million with cash runway into second half of 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

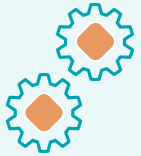
Well-Documented Safety Profile

- 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 $GABA_A$

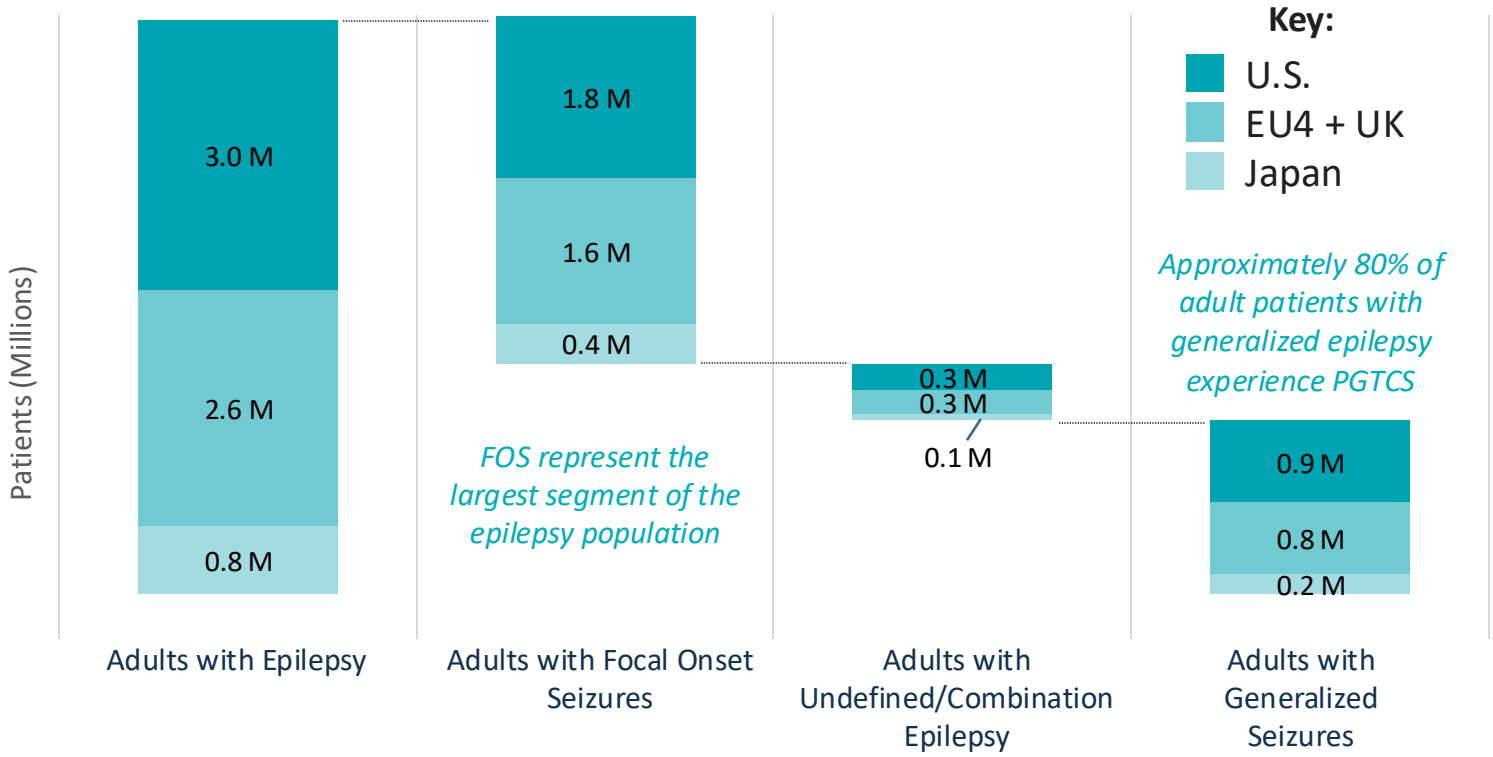
Source: 1. "Long-Term Safety and Efficacy of Azetukalner, a Novel, Potent KV7 Potassium Channel Opener, in Adults With Focal Epilepsy: ≥48-Month Interim Analysis of the Ongoing 7-Year X-TOLE Open-Label Extension." 2025 Annual Meeting of the American Epilepsy Society (AES). 2. French JA et al. JAMA Neurol.2023;80(11):1145-1154.cc

Azetukalner & Epilepsy Market Opportunity

Significant Global Epilepsy Burden

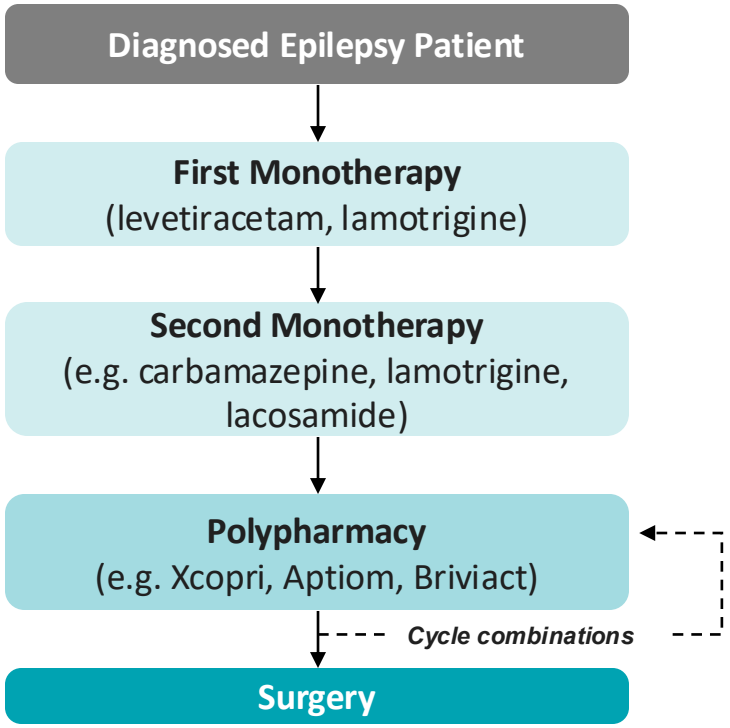
- Epilepsy is the **fourth most common neurological condition**
- Hallmark symptoms include:
  - **focal seizures** that start in one brain hemisphere (either aware or unaware)
  - **generalized seizures** the most common of which are tonic-clonic/convulsive seizures
- Despite the availability of multiple anti-seizure medications (ASMs), a **substantial unmet medical need exists**
- 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

Treatment Decisions Are Highly Individualized and Complex



Focal and general epilepsy have similar treatment considerations, with select ASMs (e.g. valproate) used more frequently in FOS than in generalized

Treatment goal aims to optimize efficacy while managing tolerability

- Levetiracetam and lamotrigine are commonly used in early lines of treatment
- Monotherapy switching in second line driven by desire for better seizure control or tolerability/AE issues, including mood issues
- Comorbid conditions influence prescribing decisions

Patients continuing to experience sub-optimal response (poor efficacy, tolerability) frequently receive polypharmacy

- Combinations typically involve mechanistic differentiation from early lines of therapy
- Branded therapies can potentially be accessed if a patient has tried and failed 1-2 generic ASMs

Significant opportunity remains with up to 50% of epilepsy patients requiring additional treatment options

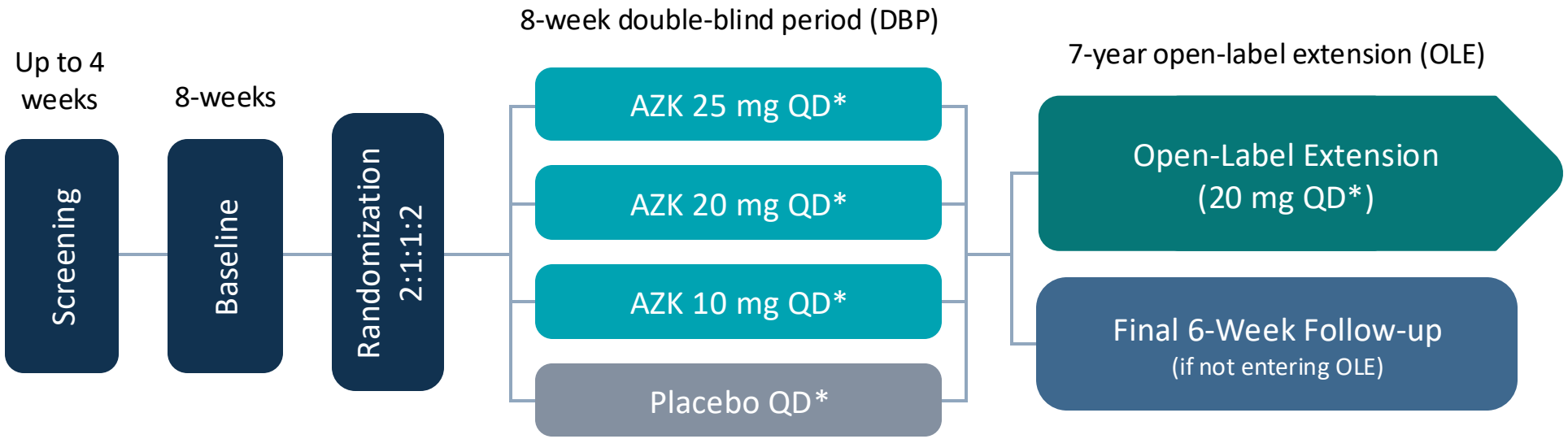
Sources: Epilepsy Foundation; Epilepsy Currents, Englot (2018); National Association of Epilepsy Centers; National Institute of Neurological Disorders and Stroke; Barnard S, et al. Treatment outcomes in newly diagnosed focal epilepsy. AES. 2024; Chen Z, et al. Long-term outcomes with ASMs. JAMA Neurol. 2018; Kwan P, et al. Definition of drug-resistant epilepsy. Epilepsia. 2010; Company-sponsored market research.

Azetukalner Data in Epilepsy

X-TOLE, X-TOLE2, X-TOLE3 AND X-ACKT CLINICAL STUDIES

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

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



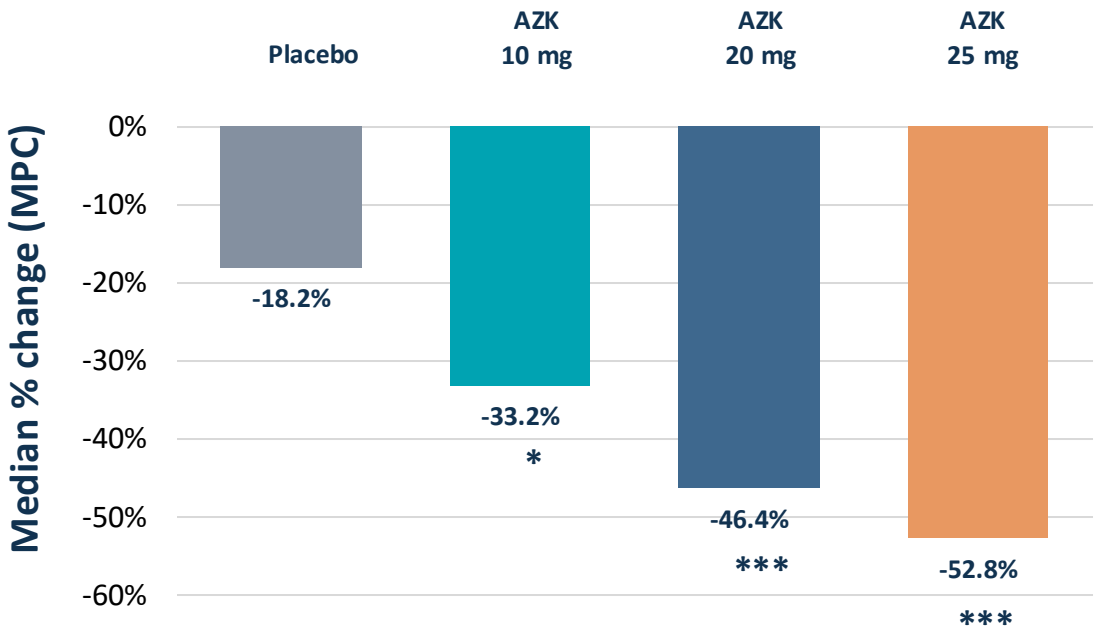
*Administered as a once-daily capsule with food with no titration period.

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

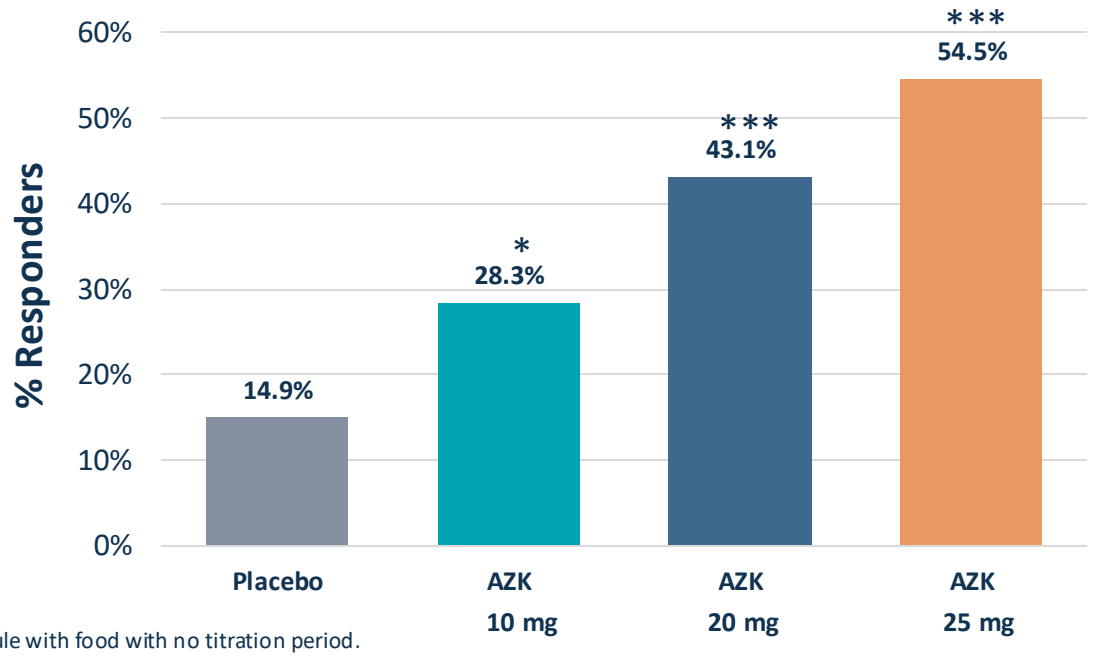
X-TOLE™

Change from baseline in seizure frequency



*p<0.05, ***p<0.001

Responder rate (RR50)



*p<0.05, ***p<0.001

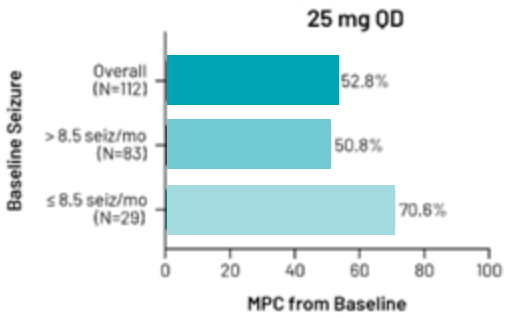
Azetukalner was administered as a once-daily capsule with food with no titration period.

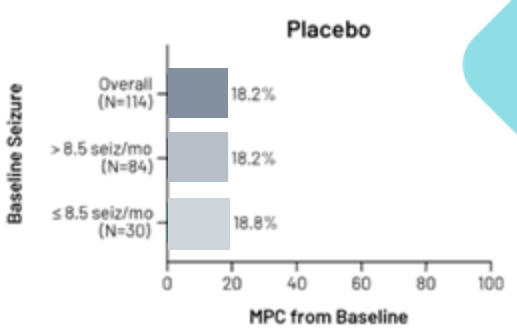
Source: "Phase 2b Efficacy and Safety of XEN1101, a Novel Potassium Channel Modulator, in Adults with Focal Epilepsy (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).

X-TOLE Sub-Group Analyses (Double-Blind Period)

Baseline Seizure Sub-Group Analysis

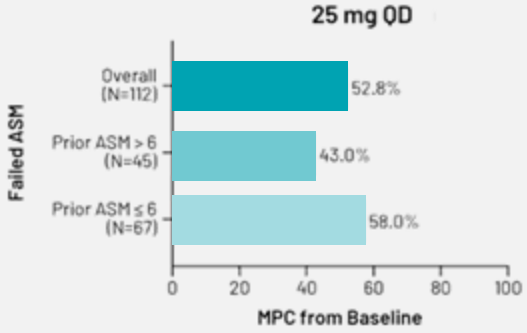
- Seizure reduction was 70.6% for participants with ≤ 8.5 seizures/month at baseline compared to 50.8% for those with > 8.5 seizures/month

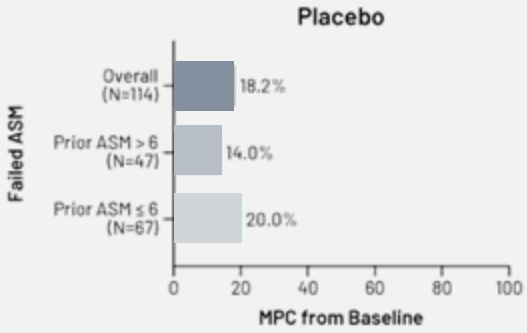




Prior Failed ASMs Sub-Group Analysis

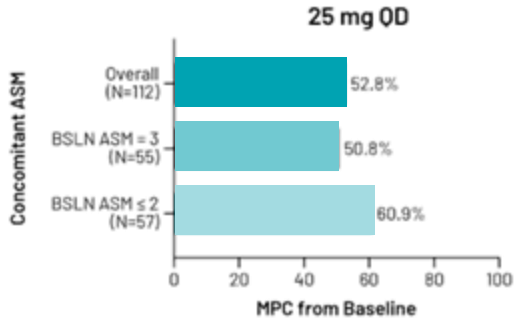
- Median monthly FOS reduction was 58.0% in participants who failed ≤ 6 ASMs at baseline and 43.0% in participants who failed > 6 ASMs

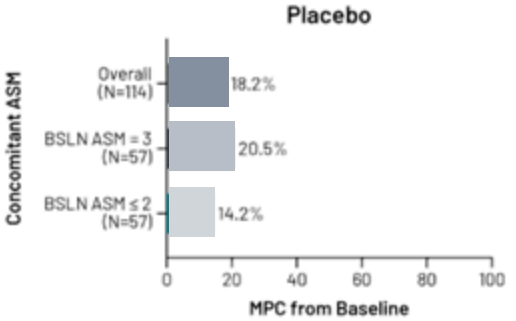




Concomitant ASMs Sub-Group Analysis

- Median monthly FOS reduction was 60.9% for participants with 1-2 concomitant ASMs and 50.8% for participants with 3 concomitant ASMs



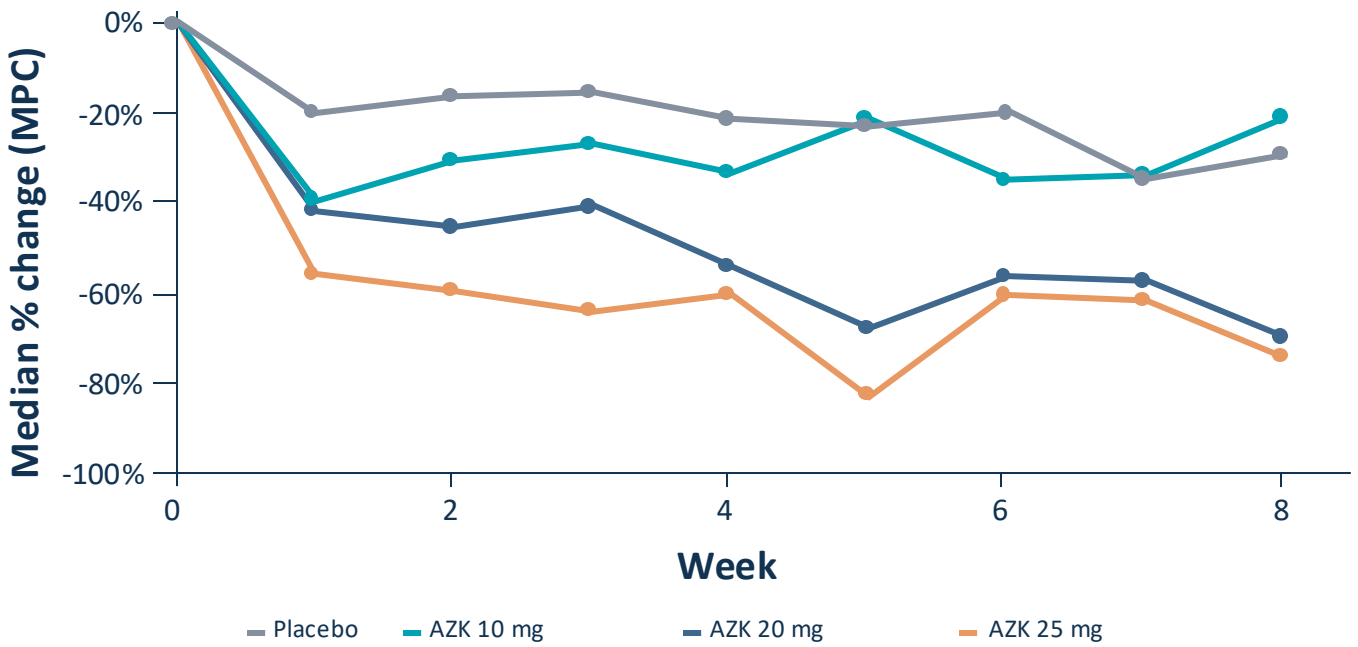


Notes: Azetukalner (XEN1101) was administered as a once-daily capsule with food. The post hoc analysis was categorized by ≤ 8.5 and > 8.5* seizures per month for baseline seizure burden, ≤ 6 and > 6 prior failed ASMs (median), and = 3 or ≤ 2 concomitant ASMs (pre-specified).

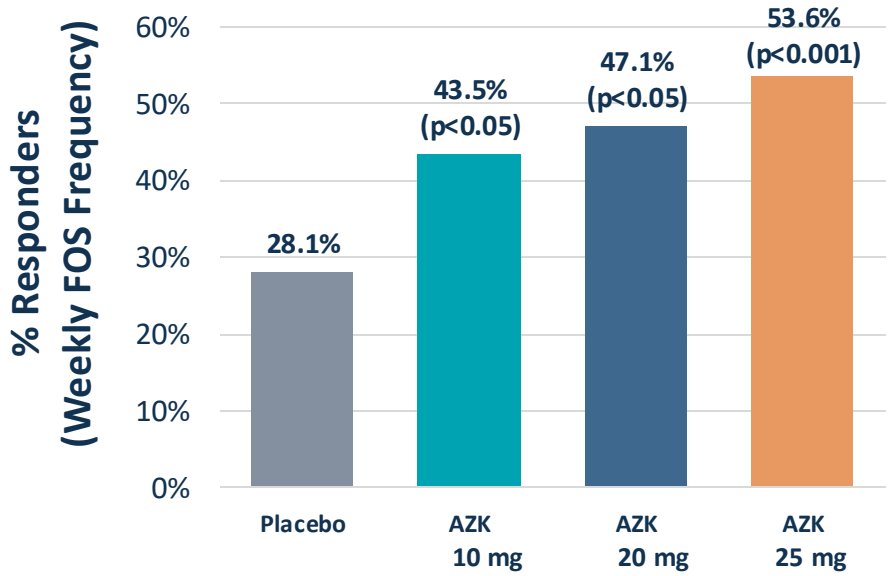
Source: "The Impact of Disease Severity on Efficacy From a Phase 2b Study of XEN1101, a Novel Potassium Channel Opener, in Adults With Focal Epilepsy (X-TOLE)." 2022 Annual Meeting of the American Epilepsy Society (AES).

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



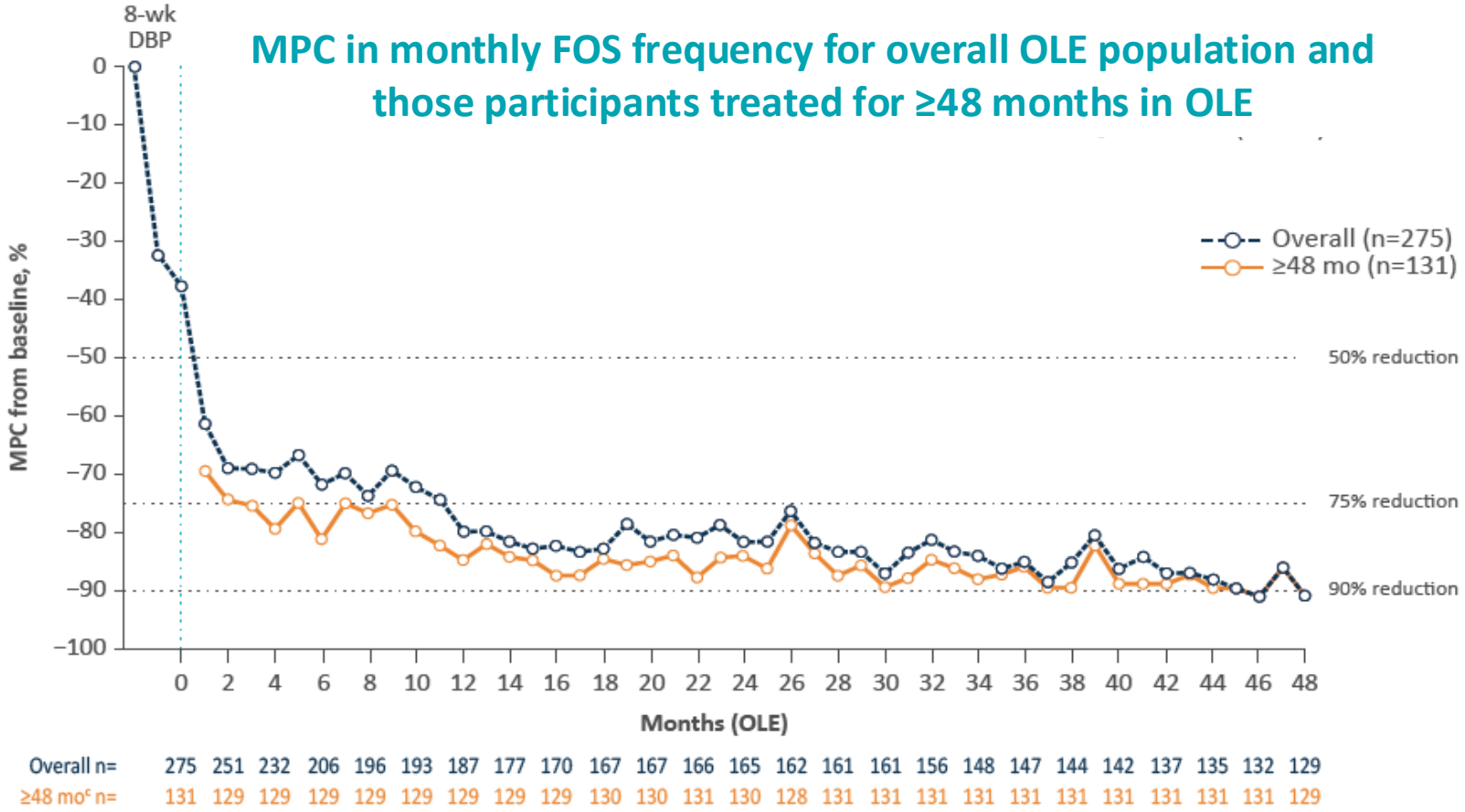
*Azetukalner was administered as a once-daily capsule with food with no titration period.

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

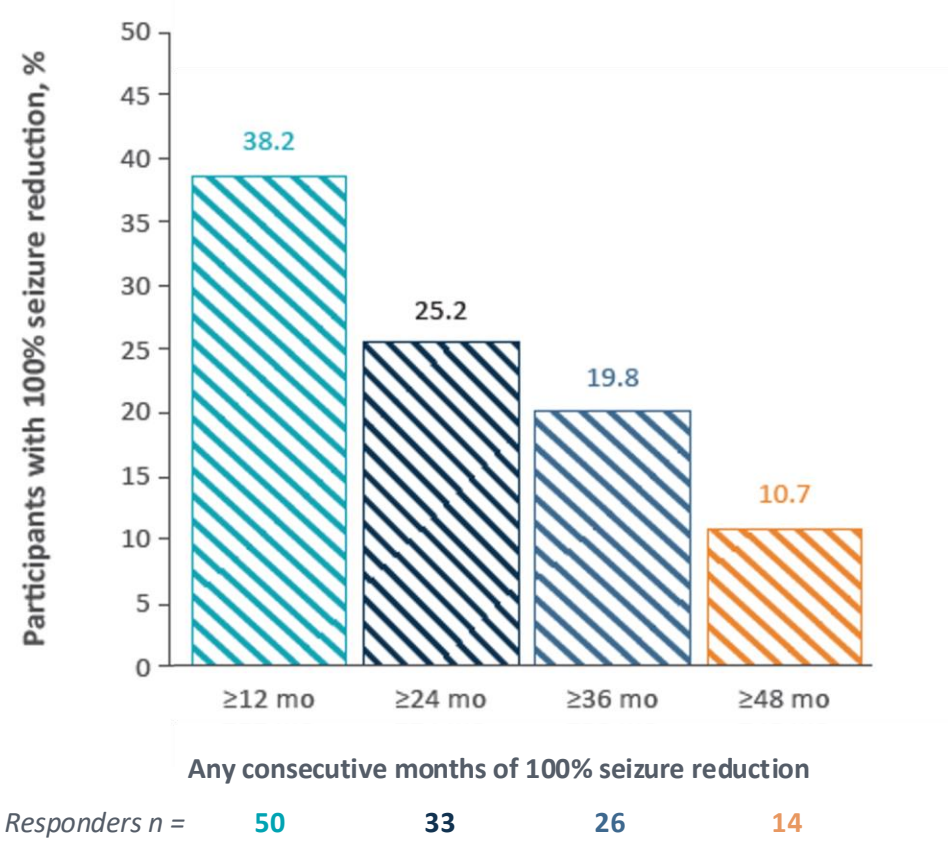


- **90.9% reduction** in monthly FOS frequency from DBP baseline at OLE month 48
- Higher monthly reductions in FOS frequency in participants receiving **1-2 ASMs at DBP baseline (n=60, 100%)** vs. those receiving 3 ASMs (n=69, 81.8%) (data not shown)

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 K_V7 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

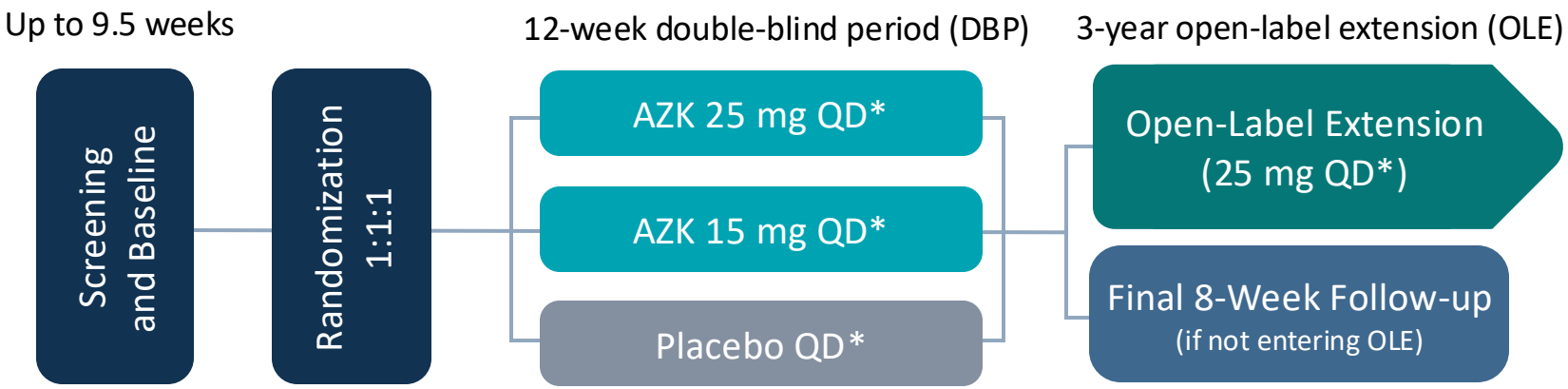
- Azetukalner was generally well tolerated in OLE, long-term safety in the OLE is comparable with the safety observed in the DBP
- As of October 6, 2025, the OLE has generated >775 patient-years of safety data exposure

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 K_V7 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™



- **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

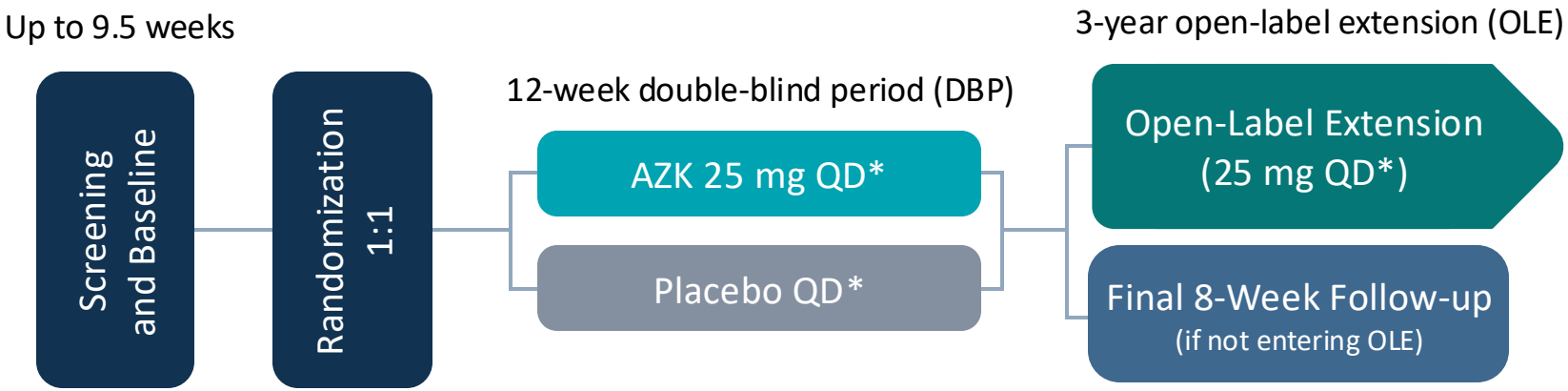
*Administered as once-daily capsule with food with no titration period.

Phase 3 X-TOLE2 FOS topline data expected first half of 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

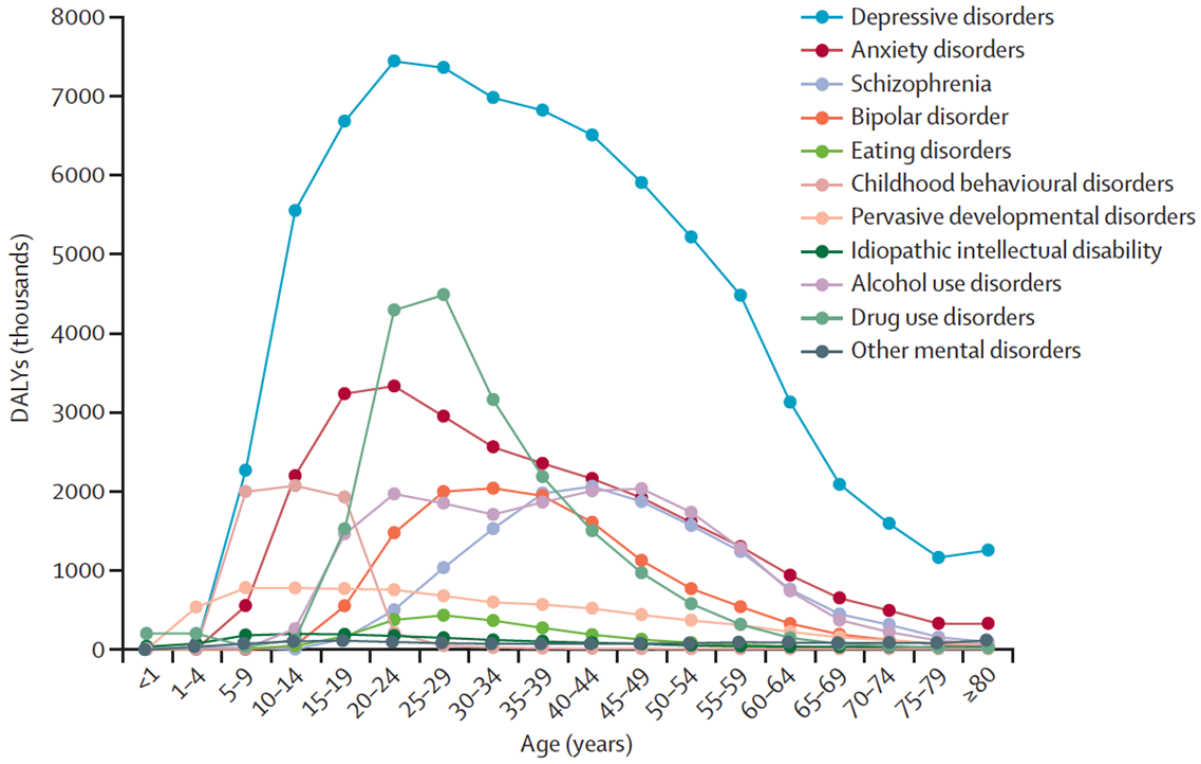
*Administered as once-daily capsule with food with no titration period. Participants aged ≥12 years and <18 years will receive either azetukalner 15mg, azetukalner 25 mg, or placebo; participants aged ≥18 years will receive either azetukalner 25 mg or placebo.

Expanding Azetukalner in Neuropsychiatry

MDD is a Highly Prevalent Mental Health Disorder

- In 2022, the MDD diagnosed prevalent population in the U.S. was approximately 21 million adults
  - ~55% treated with pharmacotherapy
  - 1 in 3 patients are inadequately managed on pharmacotherapy
- Anhedonia is a common comorbidity of MDD
  - Associated with poorer treatment outcomes

Depression Accounts for Greatest Disability Among All Central Nervous System Disorders



Disability-adjusted life years (DALYs) for each mental and substance use disorder in 2010, by age

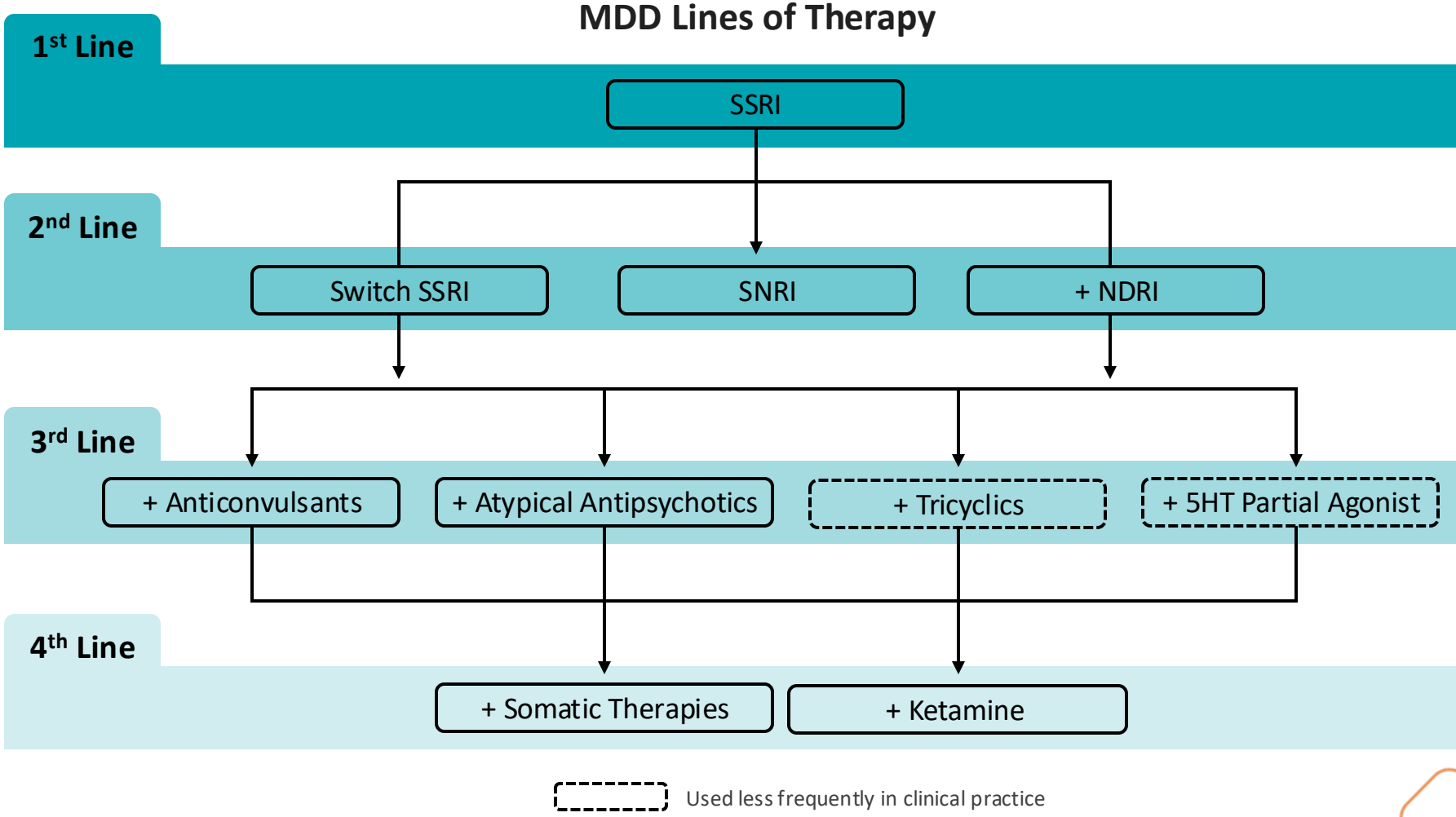
Sources: Whiteford et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. Lancet. 2013; Kern et al. Treatment patterns and sequences of pharmacotherapy for patients diagnosed with depression in the United States: 2014 through 2019. BMC Psychiatry. 2020; Fava, M. Definition and epidemiology of treatment-resistant depression. Psychiatry Clin North Am. 1996.

Opportunity to Improve MDD Treatment Paradigm

Treatment Considerations

- Physicians typically use multiple SSRIs/SNRIs, prior to progressing to branded therapy
- Poorly managed patients may seek alternative MOAs in 3L+
- Opportunity exists for novel mechanisms that offer efficacy in anhedonia with a differentiated safety profile

MDD Lines of Therapy

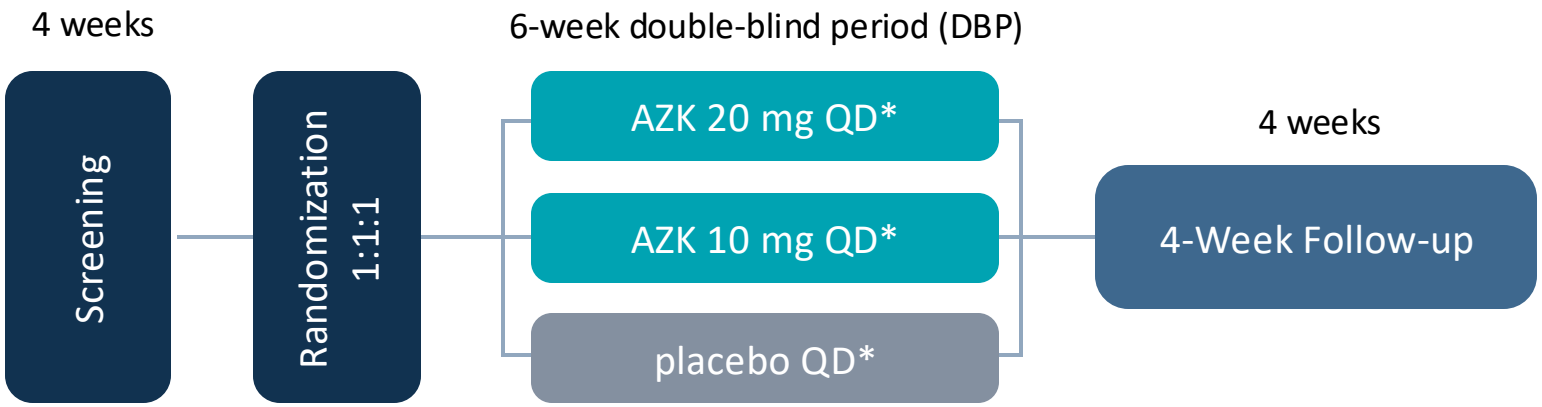


Source: Xenon-sponsored market research

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™



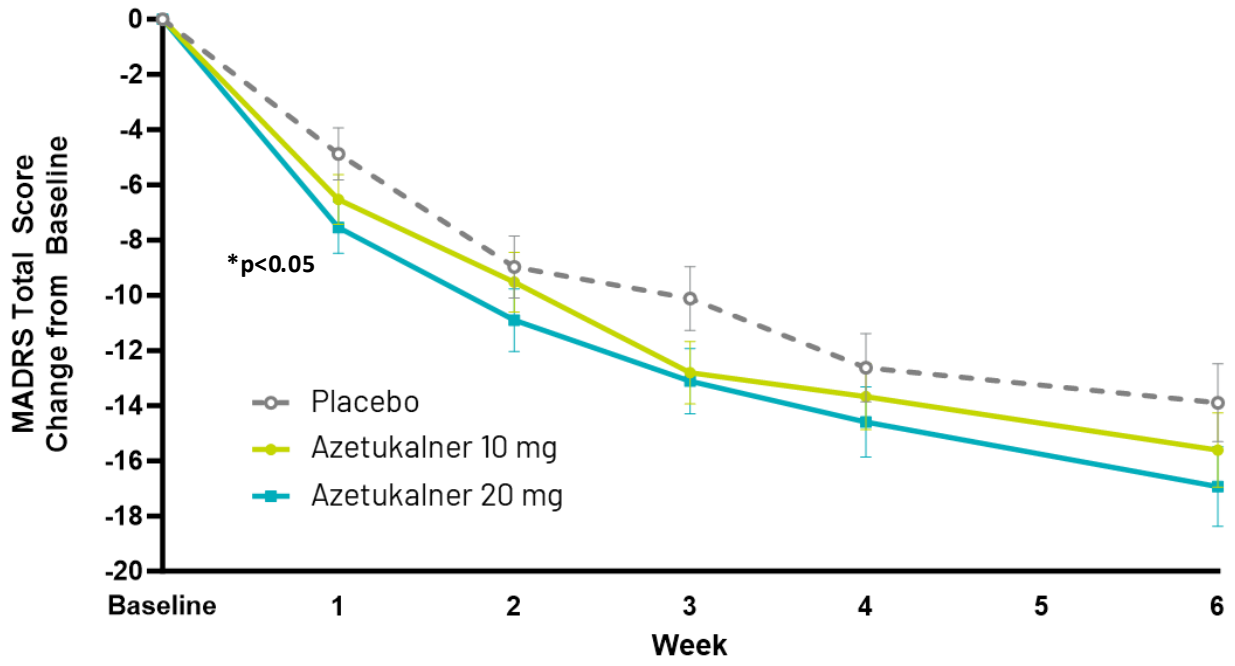
- **Primary Objective:** Montgomery-Åsberg Depression Rating Scale (MADRS) score change through week 6
- **Key Secondary Objective:** Snaith-Hamilton Pleasure Scale (SHAPS) score change through week 6

*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)



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

	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

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

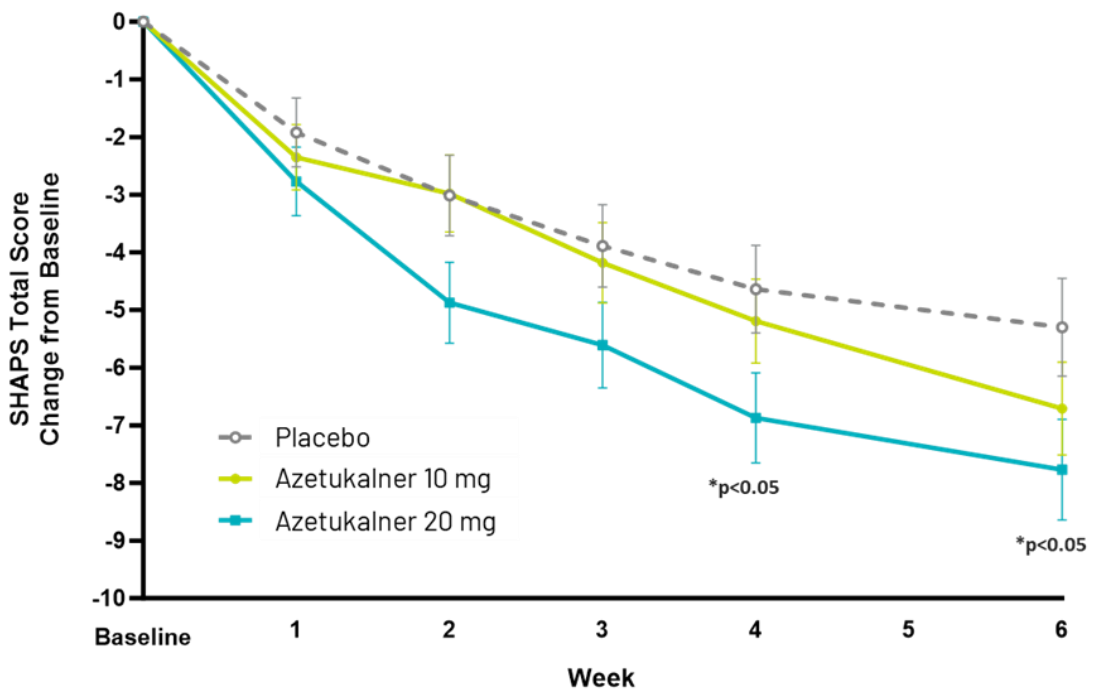
Azetukalner (XEN1101) was administered as a once-daily capsule with food with no titration period.

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

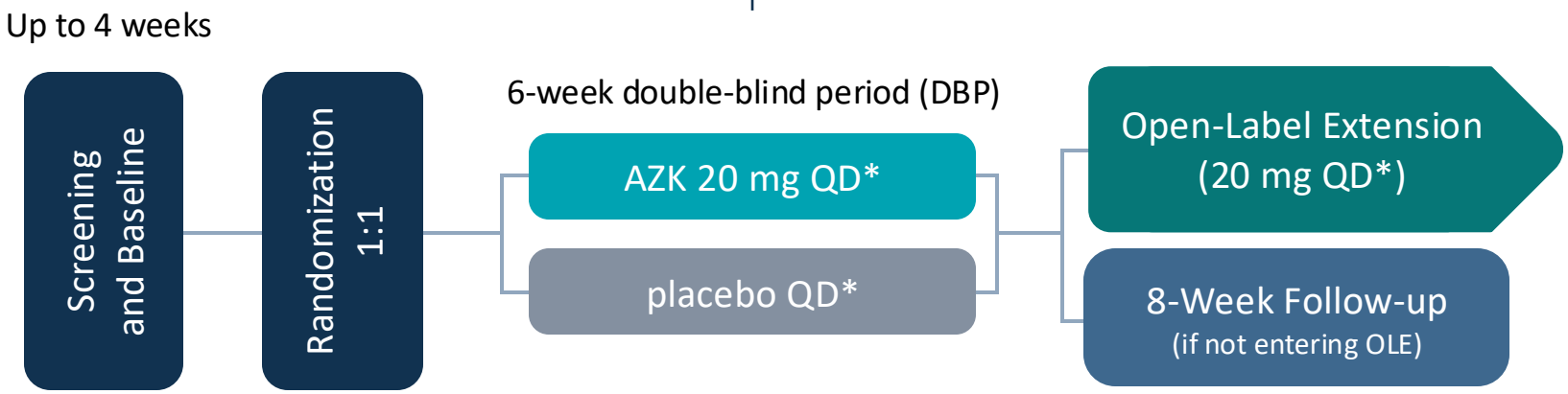
Azetukalner was generally well-tolerated with similar rates of overall adverse events reported across all treatment arms

- 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™



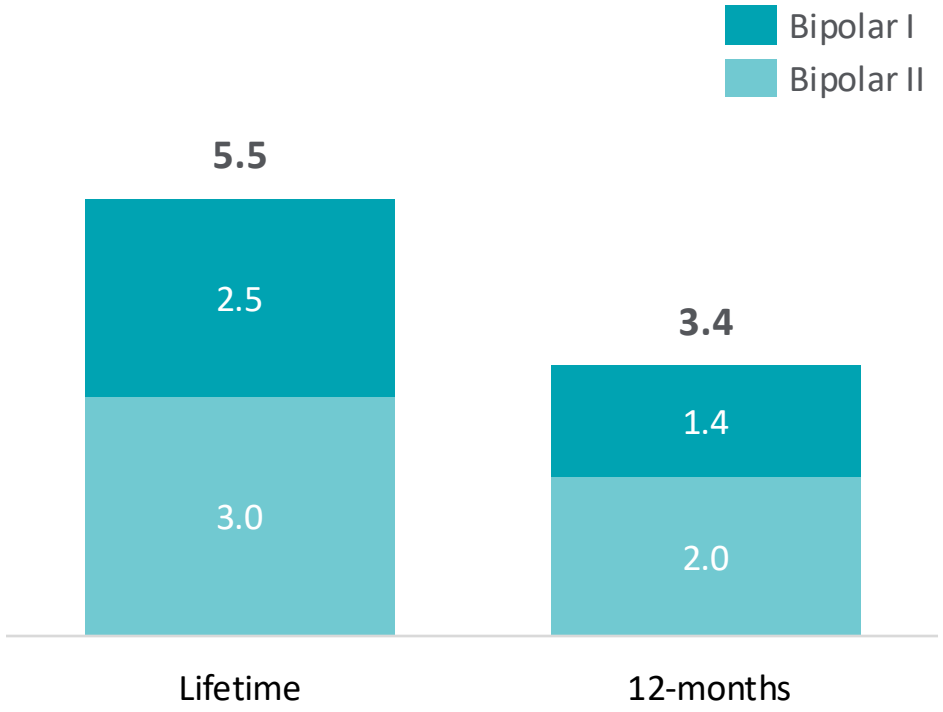
*Administered as once-daily capsule with food with no titration period.

- **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

Limited Options to Address Life-long Nature of Bipolar Depression

Estimated U.S. Bipolar disorder prevalence
Millions of adults

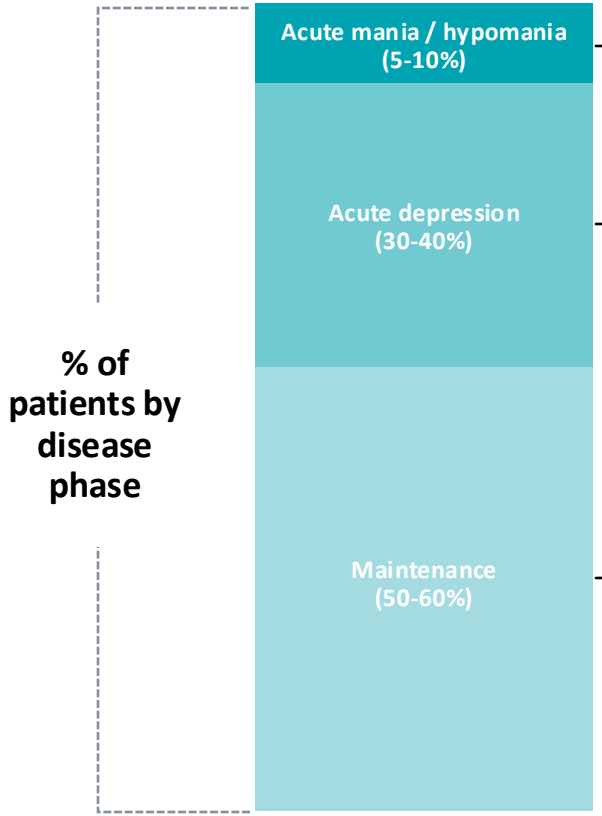


- Bipolar disorder is a life-long disease that requires chronic management with pharmacotherapy
- Hallmark of bipolar disorder is its cyclical pattern, where individuals alternate between mania/hypomania and depression, often with periods of normal mood in between
- Lifetime prevalence is estimated at 5.5M patients
  - 12-month prevalent population (estimated at 3.4 million patients in the U.S.) excludes maintenance patients who did not have an acute bipolar episode in the last 12 months

Note: [1] 12-month prevalence is defined as patients who had bipolar disorder episodes in the 12 months before the clinical interview
Source: Hoertel et al., J. Affect Disord. (2013); Merikangas et al., Arch. Gen. Psychiatry (2007); Merikangas et al., Arch. Gen. Psychiatry (2011); Angst et al., Am. J. Psychiatry (2010); Kessler et al., Int. J. Methods Psychiatr. Res. (2012); and corporate presentations

Bipolar Depression is Debilitating With Limited Tx Options

- Depressive episodes can be longer and more frequent than manic/hypomanic episodes
- Limited effective options (antipsychotics, mood stabilizers) results in patchwork of management options
  - While SSRIs are the standard-of-care in MDD, physicians must avoid agents that can induce mania and/or exacerbate psychosis (e.g. SSRIs) in BPD patients



Acute mania / hypomania (~5-10%)**:** acute manic patients make up a small portion of the overall patient population due to the infrequent nature of manic episodes

Acute depression (~30-40%): acute depressive patients are a significant population as depressive episodes are more common in bipolar disorder

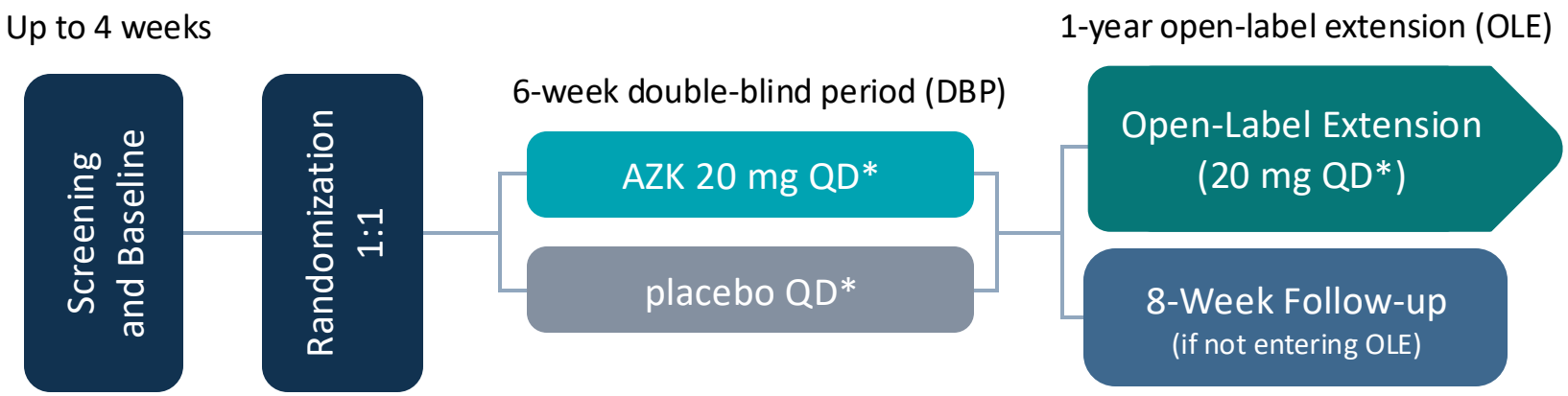
Maintenance (~50-60%): stabilized patients who are not experiencing an active manic or depressed state are on maintenance therapy

Note: [1] 12-month prevalence is defined as patients who had bipolar disorder episodes in the 12 months before the clinical interview
Source: Hoertel et al., J. Affect Disord. (2013); Merikangas et al., Arch. Gen. Psychiatry (2007); Merikangas et al., Arch. Gen. Psychiatry (2011); Angst et al., Am. J. Psychiatry (2010); Kessler et al., Int. J. Methods Psychiatr. Res. (2012); and corporate presentations; company-sponsored market research

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

Early-Stage Programs

Potassium & Sodium Channel Science

Xenon's Ongoing Early-Stage and Product Life Cycle Work

- Leveraging Xenon's deep ion channel expertise to develop promising drug candidates that target sodium and potassium channels
  - XEN1120, a K_V7 channel opener in development for pain: Phase 1 study underway in healthy participants
  - XEN1701, a $Na_V1.7$ channel inhibitor in development for pain: Phase 1 study underway in healthy participants
  - IND-enabling studies are underway for our lead $Na_V1.1$ candidate

Potassium Channel Program

- Strong conviction in broad applicability of K_V7 mechanism and strength of Xenon's discovery platform
- Next gen molecules to be explored in epilepsy and MDD
- Further potential pipeline expansion into pain and other psychiatric indications beyond MDD

Sodium Channel Program

- Leveraging Xenon's extensive knowledge and prior work to advance $Na_V1.7$ program in pain
  - Xenon scientists contributed to early work linking loss of function in SCN9A gene ($Na_V1.7$) to pain, based on strong human genetic validation
- $Na_V1.1$ channel work in epilepsy, based on genetic evidence of underlying pathophysiology of Dravet Syndrome

Maturing Pipeline with Two Novel Pain Programs in Phase 1

K_V7 Program

- Designated lead molecule, XEN1120
- Phase 1 SAD/MAD study underway
  - Preliminary data from the SAD portion of the study suggest that XEN1120 has reached drug concentrations that are consistent with pain reductions in preclinical models
- Study completion expected in 2026 to support initiating a Phase 2 PoC study in acute pain
- Robust pipeline of additional K_V7-targeted compounds being advanced through IND-enabling studies
  - Distinct molecules targeting unique:
    - Binding sites/mechanisms
    - Tissue distribution profiles

$Na_V1.7$ Program

- Designated lead molecule, XEN1701
- Phase 1 SAD/MAD study underway
  - Preliminary data from SAD portion of study suggest XEN1701 has reached drug concentrations 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 PoC study in acute pain
- Robust pipeline of additional NaV1.7-targeted compounds being advanced through IND-enabling studies
  - Differentiated compound profile:
    - CNS exposure
    - Free fraction and tissue distribution
    - Selectivity

SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PoC: proof-of-concept

Pain Landscape Segmented By Type and Duration

	Nociceptive		Neuropathic	Mixed	Nociplastic
Type / origin	Tissue injury	Tissue injury	Nervous system dysfunction	Contribution from injury & nervous system dysfunction	Genetic, environmental and psychosocial factors

	Acute	Chronic
Duration*	< 3 months	Persists for 3+ months

Example indications

- Peri-operative
- Post discharge (procedure)
- Acute musculoskeletal
- Trauma (e.g., fractures)
- Other (e.g., visceral)
- Chronic lower back pain
- Osteoarthritis
- Other arthritis (e.g., RA)
- Other (e.g., idiopathic)
- Diabetic neuropathic pain
- Lumbosacral radiculopathy
- Post-herpetic neuralgia
- Trigeminal neuralgia
- Idiopathic / hereditary neuropathy
- Cancer pain
- Fibromyalgia

Note: * The CDC defines chronic pain in their clinical practice guidelines as pain > 3 months. Source: IQVIA; Pharmaprojects; SymphonyRx; TD Cowen Pain Management Report; Precedence Research; Allied Market Research; BCC Research; CDC

Prevalence and Treatment Paradigms Across Pain Types

Acute Pain

1L

NSAIDs, acetaminophen
(e.g., diclofenac, Tylenol)

1L/2L

Opioid analgesics
(tramadol, hydrocodone)

~1 in 4 Americans experience acute pain annually, with ~50% being prescribed opioids at some point during their management

~80M
Annual U.S. Treated Patients
(Treated incidence)

Chronic Nociceptive Pain*

NSAIDs; Neuromodulators
(e.g., diclofenac, diazepam, Cymbalta)

1L

Add-on *– patients stay on 1L*

Opioids
(Weak & strong opioid analgesics: tramadol, tapentadol, morphine, oxycodone)

2&3L

Interventional procedures

4L+

~35-40M
Annual U.S. Diagnosed Patients
(Prevalence)

Neuropathic Pain

Neuromodulators
(e.g., TCAs, anticonvulsants, Cymbalta)

1L

Add-on *– patients stay on 1L*

Opioids
(Weak & strong opioid analgesics: tramadol, tapentadol, morphine, oxycodone)

2&3L

Interventional procedures

4L+

~10M
Annual U.S. Diagnosed Patients
(Prevalence)

Current pain treatments rely on NSAIDs, neuromodulators and opioids, which pose risks of addiction and poor tolerability

Note: *Patients cycle through opioid treatment in chronic pain; patients often cycle between medications and therapeutic lines in all three pain categories and occasionally use medicines together. Source: External expert interviews; Mayo Clinic; Johns Hopkins; Cleveland Clinic

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 first half of 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

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