Xenon Announces Azetukalner NDA Submission to FDA for Focal Seizures and Provides Update on Psychiatry Clinical Program

September 17, 2026

- *New Drug Application for azetukalner in focal seizures submitted to U.S. Food and Drug Administration; X-TOLE3 and X-ACKT continue to enroll focal seizure and PGTCS patients, respectively*
- *Enrollment in X-NOVA2 study in MDD completed with approximately 360 total patients; topline data readout expected Q1 2027*
- *The Company has voluntarily initiated a temporary pause of enrollment of new patients in ongoing psychiatry studies; patients currently enrolled in the ongoing studies remain active*
- *Conference call today at 4:30 pm ET*

VANCOUVER, BC and BOSTON, MA, Sept. 17, 2026 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq: XENE), a neuroscience-focused biopharmaceutical company dedicated to drug discovery, clinical development, and commercialization of life-changing therapeutics for patients in need, today announced it has submitted a New Drug Application (NDA) for azetukalner in focal seizures (FS) to the U.S. Food and Drug Administration (FDA).

The NDA submission is based on positive clinical data from two global, randomized, double-blind, placebo-controlled trials for azetukalner in focal seizures, including the Phase 2b X-TOLE study and Phase 3 X-TOLE2 study. Across the two studies, treatment with all four doses of azetukalner demonstrated a statistically significant reduction from baseline in monthly seizure frequency compared with placebo, and azetukalner was generally well-tolerated with a consistent safety profile observed in both studies. These safety results are comparable with the long-term safety observed in the X-TOLE open label extension (OLE) study, with the entire epilepsy program generating more than 1,500 patient-years of safety and exposure data.

“We are very pleased to announce completion of the NDA submission for azetukalner in focal seizures in epilepsy. Azetukalner has the potential to deliver much needed innovation to treat people living with focal seizures, with strong efficacy, a differentiated mechanism of action that may enable rational polytherapy, once-daily dosing with no dose adjustments for other antiseizure medications, and a consistent and generally well-tolerated safety profile,” said Ian Mortimer, President and CEO of Xenon. “This is a significant milestone for Xenon as we continue to work toward the potential of our first approval and launch and becoming a fully integrated neuroscience company.”

The ongoing Phase 3 X-TOLE3 and X-ACKT studies of azetukalner in focal seizures and primary generalized tonic-clonic seizures (PGTCS), respectively, continue to enroll patients to support expansion of use across seizure types and global regions.

In addition, the Company announced today that it has implemented a voluntary pause on enrollment for new patients in its ongoing clinical studies in major depressive disorder (MDD) and bipolar depression (BPD), following an analysis of neuropsychiatric adverse events in these studies. Participants currently enrolled in the randomized controlled psychiatry studies and associated OLE studies will continue on study. The observed events, the rate of these events and their severity, are consistent with the known safety and tolerability profile of azetukalner and its mechanism; however, such adverse events had not previously been seen in the Phase 2 X-NOVA clinical study in MDD. The enrollment pause is being implemented as a precautionary measure by Xenon in consultation with its Data Safety Monitoring Board (DSMB) and is expected to be temporary. Xenon is working to evaluate potential dosing modifications to help mitigate these adverse events. This voluntary action does not impact ongoing epilepsy studies.

X-NOVA2 enrollment has reached approximately 80% of its initial target of 450 patients, which is sufficiently powered to demonstrate a clinically meaningful change in the study’s primary endpoint of HAM-D17. The Company plans to complete the six-week dosing period for patients currently enrolled in the trial and unblind the data. Topline data for X-NOVA2 are now expected in Q1 2027.

"We remain very confident in the product profile of azetukalner as a potential new treatment option for patients with epilepsy based on strong efficacy and safety data and a consistent safety profile across over 1,500 patient-years of data,” said Chris Kenney, Chief Medical Officer of Xenon. “For potential expansion in psychiatry, we would like to evaluate whether modifying the dose regimen may help enhance azetukalner’s tolerability profile in this indication. Completing the X-NOVA2 study will help assess the efficacy and tolerability of azetukalner in MDD, which will provide important data to guide us in the future clinical development in psychiatry indications."

Conference Call Information

Xenon will host a conference call and webcast today at 4:30 pm Eastern Time (1:30 pm Pacific Time) to discuss the azetukalner NDA submission and provide an update on the psychiatry clinical programs. A listen-only webcast can be accessed on the Investors section of the Xenon website, with a replay available following the event. Participants can access the conference call by

dialing (800) 715-9871 or (646) 307-1963 for international callers and referencing conference ID 8451337.

About Azetukalner
Azetukalner is a novel, potent K_V7 potassium channel opener currently in development for the treatment of epilepsy, major depressive disorder and bipolar depression. It represents the most advanced, clinically validated potassium channel modulator in late-stage clinical development. Azetukalner is designed to open potassium channels in the central nervous system, allowing potassium ions to flow and hyperpolarizing neurons. This process helps reduce excessive neuronal firing, which is a key contributor to several neurologic and psychiatric disorders.

About Epilepsy and Focal Seizures
Epilepsy is a neurological condition characterized by abnormal electrical activity in the brain that leads to spontaneous, recurrent and unprovoked seizures. It is the fourth most common neurological condition and affects approximately three million adults in the U.S. Focal epilepsy is the most common form of epilepsy. It is characterized by recurrent seizures that originate in a specific area of the brain (focal seizures), leading to various motor, sensory, autonomic, or cognitive symptoms depending on the affected region.

Epilepsy is often managed with polytherapy – or concurrent use of multiple antiseizure medications (ASMs) – to improve seizure control. However, despite more than 30 available epilepsy treatments, up to half of people with focal epilepsy still live with uncontrolled seizures. Epilepsy treatment is further complicated by often burdensome drug interactions and lengthy titration and dose-adjustment periods. These challenges highlight the critical need for a new therapeutic approach.

Phase 3 Epilepsy Studies
The clinical development program for azetukalner in epilepsy includes three Phase 3 clinical studies in focal onset seizures (FOS) and primary generalized tonic-clonic seizures (PGTCS). The completed X-TOLE2 study and the ongoing X-TOLE3 study were both designed as multicenter, randomized, double-blind, placebo-controlled studies to evaluate the clinical efficacy, safety, and tolerability of 15 mg or 25 mg of azetukalner administered orally with food as adjunctive treatment in approximately 360 patients per study with FOS. The primary efficacy endpoint is median percent change (MPC) in monthly seizure frequency from baseline through the 12-week double-blind period (DBP) of azetukalner compared to placebo.

X-ACKT is a multicenter, randomized, double-blind, placebo-controlled study evaluating the clinical efficacy, safety, and tolerability of 25 mg of azetukalner administered with food as adjunctive treatment in approximately 160 patients with PGTCS. The primary efficacy endpoint is MPC in monthly PGTCS frequency from baseline through the 12-week DBP of azetukalner compared to placebo. Upon completion of the DBP in the Phase 3 epilepsy studies, eligible patients may enter an open-label extension (OLE) study for up to six years.

Phase 3 MDD & BPD Studies
The Phase 3 X-NOVA major depressive disorder (MDD) program includes three multicenter, randomized, double-blind, placebo-controlled clinical studies to evaluate the clinical efficacy, safety, and tolerability of 20 mg of azetukalner administered orally with food over the 6-week double-blind period (DBP) as monotherapy treatment in approximately 450 patients per study with moderate-to-severe MDD. The primary efficacy endpoint is the change from baseline in the HAM-D17 score at week 6 in patients who received azetukalner compared to placebo. Upon completion of the DBP, eligible patients may enter an open-label extension (OLE) study for up to 12 months.

The Phase 3 X-CEED Bipolar Depression **(**BPD) program includes two multicenter, randomized, double-blind, placebo-controlled clinical studies to evaluate the clinical efficacy, safety, and tolerability of 20 mg of azetukalner administered orally with food over the 6-week double-blind period (DBP) as monotherapy treatment in approximately 400 patients per study with BPD I or II. The primary efficacy endpoint is the change from baseline in the MADRS score at week 6 in patients who received azetukalner compared to placebo. Upon completion of the DBP, eligible patients may enter an open-label extension (OLE) study for up to 12 months.

About Xenon Pharmaceuticals Inc.
Xenon Pharmaceuticals (Nasdaq: XENE) is a neuroscience-focused biopharmaceutical company dedicated to drug discovery, clinical development, and commercialization of life-changing therapeutics for patients in need. Xenon's lead molecule, azetukalner, is a novel, potent K_V7 potassium channel opener in late-stage clinical development for the treatment of epilepsy, major depressive disorder and bipolar depression. Xenon is also advancing an early-stage portfolio of multiple promising potassium and sodium channel modulators, including K_V7 and $Na_V1.7$ programs in Phase 1 development for the potential treatment of pain. Xenon has offices in Vancouver, British Columbia, and Boston, Massachusetts. For more information, visit www.xenon-pharma.com and follow us on LinkedIn and X.

Safe Harbor Statement
This press release contains 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 status 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 achieve milestones in our pipeline and development programs, including the completion of trial enrollment and timing of topline data readout from any clinical studies; the timing and results of our interactions with regulators; and our ability to successfully develop, obtain regulatory approval for, and commercialize azetukalner and our other product candidates. 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 delay the initiation or completion of clinical studies or impose additional requirements prior to approval; 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.

Contacts

For Investors:
Laura Perry/Emily Huang
Argot Partners
Xenon@argotpartners.com

For Media:
Colleen Alabiso
Senior Vice President, Corporate Affairs
media@xenon-pharma.com