Xenon Showcases New 48-Month Azetukalner OLE Study Data in Epilepsy at AES 2025

December 5, 2025

- *Monthly reductions in seizure frequency of 90.9% among participants treated for ≥48 months in the OLE, with 38% achieving ≥1 year of seizure freedom*
- *New X-TOLE OLE data analysis supports the ability to attain and regain extended periods of seizure freedom with long-term use of azetukalner, even in patients with difficult-to-treat disease*
- *Four real-world study posters illustrate significant burden of depression and ASM titration on people living with epilepsy; poster on impact of depression on outcomes and treatment patterns in patients with newly diagnosed epilepsy highlighted in AES press program*
- *New pre-clinical data in Dravet syndrome suggest potential to improve motor function through $Na_V1.1$ potentiation*

VANCOUVER, British Columbia and BOSTON, Dec. 05, 2025 (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 new data highlighting its commitment in epilepsy, including interim 48-month data from its ongoing X-TOLE open-label extension (OLE) study of azetukalner in patients with focal onset seizures (FOS), multiple real world studies on the burden of depression and anti-seizure medication (ASM) titration in epilepsy, and new data for its pre-clinical program in Dravet syndrome. These data are being presented at the American Epilepsy Society Annual Meeting (AES 2025), taking place December 5-9, 2025 in Atlanta, Georgia.

“We are excited to share the latest update from our ongoing X-TOLE OLE study of azetukalner. The data show impressive monthly reductions in seizure frequency of over 90% at 48 months in the OLE, with a 100% monthly reduction observed among patients receiving 1-2 ASMs at baseline, and an AE profile comparable to the double-blind period,” said Chris Kenney, MD, Chief Medical Officer at Xenon. “We are also sharing a new analysis characterizing intervals of seizure freedom in the X-TOLE OLE, which we believe presents a clinically relevant real-world view of seizure freedom. These data indicate that even after patients had a breakthrough seizure, most could regain extended periods of seizure freedom with continued azetukalner treatment. Additionally, new findings reveal that a meaningful proportion of participants achieved prolonged intervals of seizure freedom of 12 months or longer at their most recent study visit. We believe these interim OLE data continue to support azetukalner’s best-in-class potential among both approved and investigational anti-seizure medicines.”

“The breadth of research we’re presenting this year reflects the commitment we are making in epilepsy and the momentum we are building across our organization,” said Ian Mortimer, President and Chief Executive Officer of Xenon. “AES represents an opportunity to connect with key patient advocates and HCPs in the epilepsy community in advance of sharing near-term Phase 3 data from our X-TOLE2 study in focal onset seizures in early 2026. This will be an important milestone for our team and, more importantly, for the epilepsy patient and physician communities we serve.”

For more information about Xenon’s planned participation at AES 2025, please visit this link. Posters will be available after the live presentations.

Long-Term Data for Azetukalner in Epilepsy

Poster Presentation #3.356: ***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***

- **Sustained reductions in seizure frequency**: Among participants treated for ≥48 months in the OLE (n=131), monthly median percent change (MPC) in FOS frequency increased from a 69.8% reduction in the first month of the OLE to a 90.9% reduction at OLE study month 48. At OLE month 48, higher monthly MPC reductions in FOS frequency from the double-blind period (DBP) baseline were observed for participants in the OLE who were receiving 1-2 ASMs at DBP baseline (n=60, 100%) compared with those receiving 3 ASMs (n=69, 81.8%).

- **Attained seizure freedom:** Among the participants treated for ≥48 months in the OLE (n=131), seizure freedom for any ≥12-, ≥24-, ≥36-, and ≥48-month consecutive durations was attained by 38.2%, 25.2%, 19.8% and 10.7% of the participants respectively.

- **Consistent tolerability and safety profile**: Long-term safety of azetukalner in the OLE was comparable with the safety observed in the DBP.

Poster Presentation #1.377: ***Characterization of Long-Term Seizure Freedom in the Ongoing Open-Label Extension of X-TOLE: Potential Implications for Future Clinical Practice***

- Analysis from the interim X-TOLE OLE data found that seizure freedom can be attained and, if lost, regained with long-term azetukalner treatment, even in patients with difficult-to-treat disease. Of the 131 participants who were treated in the OLE for ≥48 months who had a breakthrough seizure after one interval, or epoch, of ≥6 consecutive months of seizure freedom in the OLE (n=33), 69.7% (n=23) and 57.6% (n=19) regained ≥6 and ≥12 months of subsequent seizure freedom, respectively, with continued azetukalner treatment. Of the participants who had a breakthrough seizure (n=33), there was a mean duration of regained seizure freedom of 18.9 months. Additionally, new findings reveal that a meaningful proportion of participants achieved prolonged intervals of seizure freedom of 12 months or longer at their most recent study visit. Collectively, these findings highlight that assessing only a single epoch of seizure freedom may underestimate the full scope of treatment response over time and offer a deeper understanding of treatment response patterns, which may inform future clinical decision-making.

Epilepsy Real World Studies

Poster Presentation #1.364: ***Depression Symptom Experience Among Patients with Epilepsy Reporting a Diagnosis of Focal Seizures (FS): A Patient-Reported Outcomes Study***

- People living with epilepsy reporting focal seizures experience a considerable mental health burden, including those reporting no formal diagnosis of depression, with most patients reporting depressed mood (80.6%) and anhedonia (81.8%). These findings highlight the potential unrecognized burden of depression in focal epilepsy and support recent guidelines for the routine screening of depression in clinical practice.

Poster Presentation #1.365: ***Impact of Depression on Outcomes and Treatment Patterns in Patients with Newly Diagnosed Epilepsy: A Retrospective Claims Analysis***

- In patients newly diagnosed with epilepsy, the presence of depression was associated with a higher prevalence of psychiatric and systemic comorbidities, shorter duration of initial therapy, and an increased risk of treatment failure. These data underscore the importance of tailored treatment strategies for this patient subgroup.

Poster Presentation #2.325: ***Multivariable Models Reporting Increased Economic and Humanistic Burden Among Patients with Epilepsy Reporting Focal Seizures (FS) Experiencing Moderate to Severe Depression Symptoms***

- People living with epilepsy reporting focal seizures with moderate to severe depression symptoms experience heightened disease burden. Even after accounting for key disease-related and demographic factors, those with depression symptoms experienced significantly lower quality of life and higher healthcare resource utilization, underscoring the need for routine screening for depression among people living with epilepsy.

Poster Presentation #2.367: ***Clinical Practice and Patient Burden Associated with Anti-Seizure Medication Titration: A Thematic Analysis***

- In an analysis assessing both patient and HCP perspectives on the practical realities of ASM titration, with focus on identifying key unmet needs and defining the burden on patients and HCPs, data revealed titration was associated with greater complexity of clinical management, increased strain on healthcare resources, and a substantial and potentially overlooked burden on patients and physicians.

Early-stage Pipeline Data

Poster Presentation #3.181: ***Selective Potentiation of $Na_V1.1$ Channels by XPC-837 in Dravet Mice Suppresses Spontaneous Seizures, Prevents SUDEP and Increases Long Term Potentiation (LTP)***

- Acute dosing of XPC-837, an orally administered $Na_V1.1$ potentiator, improved motor performance in the mouse rotarod assay, supporting the potential for improvements in Dravet patient motor function. In other pre-clinical models of Dravet syndrome, chronic dosing with XPC-837 suppressed spontaneous seizures, prevented sudden unexpected death in epilepsy (SUDEP), produced a more mature dendritic spine morphology, and increased long-term potentiation, a potential cellular correlate of learning and memory. In addition, transcriptomic profiling provided evidence that XPC-837 may normalize *SCN1A* disease-related gene expression back toward wild type levels.

Scientific Exhibit
In addition to booths #133 and #233 in the Exhibit Hall, Xenon is also hosting a Scientific Exhibit to provide an overview of its clinical- and pre-clinical-stage research programs on Sunday, December 7, 2025 from 2:00 – 5:00 pm ET in Room B304/B305.

Satellite Symposium
Xenon is hosting a symposium in partnership with the Epilepsy Foundation of America (EFA) entitled *Exploring Depression and Anxiety in Epilepsy: A Practical Dialogue with Patients and Providers* on Saturday, December 6, 2025 from 6:00 – 9:00 pm ET in Room B213. The panel presentation will feature several representatives from the EFA, as well as Dr. Jacqueline A. French, epileptologist and neurologist with the NYU Langone Comprehensive Epilepsy Center, Dr. Andres M. Kanner, Professor of Clinical Neurology and Director of the Comprehensive Epilepsy Center and Chief of the Epilepsy Division at the Department of Neurology of the University of Miami, Miller School of Medicine, and Dr. Heidi Marie Munger Clary, Associate Professor of Neurology, Epilepsy Fellowship Director and Director of Faculty Research Development at Wake Forest University School of Medicine.

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, selective Kv7 potassium channel opener in Phase 3 clinical trials for the treatment of epilepsy, major depressive disorder (MDD) and bipolar depression (BPD). Xenon is also advancing an early-stage portfolio of multiple promising potassium and sodium channel modulators, including Kv7 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 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; 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.

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Source: Xenon Pharmaceuticals Inc.