Xenon Reports First Quarter 2025 Financial Results and Provides Business Update

May 12, 2025

– Phase 3 azetukalner X-TOLE2 FOS study patient recruitment expected to complete in the next few months with topline data anticipated in early 2026

– Phase 3 azetukalner X-NOVA3 MDD and Phase 3 BPD studies on track to initiate mid-year

– Results from completed Mount Sinai IST in MDD confirm azetukalner drug activity as seen in X-NOVA

– Phase 1 study in healthy volunteers initiated for follow-on Kv7 channel opener XEN1120

– IND filing and Phase 1 study start for XEN1701, lead Nav1.7 candidate, anticipated in Q3 2025

– Conference call at 4:30 pm ET today

VANCOUVER, British Columbia and BOSTON, May 12, 2025 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq: XENE), a neuroscience-focused biopharmaceutical company dedicated to discovering, developing, and delivering life-changing therapeutics for patients in need, today reported financial results for the first quarter ended March 31, 2025, and provided a business update.

"We continue to make steady progress across our Phase 3 epilepsy program, with patient recruitment into our X-TOLE2 study expected to complete in the next few months, positioning us to report topline results in early 2026. While this timing represents a modest shift from our prior guidance, we are encouraged that we are nearing the end of this important study which represents a significant milestone for Xenon, getting us one step closer to a potential first commercial product launch," said Ian Mortimer, President and Chief Executive Officer of Xenon.

"Outside of epilepsy, we have made tremendous progress across our pipeline, including with azetukalner expansion into neuropsychiatry and significant advancements in our earlier-stage programs. Enrollment in our first Phase 3 MDD study, X-NOVA2, is progressing well and our second MDD study, X-NOVA3, along with our first Phase 3 study in bipolar depression are on track for initiation in the near term. In addition, there is great excitement and momentum across our early-stage programs, with the initiation of a Phase 1 study for our first follow-on Kv7 candidate, XEN1120, that we expect to study in pain, and we anticipate a regulatory filing followed by a Phase 1 study start for our lead Nav1.7 candidate, XEN1701, in the third quarter. It's an incredibly exciting time for Xenon as we advance multiple late-stage development programs and continue to progress multiple early-stage programs, with important milestones expected across our pipeline over the coming year," stated Mr. Mortimer.

Business Highlights and Anticipated Milestones

Azetukalner Clinical Development

Azetukalner, a novel, highly potent, selective Kv7 potassium channel opener, represents the most advanced, clinically validated potassium channel modulator in late-stage clinical development for the treatment of multiple indications that include epilepsy, including focal onset seizures (FOS) and primary generalized tonic-clonic seizures (PGTCS), as well as neuropsychiatric disorders including major depressive disorder (MDD) and bipolar depression (BPD).

Epilepsy Programs

- Phase 3 X-TOLE2/3 azetukalner clinical studies in FOS continue to advance, with the first topline data readout anticipated in early 2026.
- Phase 3 X-ACKT clinical study continues to enroll patients and is intended to support potential regulatory submissions in an additional epilepsy indication of PGTCS.
- Xenon presented at the American Academy of Neurology Annual Meeting (AAN), including 36-month data from the ongoing X-TOLE open-label extension (OLE) study of azetukalner in patients with FOS, which demonstrated sustained monthly reduction in seizure frequency, impressive seizure freedom rates, and a consistent AE profile suggesting long-term efficacy and tolerability of azetukalner.

Neuropsychiatric Programs

- X-NOVA2, the first of three planned Phase 3 clinical trials evaluating azetukalner in patients with MDD is currently enrolling patients, and X-NOVA3 is expected to initiate mid-year.

- Xenon announced plans for a Phase 3 BPD program earlier this year, with initiation of the first azetukalner clinical study in BPD I and BPD II depression expected by mid-year.
- The investigator-sponsored Phase 2 proof-of-concept study of azetukalner in MDD led by Icahn School of Medicine at Mount Sinai did not meet its primary neuroimaging endpoint. Compared to placebo, azetukalner demonstrated drug activity and was associated with a numerically higher improvement in MADRS and SHAPS scores across all time periods measured, consistent with results seen in Xenon's Phase 2 X-NOVA study. Azetukalner was generally well tolerated, with a low rate of treatment discontinuations due to adverse events (AEs), one serious adverse event deemed unrelated to study drug, and an AE profile consistent with prior studies and the known mechanism. An abstract reviewing the results of this study has been submitted to the American Society of Clinical Psychopharmacology (ASCP) Annual Meeting to be held May 27-30, 2025.

Early-Stage Pipeline: Next-Generation Ion Channel Modulators

Xenon continues to expand its portfolio by leveraging its extensive expertise to discover and develop potassium and sodium channel therapeutics, with the goal of filing multiple INDs, or equivalent, in 2025.

- A Clinical Trial Application was recently accepted for XEN1120, a Kv7 channel opener, with a Phase 1 study in healthy adult participants now underway. Work remains ongoing with additional Kv7 development molecules and chemistries. Kv7 may have utility in a broad range of therapeutic indications including seizure disorders, pain, and neuropsychiatric disorders, such as MDD and BPD.
- IND-enabling work is underway with multiple Nav1.7 development candidates, with an IND (or equivalent) filing and Phase 1 study initiation for the Xenon's lead candidate, XEN1701, expected in the third quarter. Nav1.7 is an important pain-related target, based on strong human genetic validation, that may represent a new class of medicines without the limitations of opioids.
- The Company expects a lead candidate within its Nav1.1 program to enter IND-enabling studies in 2025. Pre-clinical data suggests that targeting Nav1.1 could potentially address the underlying cause and symptoms of Dravet Syndrome.
- Xenon plans to host multiple R&D webinars this summer to highlight certain early-stage pipeline programs. The first webinar will take place in June and focus on our approach to treating pain with drug candidates targeting both Nav1.7 and Kv7. Additional details to follow in the coming weeks.

Partnered Program

- As part of Xenon's ongoing collaboration with Neurocrine Biosciences, a Phase 1 study is underway of NBI-921355, an investigational, selective inhibitor of voltage-gated sodium channels Nav1.2 and Nav1.6 in development for the potential treatment of certain types of epilepsy.

First Quarter Financial Results

- Cash and cash equivalents and marketable securities were $691.1 million as of March 31, 2025, compared to $754.4 million as of December 31, 2024. Based on current operating plans, including the completion of the azetukalner Phase 3 epilepsy studies and supporting late-stage clinical development of azetukalner in MDD and BPD, Xenon anticipates having sufficient cash to fund operations into 2027. As of March 31, 2025, there were 76,586,359 common shares and 2,173,081 pre-funded warrants outstanding.
- Revenue of $7.5 million was recognized for the quarter ended March 31, 2025, compared to nil for the same period in 2024. The increase was due to a milestone payment recognized in connection with the Neurocrine collaboration.
- Research and development expenses for the quarter ended March 31, 2025 were $61.2 million, compared to $44.3 million for the same period in 2024. The increase of $17.0 million was primarily attributable to continued enrollment in the azetukalner Phase 3 epilepsy clinical trials and Phase 3 X-NOVA2 clinical trial in MDD, increased personnel-related costs due to an increase in employee headcount, and pre-clinical and discovery programs to advance multiple potential drug candidates targeting Kv7, Nav1.7, and Nav1.1.
- General and administrative expenses for the quarter ended March 31, 2025 were $19.0 million, compared to $14.8 million for the same period in 2024. The increase of $4.2 million was primarily attributable to personnel-related costs due to an increase in employee headcount.
- Other income for the quarter ended March 31, 2025 was $8.1 million, compared to $11.5 million for the same period in 2024. The decrease of $3.4 million was primarily attributable to lower interest income.
- Net loss for the quarter ended March 31, 2025 was $65.0 million, compared to $47.9 million for the same period in 2024. The increase in net loss was primarily attributable to higher research and development expenses driven by the azetukalner program, increased personnel-related costs across the organization, and lower interest income.

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 its first quarter 2025 results. 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 5532604.

About Azetukalner Phase 3 Epilepsy Program

Xenon's Phase 3 epilepsy program includes three Phase 3 clinical trials in focal onset seizures (FOS) and primary generalized tonic-clonic seizures (PGTCS). Designed closely after the Phase 2b X-TOLE clinical trial, the Phase 3 X-TOLE clinical trials are multicenter, randomized, double-blind, placebo-controlled studies evaluating 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 with FOS per study. The primary efficacy endpoint is the 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 the 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 OLE study for up to three years.

About Azetukalner Phase 3 MDD Program

Xenon's Phase 3 MDD program includes three multicenter, randomized, double-blind, placebo-controlled clinical trials 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 with moderate-to-severe major depressive disorder (MDD) per study. 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 OLE study for up to 12 months.

About Xenon Pharmaceuticals Inc.

Xenon Pharmaceuticals (Nasdaq: XENE) is a neuroscience-focused biopharmaceutical company dedicated to discovering, developing, and delivering life-changing therapeutics. We are advancing an ion channel product portfolio to address areas of high unmet medical need, including epilepsy and depression. Azetukalner, a novel, highly potent, selective Kv7 potassium channel opener, represents the most advanced, clinically validated potassium channel modulator in late-stage clinical development for multiple indications. For more information, please visit www.xenon-pharma.com.

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 trials; 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 trial 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 trials 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 trials 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 trial results may not be replicated in later clinical trials; 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 trials; the impact of market, industry, and regulatory conditions on clinical trial 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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XENON PHARMACEUTICALS INC.
Condensed Consolidated Balance Sheets
(Expressed in thousands of U.S. dollars)

	March 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents and marketable securities	$ 549,629	$ 626,905
Other current assets	15,908	8,359
Marketable securities, long-term	141,498	127,496
Other long-term assets	36,245	35,379
Total assets	$ 743,280	$ 798,139
Liabilities		
Current liabilities:		
Accounts payable and accrued liabilities	$ 30,648	$ 34,221
Other current liabilities	1,382	1,369
Other long-term liabilities	7,293	7,646
Total liabilities	$ 39,323	$ 43,236
Shareholders' equity	$ 703,957	$ 754,903
Total liabilities and shareholders' equity	$ 743,280	$ 798,139

XENON PHARMACEUTICALS INC.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(Expressed in thousands of U.S. dollars except share and per share amounts)

	Three Months Ended March 31,	
	2025	2024
Revenue	$ 7,500	$ —
Operating expenses:		
Research and development	61,200	44,250
General and administrative	19,038	14,791
	80,238	59,041
Loss from operations	(72,738)	(59,041)
Other income	8,118	11,522
Loss before income taxes	(64,620)	(47,519)
Income tax expense	(427)	(412)
Net loss	$ (65,047)	$ (47,931)
Other comprehensive income (loss):		
Unrealized gain (loss) on available-for-sale securities	$ 776	$ (1,692)
Comprehensive loss	$ (64,271)	$ (49,623)
Net loss per common share:		
Basic and diluted	$ (0.83)	$ (0.62)
Weighted average common shares outstanding:		

Basic and diluted	78,687,503	77,594,599

Source: Xenon Pharmaceuticals Inc.