Xenon Reports Fourth Quarter & Full Year 2024 Financial Results and Business Update

February 27, 2025

– Phase 3 topline data from azetukalner FOS epilepsy program planned for H2 2025 in support of NDA filing and potential commercial launch

– First of three planned Phase 3 azetukalner MDD studies underway, with second study on track to initiate mid-year

– Phase 3 azetukalner bipolar depression program planned for clinical trial initiation mid-year

– Early-stage portfolio advancing with Kv7 and Nav1.7 IND filings anticipated in 2025

– Neurocrine collaboration achieves milestone with initiation of Phase 1 study of Nav1.2/Nav1.6 inhibitor

– Conference call at today

VANCOUVER, British Columbia and BOSTON, Feb. 27, 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 provided a business update and reported financial results for the fourth quarter and full year ended December 31, 2024.

“We expect the next 12 to 24 months will represent a catalyst-rich period for Xenon as we continue to advance our deep pipeline of promising late- and early-stage programs across multiple neurological and neuropsychiatric indications. The anticipated readout from our Phase 3 study in focal onset seizures signifies an important inflection point and could set the stage for our first potential commercial product launch in epilepsy. In addition to building upon our growing leadership in the epilepsy community, we firmly believe that azetukalner has broad potential in neuropsychiatric indications based upon strong mechanistic and scientific rationale, and we are pleased to be enrolling patients in our Phase 3 MDD program, with plans to now initiate a registrational program studying the use of azetukalner in bipolar depression,” said Ian Mortimer, President and Chief Executive Officer of Xenon. “We also expect multiple regulatory filings in 2025 coming out of our early-stage portfolio – which includes Kv7 and Nav1.7 candidates that are progressing through IND-enabling studies – to support the initiation of first-in-human trials across multiple targets. In addition, we are pleased to confirm a promising Nav1.2/Nav1.6 sodium channel inhibitor discovered in Xenon labs has progressed into a Phase 1 study as part of our collaboration with Neurocrine Biosciences, triggering a milestone payment to us,” 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 the second half of 2025.
- 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.
- Building upon more than 700+ patient-years of data to date from the ongoing X-TOLE open-label extension (OLE) study, Xenon continues to generate long-term scientific evidence supporting azetukalner’s compelling efficacy and safety profile, with approximately one in three patients on drug for at least 36 months achieving seizure freedom for a period of one year or longer.
- Xenon continues to present data at leading medical conferences, including the upcoming medical congresses of the American Society for Experimental Neurotherapeutics (ASENT) and the American Academy of Neurology (AAN) taking place in the first half of this year.

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 announces plans for a Phase 3 BPD program with initiation of the first of two azetukalner clinical studies in bipolar I and bipolar II depression expected by mid-year. Initiation of this program is based on a strong scientific rationale – supported by promising clinical data with azetukalner and the Kv7 mechanism in MDD and preclinical research examining the genetic links between BPD and Kv7 and evidence of Kv7 downregulation in BPD – as well as a large unmet medical need.
- Patient enrollment in the investigator-sponsored Phase 2 proof-of-concept study of azetukalner in MDD led by Icahn School of Medicine at Mount Sinai is complete, and topline results are anticipated in the first half of 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.

- IND-enabling work is underway with multiple Kv7 development candidates. Kv7 may have utility in a broad range of therapeutic indications including seizures, pain, and neuropsychiatric disorders, such as MDD and BPD.
- IND-enabling work is underway with a lead Nav1.7 development candidate. 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 will 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.

Partnered Program

- As part of Xenon's ongoing collaboration with Neurocrine Biosciences to develop treatments for epilepsy, NBI-921355, a Nav1.2 and Nav1.6 sodium channel inhibitor in development for the potential treatment for certain types of epilepsy, has progressed into a Phase 1 clinical study in healthy adult participants, triggering an anticipated $7.5 million milestone payment to Xenon.

Corporate

- Xenon announced that Sherry Aulin plans to step down as Chief Financial Officer due to personal reasons. Ms. Aulin is expected to continue to serve as CFO until June 30, 2025, and then act as an advisor through the end of August to ensure a smooth transition.

"Sherry has made invaluable contributions to the organization over the last decade and was instrumental in helping build Xenon as we evolved from a discovery organization to what is now a late-stage clinical organization readying for our first potential drug approval and commercial launch," said Mr. Mortimer. "On behalf of the Board and our entire Xenon team, I want to thank Sherry for her successful leadership as CFO and commitment to ensure a smooth transition at this important time for the company."

"While I am stepping down for personal reasons, I remain excited about Xenon's future, as it enters this transformational period driving towards commercialization, as well as the significant impact Xenon's therapeutics could potentially have on the lives of patients around the world. It has been a privilege to serve as CFO of Xenon, and I am truly honored to have worked alongside such a talented team, and very confident that Xenon is positioned for success," said Ms. Aulin.

- Cash and cash equivalents and marketable securities were $754.4 million as of December 31, 2024, compared to $930.9 million as of December 31, 2023. 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 December 31, 2024, there were 76,416,086 common shares and 2,173,081 pre-funded warrants outstanding.
- Research and development expenses were $59.5 million for the fourth quarter of 2024, and $210.4 million for the year ended 2024, compared to $41.1 million and $167.5 million for the same periods in 2023, respectively. The increase in research and development expenses for the year was primarily attributable to the azetukalner program and increased expenses related to the ongoing Phase 3 epilepsy clinical trials, the initiation of the first Phase 3 MDD clinical trial, as well as manufacturing activities to support current and future clinical trials and a potential NDA submission, and increased personnel-related costs due to an increase in employee headcount and higher stock-based compensation expense.
- General and administrative expenses were $18.0 million for the fourth quarter of 2024, and $68.9 million for the year

ended 2024, compared to $12.6 million and $46.5 million for the same periods in 2023, respectively. The increase in general and administrative expenses for the year was primarily attributable to personnel-related costs due to an increase in employee headcount and higher stock-based compensation expense, and an increase in professional and consulting fees.

- Other income was $7.9 million for the fourth quarter of 2024, and $40.9 million for the year ended 2024, compared to $8.7 million and $31.4 million for the same periods in 2023. The increase in other income for the year was primarily attributable to higher interest income.
- Net loss was $65.7 million for the fourth quarter of 2024, and $234.3 million for the year ended 2024, compared to $44.7 million and $182.4 million for the same periods in 2023, respectively. The increase in net loss for the year was primarily attributable to higher research and development expenses driven by the azetukalner program, as well as increased personnel-related costs and stock-based compensation expense across the organization, partially offset by an increase in 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 fourth quarter and full year 2024 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 8120798.

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)

	, 2024	, 2023
Assets		
Current assets:		
Cash and cash equivalents and marketable securities	$ 626,905	$ 638,082
Other current assets	8,359	6,880
Marketable securities, long-term	127,496	292,792
Other long-term assets	35,379	27,044
Total assets	$ 798,139	$ 964,798
Liabilities		
Current liabilities:		
Accounts payable and accrued liabilities	$ 34,221	$ 25,974
Other current liabilities	1,369	1,299
Other long-term liabilities	7,646	9,604
Total liabilities	$ 43,236	$ 36,877
Shareholders' equity	$ 754,903	$ 927,921
Total liabilities and shareholders' equity	$ 798,139	$ 964,798

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,		Year Ended,	
	2024	2023	2024	2023
Operating expenses:				
Research and development	$ 59,472	$ 41,076	$ 210,394	$ 167,512
General and administrative	18,005	12,619	68,904	46,542
	77,477	53,695	279,298	214,054
Loss from operations	(77,477)	(53,695)	(279,298)	(214,054)
Other income	7,944	8,747	40,879	31,369
Loss before income taxes	(69,533)	(44,948)	(238,419)	(182,685)
Income tax recovery	3,848	205	4,089	292
Net loss	(65,685)	(44,743)	$ (234,330)	$ (182,393)
Other comprehensive income (loss):				
Unrealized gain (loss) on available-for-sale securities	$ (2,948)	$ 2,876	$ (1,535)	$ 2,923
Comprehensive loss	$ (68,633)	$ (41,867)	$ (235,865)	$ (179,470)
Net loss per common share:				
Basic and diluted	$ (0.84)	$ (0.64)	$ (3.01)	$ (2.73)
Weighted average common shares outstanding:				
Basic and diluted	78,386,640	69,968,038	77,894,643	66,889,005

Source: Xenon Pharmaceuticals Inc.