Xenon Pharmaceuticals Reports Second Quarter 2022 Financial Results and Provides Corporate Update

August 9, 2022

Xenon remains on track to initiate the XEN1101 Phase 3 program within second half of this year

Cash runway extended into 2026 following successful completion of equity offering in June

Conference Call at 4:30 pm ET Today

BURNABY, British Columbia, Aug. 09, 2022 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a neurology-focused biopharmaceutical company, today reported financial results for the second quarter ended June 30, 2022 and provided a corporate update.

Mr. Ian Mortimer, Xenon's President and Chief Executive Officer, stated, "With the benefit of a strong balance sheet, which was further bolstered by a recent equity offering, we are sharply focused on executing our clinical development plans across our pipeline. This past quarter marked several important milestones for our XEN1101 program. Following a positive 'End-of-Phase 2' meeting with the FDA, we are excited to advance our XEN1101 Phase 3 program, starting with the initiation of 'X-TOLE2' in the second half of this year. Additionally, we have strong scientific rationale supporting the use of XEN1101 to address primary generalized tonic clonic seizures, and we are looking forward to initiating our Phase 3 'X-ACKT' clinical trial in PGTCS. Ultimately, our goal is to deliver a new, differentiated therapeutic option for epilepsy patients."

Mr. Mortimer continued, "Our team has completed additional sub-analyses of efficacy data from our Phase 2b 'X-TOLE' trial, which further support our Phase 3 development plans for XEN1101, including a 'time course to efficacy' analysis demonstrating that all doses of XEN1101 rapidly reduced the frequency of focal onset seizures within one week compared to placebo. Additionally, within our analysis of the open label extension (OLE) population, we are seeing seizure frequency continuing to improve after the double-blind period with patients experiencing increased periods of seizure freedom."

Mr. Mortimer added, "In addition, our Phase 2 'X-NOVA' study is underway examining XEN1101 in major depressive disorder in parallel with an investigator-led Phase 2 MDD study led by our collaborators at Mount Sinai. Our Phase 3 'EPIK' study is also ongoing examining the use of XEN496 in a rare, pediatric epilepsy called KCNQ2-DEE, and is anticipated to be completed in 2023."

Highlights and Anticipated Milestones

Proprietary Programs

XEN1101 for Epilepsy (Focal Onset Seizures)
XEN1101 is a differentiated Kv7 potassium channel opener being developed for the treatment of epilepsy and major depressive disorder (MDD). In October 2021, Xenon announced positive results from its Phase 2b X-TOLE clinical trial, which evaluated the clinical efficacy, safety and tolerability of XEN1101 administered as an adjunctive treatment for adult patients with focal epilepsy. In June 2022, Xenon announced the successful completion of an End-of-Phase 2 (EOP2) meeting with the U.S. Food & Drug Administration (FDA). Based on the EOP2 meeting, Xenon and the FDA aligned on key elements of the Phase 3 program to support a New Drug Application (NDA) submission. Xenon plans to submit an NDA upon completion of the first XEN1101 Phase 3 clinical trial (X-TOLE2), if successful, and use the existing data package from the Phase 2b X-TOLE clinical trial along with additional safety data from other clinical trials to meet regulatory requirements.

Xenon plans to initiate two identical Phase 3 clinical trials called X-TOLE2 and X-TOLE3, which are designed closely after the Phase 2b X-TOLE clinical trial. X-TOLE2 is expected to be initiated in the second half of 2022 followed by the initiation of X-TOLE3 and both studies will run in parallel. These multicenter, randomized, double-blind, placebo-controlled trials will evaluate the clinical efficacy, safety, and tolerability of XEN1101 administered as adjunctive treatment in approximately 360 patients per study with focal onset seizures (FOS). The primary efficacy endpoint is the median percent change (MPC) in monthly seizure frequency from baseline through the double blind period (DBP) of XEN1101 compared to placebo. On completion of the DBP in X-TOLE2 and X-TOLE3, eligible patients may enter an open-label extension (OLE) study for up to three years. In addition, the ongoing X-TOLE OLE also continues to generate important long-term data for XEN1101 in FOS.

XEN1101 for Epilepsy (Primary Generalized Tonic Clonic Seizures)
Alignment was obtained with the FDA at the EOP2 meeting on key elements of a single Phase 3 clinical trial to pursue an additional epilepsy indication of primary generalized tonic clonic seizures (PGTCS). Following the initiation of X-TOLE2, Xenon plans to initiate a Phase 3 clinical trial, called X-ACKT, to support potential regulatory submissions in PGTCS. This multicenter, randomized, double-blind, placebo-controlled study will evaluate the clinical efficacy, safety, and tolerability of XEN1101

administered as adjunctive treatment in approximately 160 patients with PGTCS. The primary efficacy endpoint is the MPC in monthly PGTCS frequency from baseline through the DBP of XEN1101 compared to placebo. On completion of the DBP in X-ACKT, eligible patients may enter an OLE study for up to three years.

XEN1101 for Major Depressive Disorder
Based on promising pre-clinical data with XEN1101 and published clinical data generated from both an open-label study and a randomized, placebo-controlled clinical trial that explored the targeting of KCNQ channels as a treatment for MDD using ezogabine, Xenon is evaluating the clinical efficacy, safety and tolerability of XEN1101 administered as monotherapy in approximately 150 patients with MDD in a Phase 2 clinical trial called X-NOVA. Designed as a randomized, double-blind, placebo-controlled, multicenter clinical study, the primary objective is to assess the efficacy of XEN1101 compared to placebo on improvement of depressive symptoms in subjects diagnosed with moderate to severe MDD, using the Montgomery-Åsberg Depression Rating Scale (MADRS) score change through week six. Topline results from the X-NOVA study are anticipated in 2023.

In addition, Xenon is collaborating with the Icahn School of Medicine at Mount Sinai to support an ongoing investigator-sponsored Phase 2 proof-of-concept, randomized, parallel-arm, placebo-controlled multi-site study of XEN1101 for the treatment of MDD in approximately 60 subjects. The primary objective of the study is to investigate the effect of XEN1101 on the brain reward circuit as measured by the change in bilateral ventral striatum activity as assessed by functional MRI (fMRI). The secondary objectives are to test the effect of XEN1101 compared to placebo on clinical measures of depression and anhedonia using the MADRS and SHAPS scales.

XEN1101 – Additional Supporting Data
In June 2022, Xenon announced new, compelling efficacy data supporting the late-stage, Phase 3 development of XEN1101. A sub-group analysis of Phase 2b X-TOLE data showed that XEN1101 rapidly reduced FOS frequency within one week for all doses compared with placebo. At Week 1, the median percent reduction in monthly focal onset seizure frequency was 55.4% in the 25 mg group ($p<0.001$), 41.5% in the 20 mg group ($p=0.039$), and 39.1% in the 10 mg group ($p=0.002$) compared to 20.2% in the placebo group. Based on the strength of data from this time course to efficacy analysis, a key secondary endpoint in the Phase 3 trials will include the median percent change of weekly FOS at Week 1. Subjects remaining in the X-TOLE OLE for at least 3 months and 12 months experienced a greater than 70% and 80% reduction, respectively, in median monthly seizure frequency when compared to the DBP baseline.

XEN496
XEN496, a Kv7 potassium channel opener, is a proprietary pediatric formulation of the active ingredient ezogabine being developed for the treatment of KCNQ2 developmental and epileptic encephalopathy (KCNQ2-DEE). A Phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter clinical trial, called EPIK, is ongoing to evaluate the efficacy, safety, and tolerability of XEN496 administered as adjunctive treatment in approximately 40 pediatric patients aged one month to less than six years with KCNQ2-DEE. Xenon anticipates that the EPIK study will be completed in 2023.

Partnered Programs

NBI-921352
Xenon has an ongoing collaboration with Neurocrine Biosciences to develop treatments for epilepsy. Neurocrine Biosciences has an exclusive license to XEN901, now known as NBI-921352, a selective Nav1.6 sodium channel inhibitor. Neurocrine Biosciences is conducting a Phase 2 clinical trial evaluating NBI-921352 in adult patients with focal onset seizures, with data expected in 2023. In addition, a Phase 2 clinical trial is underway evaluating NBI-921352 in patients aged between 2 and 21 years with SCN8A developmental and epileptic encephalopathy (SCN8A-DEE). Pursuant to the terms of the agreement, Xenon has the potential to receive certain clinical, regulatory, and commercial milestone payments, as well as future sales royalties.

PCRX301 (formerly FX301)
In November 2021, Pacira BioSciences, Inc. completed its acquisition of Flexion Therapeutics, Inc., which included Flexion's global rights to develop and commercialize XEN402, a Nav1.7 inhibitor also known as funapide. XEN402 has been formulated for extended release from a thermosensitive hydrogel and is now known as PCRX301 (previously FX301). A Phase 1b proof-of-concept trial is underway evaluating the safety and tolerability of PCRX301 administered as a single-dose, popliteal fossa block in patients undergoing bunionectomy. Pursuant to the terms of the agreement, Xenon has the potential to receive certain clinical, regulatory, and commercial milestone payments, as well as future sales royalties.

Second Quarter 2022 Financial Results

Cash and cash equivalents and marketable securities were $788.2 million as of June 30, 2022, compared to $551.8 million as of December 31, 2021. The increase was the result of the completion of the Company's public offering in June 2022. As of June 30, 2022, there were 62,242,883 common shares and 3,103,864 pre-funded warrants outstanding.

Based on current assumptions, which include supporting the XEN1101 clinical development program including the completion of the planned Phase 3 epilepsy studies, XEN496, and pre-clinical and discovery programs, Xenon anticipates having sufficient cash to fund operations into 2026, excluding any revenue generated from existing partnerships or potential new partnering arrangements.

For the quarter ended June 30, 2022, Xenon reported total revenue of $0.5 million, compared to $2.2 million for the same period

in 2021. The decrease of $1.7 million was primarily attributable to lower research and development services revenue from Neurocrine Biosciences as the research collaboration began to wind down in 2022 and ended in June 2022.

Research and development expenses for the quarter ended June 30, 2022 were $22.1 million, compared to $18.4 million for the same period in 2021. The increase of $3.8 million was primarily attributable to higher salaries and benefits due to increased headcount, stock-based compensation expense and information technology costs allocated amongst research and development programs as well as external costs related to pre-clinical, discovery and other internal programs. The increases were partially offset by lower external costs related to our XEN1101 program.

General and administrative expenses for the quarter ended June 30, 2022 were $8.7 million compared to $6.3 million for the same period in 2021. The increase of $2.4 million was primarily attributable to higher stock-based compensation expense, salaries and benefits due to an increase in employee headcount, recruitment fees and insurance premiums.

Other expense for the quarter ended June 30, 2022 was $0.9 million compared to other income of $0.2 million for the same period in 2021. The change was primarily attributable to an unrealized loss on fair value of marketable securities for the quarter ended June 30, 2022 due to fluctuations in market yields, partially offset by higher interest income due to an increase in marketable securities and market yields on investments.

Net loss for the quarter ended June 30, 2022 was $31.2 million, compared to $22.1 million for the same period in 2021. The change was primarily attributable to an increase in research and development and general and administrative expenses, lower revenue and higher unrealized fair value loss on marketable securities compared to the same period in 2021.

Conference Call Information

Xenon will host a conference call and live audio webcast today at 4:30 pm Eastern Time (1:30 pm Pacific Time) to discuss its second quarter results and to provide a corporate update. The audio webcast will be broadcast live on the Investors section of the Xenon website. To participate in the call, please dial 1-800-715-9871, or 1-646-307-1963 for international callers, and provide conference ID number 6560707.

About Xenon Pharmaceuticals Inc.

Xenon Pharmaceuticals (NASDAQ:XENE) is a clinical stage biopharmaceutical company committed to developing innovative therapeutics to improve the lives of patients with neurological disorders. We are advancing a novel product pipeline of neurology therapies to address areas of high unmet medical need, with a focus on epilepsy. 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, 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 XEN1101 and other development programs; the timing and results of our interactions with regulators; our ability to successfully develop and obtain regulatory approval of XEN1101 and our other product candidates; anticipated enrollment in our clinical trials and the timing thereof; and our expectation that we will have sufficient cash to fund operations into 2026. 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: the impact of the ongoing COVID-19 pandemic on our research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; 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 XEN1101 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 of clinical trials; regulatory agencies may be delayed in reviewing, commenting on or approving any of our or our collaborators' clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; 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 the COVID-19 pandemic on our business; 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 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.

XENON PHARMACEUTICALS INC.
Condensed Consolidated Balance Sheets
(Expressed in thousands of U.S. dollars)

	June 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents and marketable securities	$ 788,238	$ 551,774
Other current assets	6,565	7,246
Other assets	12,577	12,987
Total assets	$ 807,380	$ 572,007
Liabilities		
Current liabilities:		
Accounts payable and accrued expenses	$ 13,736	$ 13,717
Other current liabilities	—	605
Other liabilities	7,851	7,652
Total liabilities	$ 21,587	$ 21,974
Shareholders' equity	$ 785,793	$ 550,033
Total liabilities and shareholders' equity	$ 807,380	$ 572,007

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Revenue	$ 536	$ 2,218	$ 9,302	$ 6,576
Operating expenses:				
Research and development	22,146	18,377	41,506	34,685
General and administrative	8,705	6,339	15,480	10,448
Total operating expenses	30,851	24,716	56,986	45,133
Loss from operations	(30,315)	(22,498)	(47,684)	(38,557)
Other (expense) income	(883)	172	(3,578)	399
Loss before income taxes	(31,198)	(22,326)	(51,262)	(38,158)
Income tax recovery	40	217	434	285
Net loss and comprehensive loss	(31,158)	(22,109)	(50,828)	(37,873)
Net loss attributable to preferred shareholders	—	(521)	(385)	(951)
Net loss attributable to common shareholders	$ (31,158)	$ (21,588)	$ (50,443)	$ (36,922)
Net loss per common share:				
Basic and diluted	$ (0.55)	$ (0.51)	$ (0.91)	$ (0.94)
Weighted-average common shares outstanding:				
Basic and diluted	56,192,922	42,090,207	55,522,857	39,457,413

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