Xenon Pharmaceuticals Outlines Key Milestone Opportunities for 2023

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XEN1101 Phase 3 Epilepsy Program Ongoing in Focal Onset Seizures and Recently Initiated in Primary Generalized Tonic Clonic Seizures

Strong financial position expected to fully support XEN1101 Phase 3 program development and cash runway into 2026

BURNABY, British Columbia, Jan. 09, 2023 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a neurology-focused biopharmaceutical company, today outlined recent progress in its clinical programs and key milestones for 2023.

Mr. Ian Mortimer, Xenon's President and Chief Executive Officer, stated, "We enter 2023 in a strong position with increasing momentum in our XEN1101 Phase 3 program, which represents the most advanced potassium channel modulator in clinical development for multiple indications. With our X-TOLE2 study underway in focal onset seizures, we are excited to announce the initiation of our Phase 3 X-ACKT clinical trial in primary generalized tonic clonic seizures."

Mr. Mortimer continued, "We believe XEN1101 shows immense promise based on its validated mechanism of action and a robust data package, including efficacy data from our Phase 2b X-TOLE clinical trial and read-outs from our ongoing open-label extension study. Having established alignment with the FDA on our Phase 3 program and NDA filing requirements, we remain sharply focused on advancing XEN1101 with the goal of improving outcomes for epilepsy patients where there continues to be a significant need for new, differentiated anti-seizure medications."

Mr. Mortimer added, "In parallel with the work supporting the continued advancements of our Phase 3 XEN1101 program, we also anticipate clinical data read-outs in 2023. In the third quarter of this year, we expect the topline data readout from our Phase 2 X-NOVA clinical trial, a proof-of-concept study examining the use of XEN1101 in major depressive disorder. In addition, our partners at Neurocrine expect to have a clinical read-out from their Phase 2 study in adult patients with focal onset seizures in the second half of this year."

Highlights and Anticipated Milestones

XEN1101
XEN1101 is a differentiated Kv7 potassium channel opener being developed for the treatment of epilepsy and major depressive disorder (MDD).

XEN1101 for Focal Onset Seizures
Xenon has initiated its XEN1101 Phase 3 development program, which includes two identical Phase 3 clinical trials to be run in parallel, called X-TOLE2 and X-TOLE3, that are designed closely after the Phase 2b X-TOLE clinical trial. 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.

XEN1101 for Primary Generalized Tonic Clonic Seizures
Xenon has initiated a Phase 3 clinical trial, called X-ACKT, to support potential regulatory submissions in an additional epilepsy indication of primary generalized tonic clonic seizures (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.

Upon completion of the DBP in X-TOLE2, X-TOLE3, or X-ACKT, eligible patients may enter an open-label extension (OLE) study for up to three years. In addition, the ongoing X-TOLE Phase 2b OLE continues to generate important long-term data for XEN1101.

XEN1101 for Major Depressive Disorder
Based on promising pre-clinical data with XEN1101 and published clinical data generated 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 the third quarter of this year.

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 Snaith-Hamilton Pleasure Scale (SHAPS).

Additional Programs and Corporate Updates

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 2024.

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 the second half of this year. 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.

Cash and cash equivalents and marketable securities were $752.2 million as of September 30, 2022. As previously reported and 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.

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: 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; 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 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, regulatory agencies and related review times, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; 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.

Investor/Media Contact:
Jodi Regts
Xenon Pharmaceuticals Inc.
Phone: 604.484.3353
Email: investors@xenon-pharma.com

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