



Xenon Pharmaceuticals Provides Updates on Proprietary Neurology Pipeline Programs at the Annual Meeting of the American Epilepsy Society (AES 2022)

December 2, 2022

Company Presents Additional Positive Data from Open Label Extension of Phase 2b 'X-TOLE' Clinical Trial for Focal Onset Seizures

XEN1101 Phase 3 Program to be Showcased at Scientific Exhibit Taking Place on Sunday, December 4, 2022

BURNABY, British Columbia, Dec. 02, 2022 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a neurology-focused biopharmaceutical company, today announced it will provide updates on its proprietary, neurology programs at the Annual Meeting of the American Epilepsy Society (AES 2022). In addition, the Company is presenting results from the open label extension (OLE) and sub-analyses of data from the XEN1101 Phase 2b X-TOLE clinical trial.

Mr. Ian Mortimer, Xenon's President and Chief Executive Officer stated, "We continue to advance our portfolio of neurology-focused programs. Xenon will have a significant presence at AES this year with seven poster presentations and a scientific exhibit showcasing our recently launched XEN1101 Phase 3 program and our planned clinical trials in focal onset seizures and primary generalized tonic clonic seizures. We also look forward to meeting with leading epileptologists, including Xenon trial investigators, as well as patient advocacy groups at this important meeting."

Mr. Mortimer continued, "Importantly, we have a scientific poster outlining additional data from the open-label extension of the XEN1101 Phase 2b X-TOLE study. This interim analysis shows XEN1101 continues to be generally well-tolerated, yielding long-term efficacy at the 20 mg once-daily dose, with patients experiencing continued seizure reduction during the OLE and extended periods of seizure freedom. Two other XEN1101-related posters outline additional sub-analyses of the X-TOLE data that suggest a rapid onset of efficacy of XEN1101, with statistically significant reduction in focal onset seizures within one week for all doses studied when compared to placebo. Further, based on the number of concomitant ASMs, baseline seizure frequency, and number of failed anti-seizure medications, the X-TOLE study enrolled more 'difficult-to-treat' patients than other similar focal onset seizure studies. We believe this is important as it suggests that the efficacy of XEN1101 may be robust in patients with less severe disease, which may represent the most common use of XEN1101 if commercially approved. With these promising data, we have now initiated our XEN1101 Phase 3 program, where we hope to confirm these encouraging results and continue to execute on our goal to deliver a new, differentiated therapeutic that could potentially play a key role in treating patients with epilepsy."

XEN1101 AES Poster Highlights

Poster No. 2.235 (French et al.) "XEN1101, a Novel Potassium Channel Modulator: Interim Data From an Ongoing, Long-Term, Open-Label Extension of a Phase 2B Study (X-TOLE) in Adults With Focal Epilepsy"

- During the OLE, there was a sustained monthly reduction in seizure frequency (80%–90% seizure reduction as measured by MPC) from the double-blind period (DBP) baseline, as of the analysis cutoff date of September 22, 2022.
- Seizure freedom for ≥6-month and ≥12-month consecutive durations was achieved in 17.5% and 10.5% of patients, respectively.
- XEN1101 continues to be generally well-tolerated in the OLE with adverse events (AEs) consistent with prior results and other anti-seizure medications (ASMs).
 - At the end of the first year in the OLE, patients recorded a mean (SD) weight gain of 1.1 (5.9) kg.
 - To date, two AEs of urinary retention occurred in the OLE possibly related to study drug; both patients continued in the study without requiring intervention.
 - Although not seen to date, Xenon continues to monitor for the emergence of the tissue discoloration that was associated with long-term exposure to ezogabine.

Poster No. 2.236 (Kenney et al.) "Rapid Onset of Efficacy of XEN1101, a Novel Potassium Channel Opener, in Adults With Focal Epilepsy: Results From a Phase 2b Study (X-TOLE)"

- X-TOLE met the primary and key secondary efficacy endpoints with XEN1101 demonstrating a statistically significant, dose-dependent reduction from baseline in monthly focal onset seizure (FOS) frequency compared to placebo.
- The rapid onset of efficacy for XEN1101 was associated with starting at an effective, therapeutic and well-tolerated dose. There was a statistically significant reduction in median FOS frequency within 1 week for all doses compared with placebo.
- The rapid onset of efficacy after 1 week and sustained efficacy of XEN1101, if confirmed in the Phase 3 clinical trials, suggests that XEN1101 may offer a compelling option for patients seeking adjunctive therapy.

Poster No. 2.233 (Leung et al.) "The Impact of Disease Severity on Efficacy From a Phase 2b Study of XEN1101, a Novel Potassium Channel Opener, in Adults With Focal Epilepsy (X-TOLE)"

- X-TOLE met the primary and key secondary efficacy endpoints with XEN1101 demonstrating a statistically significant, dose-dependent reduction from baseline in monthly FOS frequency compared to placebo in a difficult-to-treat population.
- Based on the number of concomitant ASMs, baseline seizure frequency, and number of failed ASMs, the X-TOLE study enrolled more difficult-to-treat patients than other FOS studies. In the 25 mg dose group, XEN1101 reduced seizure frequency in sub-groups of patients with ≤ 8.5 seizures/month, and in patients that failed ≤ 6 ASMs or were on 1-2 concomitant ASMs by 70.6%, 58.0% and 60.9%, respectively, compared with placebo (18.8%, 20.0% and 14.2%, respectively).
- These post hoc analyses suggest that efficacy may be more robust in patients with less severe disease, which may represent the most common clinical use of XEN1101 if commercially approved.

Xenon's Scientific Exhibit and Booth

In addition to the posters noted above, Xenon is hosting a scientific exhibit at AES 2022 providing an overview of its clinical and research programs on Sunday, December 4, 2022 from 2-5 pm CT in Room 207 C, Level 2 of Music City Center. The exhibit will feature an overview of the XEN1101 Phase 3 trial designs, including X-TOLE2 and X-TOLE3 for FOS and X-ACKT for primary generalized tonic clonic seizures, as well as the Phase 2 study design for X-NOVA for major depressive disorder. Other poster presentations will cover additional programs within Xenon's neurology-focused pipeline.

Xenon is also hosting a booth (#1028) in the Exhibit Hall, which is scheduled to open at 12 pm CT on Saturday, December 3, 2022 and run to 2 pm CT on Monday, December 5, 2022.

Other AES Poster Highlights

Other Xenon posters at AES 2022 include clinical work related to Xenon's XEN496 program and its ongoing Phase 3 EPIK clinical trial in pediatric patients with KCNQ2 developmental and epileptic encephalopathy:

- Poster 1.370 (Grayson et al.) "Genetic Burden of *KCNQ2* in Neonates With Epilepsy"
- Poster 1.372 (Harden et al.) "An Online Survey of Caregivers of Patients With *KCNQ2* Developmental and Epileptic Encephalopathy"
- Poster 2.334 (Butterfield et al.) "Real-World Evidence of *KCNQ2* Disease Management as Generated Through a Novel Data Platform"

Xenon is also presenting pre-clinical work from its discovery efforts related to the exploration of $\text{Na}_V1.1$ potentiators for the treatment of Dravet Syndrome:

- Poster 3.049 (Goodchild et al.) "Molecularly Selective $\text{Na}_V1.1$ Potentiators Increase PV+ Fast-Spiking Interneuron Excitability and Restore Motor Performance in a Mouse Model of Dravet Syndrome"

Posters will be added to the Xenon website consistent with AES 2022 conference guidelines.

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 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; and anticipated enrollment in our clinical trials and the timing thereof. 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.

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