# Xenon Pharmaceuticals Presents Data from Phase 2 X-NOVA Clinical Trial of Azetukalner in Major Depressive Disorder at the American Society of Clinical Psychopharmacology 2024 Annual Meeting

May 28, 2024

VANCOUVER, British Columbia, May 28, 2024 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a neuroscience-focused biopharmaceutical company, announced data presentations highlighting azetukalner (XEN1101) clinical data in major depressive disorder (MDD) at the American Society of Clinical Psychopharmacology (ASCP) 2024 Annual Meeting in Miami, FL.

Mr. Ian Mortimer, Xenon's President and Chief Executive Officer, stated, "We are pleased to present these data from our Phase 2 proof-of-concept X-NOVA study of azetukalner in MDD at the ASCP meeting. The X-NOVA results demonstrated a clinically meaningful reduction in depression, in addition to an early onset of action, a significant reduction in anhedonia, and a potentially differentiated safety profile of azetukalner as compared to other antidepressants. These compelling data, along with azetukalner's novel mechanism of action, support the potential of azetukalner to have a differentiated profile in the treatment of depression."

Mr. Mortimer continued, "We are looking forward to connecting with ASCP attendees and continuing to raise awareness of azetukalner's potentially unique attributes and highlight our late-stage clinical work in MDD, starting with the initiation of our Phase 3 MDD program in the second half of this year."

**Xenon's Presentations at ASCP:**

> **Oral Presentation:** "Efficacy and Safety of Azetukalner (XEN1101), a Novel, Kv7 Potassium Channel Opener in Adults With Moderate to Severe Major Depressive Disorder: Results From the Phase 2 Proof-of-Concept X-NOVA Study"
> Presenter: Dr. Joe McIntosh, Senior Vice President, Clinical Development, Xenon Pharmaceuticals
> May 28, 2024 at 2 pm ET in Salon 3
>
> **Poster**: "Efficacy and Safety of Azetukalner (XEN1101), a Novel, Kv7 Potassium Channel Opener in Adults With Moderate to Severe Major Depressive Disorder: Results From the Phase 2, Proof-of-Concept X-NOVA Study"
> May 29, 2024 at 11:15 am to 1 pm ET in Salon 4
> The Company's presentations summarize clinical data from its topline results from the Phase 2 proof-of-concept X-NOVA clinical trial, which evaluated the clinical efficacy, safety, and tolerability of 10 mg and 20 mg of azetukalner in 168 patients with moderate to severe MDD.

**Summary of Efficacy Data:**

- The primary endpoint of the study was a change in the Montgomery-Åsberg Depression Rating Scale, or MADRS, at week 6. The mean reduction was 13.90 in the placebo group, 15.61 in the 10 mg group and 16.94 in the 20 mg group. A clear dose response and a clinically meaningful, but not statistically significant, 3.04 difference between placebo and the azetukalner 20 mg groups ($P$=0.135) was observed.
- At week 1, the mean reduction in MADRS score from baseline (exploratory endpoint) was significantly different between placebo and azetukalner 20 mg groups (4.88 vs 7.54; $P$=0.047), demonstrating early onset of efficacy.
- The mean reduction in the Hamilton Depression Rating Scale, or HAM-D17, score from baseline to week 6 (pre-specified exploratory endpoint) was significantly different between placebo and azetukalner 20 mg groups (10.2 vs 13.3; difference –3.1, $P$=0.042).
- The mean reduction in the Snaith-Hamilton Pleasure Scale, or SHAPS, score from baseline to week 6 (secondary endpoint) was significantly different between placebo and azetukalner 20 mg groups (5.30 vs 7.77; difference –2.46, $P$=0.046).
- There were no statistically significant differences in change from baseline BAI total scores to week 6 between placebo and azetukalner groups. At baseline, the X-NOVA population, on average, demonstrated minimal to mild symptoms of anxiety (baseline mean BAI total score ≤15). In a *post hoc* analysis, amongst those participants with moderate to severe BAI scores (≥16) at baseline, numerical improvements were noted in the change from baseline BAI total scores to week 6 in the 20 mg azetukalner group compared to the placebo group (15.38 vs. 9.36; difference –6.02).
- Statistical significance was achieved in reporting of at least minimally improved symptoms of depression as assessed by physicians using the Clinical Global Impression of Improvement (CGI-I) ($P$=0.004) in the azetukalner 20 mg group compared to placebo.

**Summary of Safety and Tolerability Data:**

- Azetukalner was well tolerated with a low incidence of treatment-emergent adverse events (TEAEs), and no serious TEAEs were reported in either dose group.
- The most commonly reported TEAEs in the azetukalner 20 mg group included dizziness (17.9%), somnolence (10.7%), headache (8.9%), and disturbance in attention (8.9%), compared to the placebo group which reported dizziness (7.3%), somnolence (1.8%), headache (12.7%), and disturbance in attention (0%).
- Rates of discontinuation were similar across all treatment arms and rates of discontinuation owing to TEAEs were low with three patients in the azetukalner 20 mg group (5.4%) compared to two patients in the placebo group (3.6%).
- Azetukalner was not associated with notable weight gain or sexual dysfunction.

**About Xenon Pharmaceuticals Inc.**

Xenon Pharmaceuticals (Nasdaq:XENE) is a neuroscience-focused biopharmaceutical company committed to discovering, developing, and commercializing innovative therapeutics to improve the lives of people living with neurological and psychiatric disorders. We are advancing a novel product pipeline to address areas of high unmet medical need, including epilepsy and depression. 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 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; 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 enrollment in our clinical trials of azetukalner 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 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 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 pandemics, epidemics and other public health crises 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; 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.

"Xenon" and the Xenon logo are registered trademarks or trademarks of Xenon Pharmaceuticals Inc. in various jurisdictions. All other trademarks belong to their respective owner.

**Contacts:**

*For Investors:*
Chad Fugere
Vice President, Investor Relations
(857) 675-7275
investors@xenon-pharma.com

*For Media:*
Jodi Regts
Xenon Corporate Affairs
(604) 484-3353
media@xenon-pharma.com

XENON

Source: Xenon Pharmaceuticals Inc.