UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 21, 2022

XENON PHARMACEUTICALS INC.

(Exact name of Registrant as Specified in Its Charter)

Canada	**001-36687**	**98-0661854**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

200-3650 Gilmore Way **Burnaby, British Columbia, Canada** **(Address of Principal Executive Offices)**	**V5G 4W8** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (604) 484-3300

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Shares, without par value	XENE	The Nasdaq Stock Market LLC (The Nasdaq Global Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On June 21, 2022, Xenon Pharmaceuticals Inc. (the "Company") issued a press release announcing the positive outcome of the Company's End-of-Phase 2 meeting with the U.S. Food and Drug Administration to support the initiation of its XEN1101 Phase 3 program in adult patients with focal epilepsy.

A copy of the Company's press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press Release issued by Xenon Pharmaceuticals Inc. dated June 21, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

XENON PHARMACEUTICALS INC.

Date: June 21, 2022

By: /s/ Sherry Aulin
Sherry Aulin
Chief Financial Officer

XENON

NEWS RELEASE

Xenon Pharmaceuticals Announces Positive Outcome of End-of-Phase 2 Meeting with the FDA

XEN1101 Phase 3 program for the treatment of focal onset seizures to be initiated in the second half of 2022 and New Drug Application expected to be submitted after completion of first Phase 3 clinical trial (X-TOLE2) along with the completed Phase 2b (X-TOLE) clinical trial

Plans to initiate XEN1101 Phase 3 clinical trial (X-ACKT) in an additional epilepsy indication of primary generalized tonic clonic seizures

BURNABY, British Columbia, June 21, 2022 – Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a neurology-focused biopharmaceutical company, today announced next steps in its clinical program evaluating XEN1101 for the treatment of patients with focal onset seizures (FOS) following the completion of an End-of-Phase 2 (EOP2) meeting with the U.S. Food & Drug Administration (FDA). The outcome of the EOP2 meeting supports the advancement of XEN1101 into Phase 3 clinical development, and Xenon remains on track to initiate the Phase 3 program in the second half of 2022.

Mr. Ian Mortimer, Xenon's President and Chief Executive Officer, stated, "The successful completion of our EOP2 meeting with the FDA marks another important milestone in our XEN1101 program, and we are excited to advance XEN1101 into Phase 3 development. One of Xenon's key goals is to deliver innovative medicines that improve the lives of patients with epilepsy. Supported by the strong data generated from our Phase 2b 'X-TOLE' clinical trial, we believe XEN1101 has the potential to offer a highly differentiated and competitive profile when compared to other anti-seizure medications based on its unique potassium channel mechanism of action combined with once-a-day dosing in the evening with no titration. We look forward to initiating our Phase 3 program to support a planned NDA submission for XEN1101 with the goal of providing a new therapeutic option for patients with FOS."

The EOP2 meeting was supported by nonclinical and clinical data, including results from the previously completed Phase 1 trials and the positive Phase 2b X-TOLE clinical trial evaluating XEN1101 in adult patients with FOS. The X-TOLE topline efficacy data demonstrated that the primary and secondary seizure reduction endpoints were statistically significant across all three dose groups, with p-values of <0.001 for the 20 mg and 25 mg groups, and XEN1101 was generally well tolerated.

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. Additionally, alignment was obtained with the FDA on key elements of a single Phase 3 clinical trial to pursue an additional epilepsy indication of primary generalized tonic clonic seizures (PGTCS).

Dr. Christopher Kenney, Xenon's Chief Medical Officer, commented, "We are pleased with the constructive EOP2 meeting with the FDA and are excited to initiate our XEN1101 Phase 3 program in the second half of 2022. We have been evaluating other potential epilepsy indications for XEN1101 and have a strong scientific rationale supporting the use of XEN1101 to address PGTCS. Our research with key opinion leaders indicates there is a strong unmet need for new drugs with novel mechanisms of action, particularly for patients experiencing persistent PGTCS despite treatment with other anti-seizure medications. We expect to initiate our single Phase 3 'X-ACKT' clinical trial to generate the necessary data to support a potential regulatory submission with the goal of providing a new treatment option for patients with PGTCS."

About XEN1101 Phase 3 Plans in Focal Onset Seizures

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 and safety of XEN1101 administered as adjunctive treatment in patients with FOS. Approximately 360 patients will be randomized 1:1:1 for once-daily dosing of XEN1101 (15 mg), XEN1101 (25 mg) or placebo in each trial. Eligibility criteria include adults aged 18 to 75 years old taking one to three anti-seizure medications (ASMs) with a seizure frequency of $\geq$4 seizures per month at baseline. Patients will undergo an 8-week baseline period to assess seizure frequency and eligibility for randomization, followed by a 12-week double blind period (DBP). There is no titration period. The primary efficacy endpoint is the median percent change (MPC) in monthly seizure frequency from baseline through the DBP of XEN1101 compared to placebo. Key secondary endpoints include the proportion of patients experiencing $\geq$50% reduction in seizure frequency from baseline for XEN1101 versus placebo, MPC at Week 1 compared to baseline to assess the rapidity of seizure reduction and the Patient Global Impression of Change (PGI-C) at Week 12. On completion of the DBP in X-TOLE2 and X-TOLE3, eligible patients may enter an open-label extension study for up to three years. In addition, the ongoing X-TOLE open-label extension also continues to generate important long-term data for XEN1101 in FOS.

About XEN1101 Phase 3 Plans in Primary Generalized Tonic Clonic Seizures (PGTCS)
Following the initiation of X-TOLE2, Xenon plans to initiate a single Phase 3 clinical trial, called X-ACKT, to support potential regulatory submission in PGTCS. This multicenter, randomized, double-blind, placebo-controlled study will evaluate the clinical efficacy and safety of XEN1101 administered as adjunctive treatment in patients with PGTCS. Approximately 160 subjects will be randomized 1:1 for once-daily dosing of XEN1101 (25 mg) or placebo. Eligibility criteria include adults aged 18 to 75 years old taking one to three ASMs with a seizure frequency of ≥3 PGTCS over an 8-week baseline period. After the baseline period to assess seizure frequency and eligibility for randomization, patients will enter a 12-week DBP. There is no titration period. The primary efficacy endpoint is the MPC in monthly PGTCS frequency from baseline through the DBP of XEN1101 compared to placebo. Key secondary endpoints include the proportion of subjects experiencing ≥50% reduction in PGTCS frequency from baseline for XEN1101 versus placebo, seizure freedom and the PGI-C at Week 12. On completion of the DBP in X-ACKT, eligible patients may enter an open-label extension study for up to three years.

About Primary Generalized Tonic Clonic Seizures
Seizures are generally described in two major groups: generalized onset seizures and focal onset seizures. Primary generalized seizures initiate in both hemispheres of the brain simultaneously and are the second most common type of seizure experienced by people with epilepsy. PGTCS, also known as grand mal seizures or convulsions, are severe and life-threatening seizures comprised of tonic and clonic phases. Approximately 30% of patients with epilepsy have generalized seizures, which results in a total adult generalized seizure patient population of approximately 0.9 million patients in the U.S., of which at least 0.7 million patients experience PGTCS. Despite the more severe seizure phenotype, fewer ASMs are currently approved to treat PGTCS compared to FOS and approximately 30% of PGTCS patients are considered inadequately managed with initial lines of therapy warranting additional treatment options.

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, including those related to XEN1101; the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN1101; the anticipated timing of IND, or IND-equivalent, submissions and the initiation of future clinical trials for XEN1101; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in the XEN1101 programs; the timing and results of our interactions with regulators, our ability to successfully develop and obtain regulatory approval of XEN1101; 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: 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; impact of new or changing laws and regulations; the impact of the COVID-19 pandemic on our business, adverse 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" and the Xenon logo are registered trademarks or trademarks of Xenon Pharmaceuticals Inc. in various jurisdictions. All other trademarks belong to their respective owner.

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