



Xenon Expands Ion Channel Neurology Pipeline with Acquisition of New Potassium Channel Modulator for the Treatment of Epilepsy

April 26, 2017

Phase 1 expected to begin in Q4 2017, with pharmacodynamic read-out in Q1 2018 and Phase 2 proof-of-concept clinical trial beginning in mid-2018

Conference call to be held today at 9:00 am ET

BURNABY, British Columbia, April 26, 2017 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a clinical-stage biopharmaceutical company, today reported the expansion of its ion channel, neurology-focused product pipeline with XEN1101, an innovative potassium channel modulator for the potential treatment of epilepsy. Xenon acquired worldwide development and commercialization rights to XEN1101 from 1st Order Pharmaceuticals, Inc. XEN1101 is a next-generation Kv7 potassium channel opener that preclinically demonstrated improved pharmacokinetics, selectivity, and pharmacology from a new chemical platform over first-generation potassium channel modulators, such as ezogabine. Xenon anticipates filing an IND, or IND equivalent, to initiate a Phase 1 first-in-man clinical trial in the fourth quarter of 2017.

Dr. Simon Pimstone, Xenon's President and Chief Executive Officer, said, "We believe we have unique expertise to evaluate modulators of ion channel targets with strong human genetic validation, such as XEN1101. Our small molecule ion channel capabilities enable us to identify and develop selective and differentiated modulators of these targets. Consistent with our goal of building a diverse, neurology-focused portfolio of ion channel modulators, we have assessed numerous compounds being developed externally to complement our own internal discovery efforts."

Dr. Pimstone added, "Based on its mechanism of action, XEN1101 potentially represents a therapeutically differentiated alternative to the anti-epileptic medications currently available and could provide a better safety and tolerability profile when compared with earlier generation potassium channel modulators. We anticipate that XEN1101 will be in a Phase 1 clinical trial in the fourth quarter of 2017. Early clinical development is expected to include a pharmacodynamic read-out in the first quarter of 2018 and Phase 2 development beginning by mid-2018."

About XEN1101

XEN1101 acts as a neuronal Kv7 voltage-gated potassium channel opener, which has been developed to stabilize nerve cells, control action potential burst firing, and reduce brain hyperexcitability as a treatment for seizures. This mechanism has proven clinical efficacy in epilepsy as shown with ezogabine, the first generation Kv7 opener. Ezogabine demonstrated that a Kv7 potassium channel opener mechanism is an effective adjunctive treatment for treatment-resistant focal, or partial onset, seizures, which led to its market approval in Europe and the U.S. XEN1101's unique composition is chemically designed to improve upon the potency, selectivity, and pharmacokinetics of first generation molecules that have validated Kv7 as an epilepsy target, but it is not expected to have the composition-specific liabilities that have been implicated with earlier generation drugs. Ezogabine is expected to be discontinued and will no longer be commercially available past June 2017.

Human Genetic Validation of KCNQ2

The KCNQ2 gene codes for the Kv7.2 voltage gated potassium channel. Loss of function missense mutations in KCNQ2 cause an extreme single-gene epilepsy disorder characterized by multiple, daily, treatment-resistant seizures presenting within the first week of life. This human genetic validation further underpins the important role KCNQ2 plays in limiting the hyperexcitatory state of the brain and prevention of seizures in humans. XEN1101 could represent a potential treatment of this rare, severe, treatment-resistant, early infantile epileptic "KCNQ2" encephalopathy, also categorized as EIEE7.

Clinical Development of XEN1101

XEN1101 will initially be developed for treatment-resistant focal, or partial onset, seizures in adults, a strategy supported by the clinical validation of the target with ezogabine. XEN1101 has completed GLP safety pharmacology and toxicology studies, along with a pre-IND meeting with the FDA. It is anticipated that an IND, or IND equivalent, will be filed to initiate a Phase 1 clinical trial in the fourth quarter of 2017. Early clinical development is expected to include a pharmacodynamic read-out in the first quarter of 2018 and Phase 2 development beginning in mid-2018.

XEN1101 Deal Terms

XEN1101 (previously known as 1OP2198) was acquired from 1st Order Pharmaceuticals, Inc. pursuant to an asset purchase agreement. 1st Order previously acquired 1OP2198 (previously known as VRX621698) from a third party, and Xenon will assume certain financial responsibilities under that agreement. Near term upfront and milestone consideration to be paid in 2017 is expected to total approximately \$1.1 million. Future potential payments to both 1st Order and the third party include \$1 million in clinical development milestones, up to \$13 million in regulatory milestones, and up to approximately \$33.6 million in sales-based and other milestones, which includes a \$1.5 million milestone that may be payable pre-commercially, plus a mid-to-high single digit percentage royalty on commercial sales.

Mr. Christopher Crean, 1st Order Pharmaceuticals' Cofounder, President and Chief Science Officer, said, "Having been involved in the final development and approval of ezogabine, I am pleased to see Xenon move ahead with XEN1101, a promising 'next-generation' therapeutic based on a proven mechanism. I have spent a considerable part of my career in the development of potassium channel openers, and with Xenon's focus on neurology and ion channel modulators, I am hopeful that the advancement of XEN1101 will ultimately lead to a new treatment option for patients with epilepsy."

About Focal (Partial Onset) Seizures

A focal, or partial onset, seizure is localized within the brain and can either stay localized or spread to the whole brain, which is typically categorized as secondary generalized seizures. Focal seizures are the most common type of seizure experienced by people with epilepsy. The treatment of an individual patient with focal seizures is currently focused on reduction of seizure frequency, with seizure freedom as the ultimate goal. Focal seizures (simple, complex and secondarily generalized tonic-clonic) account for approximately 60% of seizures (GlobalData Report 2013) of which approximately 33% are considered resistant to current treatments (Epilepsy Foundation). It is estimated that the total addressable population for XEN1101 could include approximately 460,000 adults and 70,000 pediatric epilepsy patients.

Conference Call Information

Xenon will host a conference call and live audio webcast today at 9:00 a.m. Eastern Time (6:00 a.m. Pacific Time) to discuss its XEN1101 program. To participate in the call, please dial (855) 779-9075, or (631) 485-4866 for international callers, and provide conference ID number 14014831. The webcast will be broadcast live on the "Investors" section of Xenon's website at www.xenon-pharma.com and will be available for replay following the call for 30 days.

About Xenon Pharmaceuticals Inc.

Xenon is a clinical stage biopharmaceutical company focused on developing innovative therapeutics to improve the lives of patients with neurological disorders. Building upon our extensive knowledge of human genetics and diseases caused by mutations in ion channels, known as channelopathies, we are advancing – both independently and with our pharmaceutical collaborators – a novel product pipeline of ion channel modulators to address therapeutic areas of high unmet medical need, such as pain and 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 and Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995 and Canadian securities laws. These forward-looking statements include statements regarding the anticipated timing of the IND, or IND equivalent, submission for XEN1101 and the initiation of clinical trials for XEN1101, our ability to successfully develop and achieve milestones in the XEN1101 program, the timing of and results from our clinical trials and pre-clinical development activities related to XEN1101, the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN1101, the anticipated discontinuation of the commercial availability of ezogabine, the amounts and timing of anticipated milestone payments and royalties potentially owing to 1st Order and the associated third party, and the progress and potential of our other ongoing development programs. 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; our efforts to expand our current pipeline, including through the acquisition of XEN1101, may not be successful; any of our or our collaborators' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; adverse conditions in the general domestic and global economic markets; 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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