Xenon Pharmaceuticals Announces Initiation of XEN1101 Phase 1 Clinical Trial

October 17, 2017

Xenon's innovative, proprietary epilepsy programs continue to advance in development

Pharmacodynamic read-out expected in Q1 2018 and XEN1101 Phase 2 proof-of-concept clinical trial anticipated to begin in Q3 2018

BURNABY, British Columbia, Oct. 17, 2017 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a clinical-stage biopharmaceutical company, today announced the initiation of a Phase 1 "first-in-human" clinical trial of its proprietary epilepsy product candidate, XEN1101, which is an orally administered Kv7 potassium channel opener that has the potential to treat both adult as well as rare pediatric genetic forms of epilepsy. The Clinical Trial Application (CTA) for XEN1101 was accepted by the Medicines & Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK), and the first subject has now been dosed in the Phase 1 clinical trial.

Dr. Simon Pimstone, Xenon's President and Chief Executive Officer, said, "The initiation of clinical development of XEN1101 is a significant achievement and step forward for Xenon's proprietary epilepsy assets. We believe that XEN1101's mechanism of action represents a therapeutically differentiated alternative to the currently available anti-epileptic medications and, based on extensive pre-clinical work performed to date, may provide a better safety and tolerability profile when compared to ezogabine, an earlier generation potassium channel modulator that is no longer on the market. In addition to safety and pharmacokinetics data, the XEN1101 Phase 1 clinical trial has been designed to include a pharmacodynamic read-out incorporating a transcranial magnetic stimulation, or TMS, model, with data expected in the first quarter of 2018. The TMS model is designed to demonstrate delivery of XEN1101 into the central nervous system to observe a change in EEG or EMG activity."

Dr. Pimstone added, "I am excited that our proprietary epilepsy products, which are clearly differentiated from other currently available anti-epileptic products and those in development, are now positioned to potentially meet some critical clinical milestones over the coming months. In addition to XEN1101, we are equally excited about the advancement of XEN901, a unique selective sodium channel (Nav1.6) inhibitor for the treatment of epilepsy, and expect to file an IND equivalent application in the fourth quarter of this year. We believe that XEN1101 and XEN901 are highly innovative and differentiated anti-epileptic drug candidates with potentially broad applicability to address larger patient populations, such as adult focal seizures, as well as rare, genetically defined pediatric epilepsy disorders caused by mutations in the channels that these drugs have been designed to interact with."

About XEN1101
XEN1101 is a neuronal Kv7 voltage-gated potassium channel opener and augments the channel's critical function of dampening neuronal excitability. XEN1101 is being developed as a treatment for seizures by stabilizing neuronal cell firing and reducing brain hyperexcitability. The Kv7 potassium channel opener mechanism has been clinically validated as an effective adjunctive treatment for treatment-resistant focal onset seizures as demonstrated with ezogabine, an earlier generation Kv7 opener. However, XEN1101's unique composition is chemically designed to improve upon potency, selectivity, and pharmacokinetics, but it is not expected to have ezogabine's composition-specific skin and eye pigmentary liabilities.

XEN1101 Phase 1 Clinical Trial Design
The XEN1101 Phase 1 clinical trial is a randomized, double-blind, placebo-controlled study that will evaluate the safety, tolerability and pharmacokinetics (PK) of both single ascending doses (SAD) and multiple ascending doses (MAD) of XEN1101 in healthy subjects. In addition, the pharmacodynamic impact of single doses of XEN1101 using TMS will be studied in parallel with the SAD/MAD portions of this Phase 1 safety study. It is estimated there will be approximately 64 subjects in the planned SAD and MAD cohorts, with approximately 15 subjects taking part in the TMS cross-over study. Following the completion of the Phase 1 clinical trial and if supported by the data, it is anticipated that XEN1101 will advance into a Phase 2 proof-of-concept trial in the third quarter of 2018 evaluating its efficacy as a treatment for adult focal seizures, with a parallel plan to advance XEN1101 into rare, pediatric forms of epilepsy as soon as feasible thereafter.

About Focal Seizures
A focal 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 addressable population in the U.S. for XEN1101 could include approximately 460,000 adults and 70,000 pediatric epilepsy patients with refractory seizures.

Human Genetic Validation of KCNQ2: XEN1101 as a Potential Treatment for Orphan Pediatric Epilepsy
The KCNQ2 gene codes for the Kv7.2 voltage-gated potassium channel. Loss-of-function missense mutations in KCNQ2 cause an

extremely severe single-gene epilepsy disorder characterized by multiple, daily, treatment-resistant seizures often 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 as a target for the prevention of seizures in humans. XEN1101, which directly opens the Kv7.2 channel, represents a potential treatment of this treatment-resistant, early infantile epileptic "KCNQ2" encephalopathy, also categorized as EIEE7. In parallel with its ongoing development plans to study XEN1101 in adults with focal seizures in a Phase 2 proof-of-concept clinical trial, Xenon is exploring the options around the regulatory pathways required to study XEN1101 in pediatric patients with EIEE7.

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 are not based on historical fact, and include statements regarding the timing of and results from our clinical trials and pre-clinical development activities related to XEN1101 and our other product candidates, the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN1101 and our other product candidates, the anticipated timing of IND, or IND equivalent, submissions and the initiation of future clinical trials for XEN1101 and our other product candidates, the efficacy of our clinical trial designs, our ability to successfully develop and achieve milestones in the XEN1101 and other development programs, the anticipated benefits of XEN1101's unique composition, the design of our clinical trials and anticipated enrollment, 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 advancement of XEN1101 into clinical development, 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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Source: Xenon Pharmaceuticals Inc.