



## **Xenon Pharmaceuticals Advances Second Proprietary Epilepsy Product into the Clinic with Initiation of XEN901 Phase 1 Clinical Trial**

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BURNABY, British Columbia, Feb. 20, 2018 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a clinical-stage biopharmaceutical company, today announced the initiation of a Phase 1 clinical trial of its proprietary epilepsy product candidate, XEN901, which is an orally administered, small molecule, highly selective Nav1.6 sodium channel inhibitor. The Clinical Trial Application (CTA) for XEN901 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.

XEN901 is a potent, highly selective Nav1.6 sodium channel inhibitor being developed by Xenon for the treatment of epilepsy, including treatment resistant adult and pediatric focal seizures, as well as rare, pediatric forms of epilepsy, such as EIEE13, an early infantile epileptic encephalopathy associated with gain-of-function mutations in the SCN8A gene, which encodes the Nav1.6 sodium channel.

Dr. Simon Pimstone, Xenon's President and Chief Executive Officer, said, "With the initiation of the XEN901 Phase 1 clinical trial, Xenon now has two anti-epileptic therapeutics in clinical development, each highly validated and with novel mechanisms of action. We believe this further supports our efforts to become a leader in the development of therapeutically differentiated alternatives to the anti-epileptic medications currently available, and we believe that XEN901 is the only selective Nav1.6 inhibitor currently in clinical development. Non-selective sodium channel inhibitors are broadly used for the treatment of focal seizures but are limited by their narrow therapeutic window. We anticipate that XEN901, as a highly selective Nav1.6 inhibitor, could offer an efficacious treatment with a better therapeutic index due to its improved target selectivity."

Dr. Pimstone added, "We expect that XEN901 will follow a similar clinical development path to XEN1101, Xenon's novel Kv7 potassium channel opener for the treatment of epilepsy, which is also currently in Phase 1 development. If supported by the data, these Phase 1 clinical trials will be followed by Phase 2 proof-of-concept trials evaluating efficacy in the treatment of adult focal seizures. We are also examining the advancement of these therapies in a pediatric setting as soon as possible in order to specifically target the underlying genetic mutations in rare forms of early infantile epileptic encephalopathies that lead to marked development impairment in many cases."

Xenon has examined XEN901 in a preclinical model of genetically defined epilepsy as well as models representative of focal seizures. These studies showed that XEN901 is efficacious against seizures in both an SCN8A (Nav1.6) gain-of-function model, which is designed to be predictive of the pediatric genetic epilepsy EIEE13, and in the maximal electroshock seizure (MES) model, which is designed to be predictive of adult focal seizures. When compared to phenytoin in both the SCN8A and MES models, XEN901 achieved the same degree of efficacy as phenytoin at one thousand fold lower brain exposures. XEN901 was observed to have an improved therapeutic index relative to phenytoin as assessed by tests of rodent behavior and motor impairment.

### **XEN901 Phase 1 Clinical Trial Design**

The XEN901 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 XEN901 in healthy subjects. It is estimated there will be approximately 64 subjects in total in the planned SAD and MAD cohorts. Upon completion of the Phase 1 clinical trial, a read-out of results is anticipated in the second half of 2018, followed by a Phase 2 proof-of-concept trial evaluating XEN901's efficacy as a treatment for adult focal seizures, if supported by the data. Xenon intends to pursue a parallel plan to advance XEN901 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 entire brain, which is typically categorized as a secondary generalized seizure. 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 2017) of which approximately 33% are considered resistant to current treatments (Epilepsy Foundation). It is estimated that the addressable population in the U.S. for XEN901 could include approximately 460,000 adults and 70,000 pediatric epilepsy patients with refractory seizures.

### **About Early Infantile Epileptic Encephalopathy (EIEE13)**

XEN901's mechanism of action – which is inhibition of the Nav1.6 sodium channel – is supported by strong human genetic validation. Nav1.6 (encoded by the SCN8A gene) is the most highly expressed sodium channel in excitatory neurons in the central nervous system. When mutations in the SCN8A gene cause a gain of function, children present with a rare, extremely severe form of epilepsy. This early infantile epileptic encephalopathy is known as EIEE13 and typically presents with seizure onset between birth and 18 months of age. Most children diagnosed with EIEE13 have epilepsy that is resistant to treatment. They may have seizures every day and often need to be hospitalized. Other symptoms include learning difficulties, muscle spasms, low or high

muscle tone, poor coordination, developmental delay, and features similar to autism. The extent of physical disability leaves some children able to make little or no voluntary movement. Most children will have trouble learning to speak, and some will need assistance from feeding tubes to get the nourishment they need to grow.

#### **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](http://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 XEN901, XEN1101 and our other product candidates, the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN901, XEN1101 and our other product candidates, the anticipated timing of IND, or IND equivalent, submissions and the initiation of future clinical trials for XEN901, XEN1101 and our other product candidates, our ability to successfully develop and achieve milestones in the XEN901, XEN1101 and other development programs, the anticipated benefits of XEN901's unique composition, the efficacy of our clinical trial design 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 XEN901 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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