



Xenon Presents XEN901 Phase 1 Clinical Update and Supporting Pre-clinical Data at 14th Eilat Conference

May 15, 2018

Company to Hold Conference Call at 8:00 am ET Today

Preliminary Phase 1 Clinical Data Support Drug Exposure Levels Higher than Required in Pre-clinical Efficacy Models with Excellent Tolerability and Safety

New Pre-clinical Data Support Selective Nav1.6 Mechanism of Action and XEN901 Efficacy Superior to Standard of Care Sodium Channel Blockers

BURNABY, British Columbia, May 15, 2018 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a clinical stage biopharmaceutical company, today presented new pre-clinical data as well as preliminary clinical data from its ongoing XEN901 Phase 1 clinical trial in a podium presentation at the 14th Eilat Conference on New Antiepileptic Drugs and Devices (Eilat) held in Madrid, Spain.

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 due to gain-of-function mutations in the SCN8A gene that encodes the Nav1.6 sodium channel.

Today, Xenon presented new pre-clinical data as well as interim data from its ongoing Phase 1 clinical trial, which is evaluating the safety, tolerability and pharmacokinetics (PK) of both single ascending doses (SAD) and multiple ascending doses (MAD) of XEN901 in approximately 64 healthy subjects.

Dr. Simon Pimstone, Xenon's Chief Executive Officer, said, "Today's presentation is a culmination of years of work to identify and develop a novel and highly differentiated anti-epileptic drug (AED) with the potential to be superior to other sodium channel blockers allowing more patients to achieve seizure freedom. Although sodium channel blockers are a mainstay in the treatment of epilepsy, utilizing these drugs to their maximal effect in patients is often limited by side effects. We have generated compelling data that highlight the Nav1.6 channel as the critical sodium channel in regulating cortical hyper-excitability and the mechanism by which non-selective sodium channels are having their effect. The pre-clinical profile and selectivity of XEN901 suggest it may provide a significant advancement in efficacy, safety and tolerability when compared with other broadly used sodium channel blockers, including phenytoin, carbamazepine and lacosamide."

Dr. Pimstone added, "The interim Phase 1 clinical data presented today demonstrate a favorable PK profile, with XEN901 reaching levels of drug exposure significantly above where we see efficacy in our pre-clinical models with an excellent safety and tolerability profile. We are looking forward to completing the Phase 1 clinical trial over the next few months, and we are looking forward to advancing XEN901 into a Phase 2 clinical trial in adult focal seizures. In parallel, we are working on a strategy to advance XEN901 into rare pediatric forms of epilepsy, such as the EIEE13 pediatric population."

Summary of XEN901 Interim Phase 1 Clinical Data

- The XEN901 interim Phase 1 results include data from six SAD cohorts ranging in dose from 5 to 45 mg (n=33, placebo=8).
- Favorable PK data show dose proportionality and support twice daily or better dosing, with predicted half-life of 8 to 11 hours. The multiple dose levels tested yield drug exposure above the efficacy range for EC₇₀ in the pre-clinical Maximal Electroshock Seizure (MES) model.
- To date, all reported adverse events (AEs) are mild or moderate. Related AEs were mild and resolved spontaneously. The most common adverse event was headache. The interim preliminary safety results suggest XEN901 is overall safe and well tolerated.

Summary of XEN901 Supporting Pre-Clinical Data

- There is strong genetic validation for pursuing this particular target: children born with gain-of-function mutations in the SCN8A gene, the gene encoding the Nav1.6 channel, develop a very severe early onset form of epilepsy known as EIEE13.
- Xenon has generated compelling pre-clinical data that suggest Nav1.6 is the primary driver of efficacy for non-selective voltage-gated sodium channel targeted AEDs. By selectively targeting Nav1.6 and avoiding other sodium channel targets that do not appear relevant to seizure control, it is anticipated that XEN901 could maximize channel inhibition, yielding an enhanced effect – up to and including potential seizure freedom in a greater number of patients.

- A variety of models representative of both adult and pediatric epilepsy have shown XEN901's improved efficacy at significantly lower concentrations than approved AEDs such as carbamazepine, phenytoin, and lacosamide. Data presented today showed that XEN901 can completely suppress seizures in pre-clinical models.
- Data presented today show that XEN901's level of selectivity leads to greater than 100-fold more potent in SCN8a gain-of-function transgenic animal models of EIEE13 when compared to phenytoin, carbamazepine and lacosamide.
- XEN901 was also shown to be greater than 100-fold more potent than phenytoin, carbamazepine and lacosamide in a Maximal Electroshock Seizure (MES) model, which is used as a model for focal seizures.
- Driven by efficacy at very low plasma and brain concentrations, XEN901 demonstrates an improved therapeutic index over other sodium channel inhibitors in pre-clinical models; the preclinical safety margin for XEN901 is >100 versus <7 for phenytoin, carbamazepine and lacosamide.

The XEN901 Phase 1 clinical trial is anticipated to be completed in the second half of 2018, followed by a regulatory filing by year-end to support a Phase 2 trial evaluating XEN901 as a treatment for adult focal seizures. Xenon also intends to pursue a parallel plan to advance XEN901 into rare, pediatric forms of epilepsy, such as EIEE13, as soon as feasible thereafter. The incidence of EIEE13 has been estimated to be approximately 50 births per year in the United States.

Conference Call Information

Xenon will host a conference call and webcast today at 8:00 a.m. Eastern Time (5:00 a.m. Pacific Time) to provide a corporate update and discuss the XEN1101 and XEN901 Eilat presentations. To participate in the call, please dial (855) 779-9075, or (631) 485-4866 for international callers and provide conference ID number 5249928. 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.

We are 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 collaborators – a novel product pipeline of central nervous system, or CNS, therapies to address areas of high unmet medical need, such as epilepsy, migraine and pain. 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 our expectations regarding the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN901 and our other product candidates, the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN901 and our other product candidates, the anticipated timing of IND, or IND equivalent, submissions and the initiation of future clinical trials for XEN901 and our other product candidates, the efficacy of our clinical trial designs, our ability to successfully develop and achieve milestones in the XEN901 and other development programs, the anticipated benefits of the unique mechanisms of action of XEN901, the design of our clinical trials and anticipated enrollment, the potential for XEN901 to support twice daily or better dosing, the ability to replicate preclinical and Phase 1 data of XEN901 in head-to-head trials with competing products, 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: promising results in preclinical and early clinical trials may not be replicated in subsequent clinical trials; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; 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; we may not achieve additional milestones in our proprietary or partnered programs; the impact of competition; 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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