Xenon Pharmaceuticals Provides Updates on Proprietary Neurology Pipeline Programs at the 2019 American Epilepsy Society (AES) Annual Meeting

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Xenon's Epilepsy Programs Continue to Advance Including Ongoing XEN1101 Phase 2b Clinical Trial in Adult Focal Epilepsy and Plans for Anticipated Pediatric XEN496 Pivotal Phase 3 Clinical Trial in KCNQ2-DEE Patients

Promising New Pre-Clinical Data Support Precision Medicine Approach to Treat Dravet Syndrome with Highly Selective Potentiators of Nav1.1

Xenon Extends Invitation to View its Presentations in the "Genetic Epilepsies – Updates in the Science and Diagnosis" Exhibit in Room 318-319 on Sunday, December 8th

BURNABY, British Columbia, Dec. 06, 2019 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a clinical stage biopharmaceutical company, announced today that it will provide updates on its proprietary, neurology programs at the American Epilepsy Society (AES) Annual Meeting held in Baltimore, MD.

Dr. Simon Pimstone, Xenon's Chief Executive Officer, said, "We continue to advance our portfolio of neurology-focused candidates, and have a number of presentations on XEN496 and XEN1101 at the AES meeting in Baltimore. A pediatric-specific formulation for XEN496 has been completed, and we will conduct a pharmacokinetic study in healthy adult volunteers to support an IND filing in the first quarter of 2020 for a pediatric pivotal Phase 3 clinical trial with XEN496 in patients with KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE). Our XEN1101 Phase 2b clinical trial in adult focal epilepsy is ongoing with patient enrollment across sites in the U.S., Canada, and Europe, with top-line data expected in the second half of 2020. We believe XEN1101 has the potential to be an 'only-in-class' therapy for focal seizures, and we are investigating other potential neurological indications for this promising program. In addition to our proprietary clinical stage programs, we look forward to supporting our partner Neurocrine Biosciences as they advance XEN901 and other sodium channel inhibitors."

Dr. Pimstone continued, "We will also be presenting promising new pre-clinical data that support a precision medicine approach to treating Dravet Syndrome with highly selective potentiators of Nav1.1. We believe this mechanism could potentially address other neurologic indications where interneuron excitability is impaired."

Dr. Pimstone added, "The AES Annual Meeting is an important event allowing us to showcase our epilepsy programs and connect with key opinion leaders and patient advocacy groups. This year, in addition to the presentation of Xenon's scientific posters, we are also participating in the BioMarin Scientific Exhibit entitled "Genetic Epilepsies – Updates in the Science and Diagnosis" which is a cross-industry collaboration with BioMarin, Invitae, and Stoke Therapeutics."

Xenon is presenting updates on both of its proprietary, clinical-stage programs, XEN1101 and XEN496 – as well as presenting promising pre-clinical data – in a number of poster sessions at AES:

- XEN496 (active ingredient ezogabine) is a Kv7 potassium channel modulator being developed by Xenon. A poster entitled "Development of a Pediatric Immediate-Release Formulation of the Potassium Channel Opener XEN496 (Ezogabine)" will be presented in a scientific poster session, as well as the BioMarin exhibit, on Sunday, December 8, 2019. After examining multiple formulations with different properties, Xenon has developed XEN496 as a pediatric-specific, granule formulation to be packaged as single-dose sprinkle capsules that has excellent properties supported by both *in vitro* and *in vivo* data. A planned pharmacokinetic (PK) study will test XEN496 in healthy adult volunteers, with data expected in the first quarter of 2020.

  Xenon will also present a poster in the BioMarin exhibit entitled, "An Online Survey of Caregivers of Patients with KCNQ2 Developmental & Epileptic Encephalopathy (KCNQ2-DEE)." Xenon recently performed a caregiver survey to obtain additional phenotypic information regarding the seizure history of the disease as well as Anti-Seizure Medication (ASM) use, with a focus on ezogabine. Importantly, all seven respondents who had access to ezogabine responded that they saw improvements in their child's seizures, behavior or development while they were taking ezogabine. In addition, ezogabine was reported to be well-tolerated. Information from this survey, as well as input from key opinion leaders, will help inform the proposed Phase 3 clinical trial design and protocol.

  Xenon expects to file an Investigational New Drug (IND) application in the first quarter of 2020 to discuss with the FDA the design of a Phase 3 clinical trial in KCNQ2-DEE. The FDA has indicated that it is acceptable to study XEN496 in infants and children up to four years old, and that a single, small pivotal trial may be considered adequate in order to demonstrate XEN496's efficacy in KCNQ2-DEE, provided the study shows evidence of a clinically meaningful benefit in patients with the intended indication.

- XEN1101 is a differentiated Kv7 potassium channel modulator being developed for the treatment of epilepsy and potentially other neurological disorders. A poster entitled "Use of Transcranial Magnetic Stimulation (TMS) Data in the Design of a Dose Range Finding Efficacy, Safety, Tolerability, and Pharmacokinetics Study of XEN1101 in Patients with Focal Epilepsy" will be presented on Monday, December 9, 2019. This poster outlines the XEN1101 Phase 2 study design and concludes that incorporating TMS evidence of CNS activity in healthy volunteers may be a useful adjunct in refining dose selection for Phase 2 epilepsy studies. A Phase 2b double-blind, placebo-controlled, multicenter clinical trial (called the X-TOLE study), which is currently underway to evaluate the clinical efficacy, safety and tolerability of XEN1101 administered as adjunctive treatment in approximately 300 adult patients with focal epilepsy. The primary endpoint is the median percent change in monthly focal seizure frequency from baseline compared to treatment period of active versus placebo. Patient enrollment for this XEN1101 Phase 2b clinical trial is ongoing in the United States, Canada and Europe. Long term six and nine-month toxicology studies have now been completed, providing support to the planned 12-month open label extension for patients enrolled in the Phase 2b clinical trial. Depending upon the rate of enrollment, top-line results are anticipated in the second half of 2020.

- Xenon also continues to conduct pre-clinical work on other promising molecules to address neurological disorders. A poster entitled, "Small Molecule Potentiators of Nav1.1 Increase Action Potential Firing in Fast Spiking Cortical Inhibitory Interneurons from a Mouse Model of Dravet Syndrome" – which will be presented on Monday, December 9, 2019 – outlines promising work on highly selective small molecule potentiators of Nav1.1 that could address the underlying cause of Dravet Syndrome using a precision medicine approach. Selectively potentiating Nav1.1, the dominant sodium channel isoform expressed in inhibitory interneurons, restores the capability of *Scn1a*$^{+/-}$ interneurons to fire action potentials at high frequency. In brain slices from *Scn1a*$^{+/-}$ mice, the tested compound increased the firing rate of inhibitory neurons. A small molecule pharmaceutical with this profile could enable reversal of the fundamental defect in Dravet Syndrome and may have utility in other neurologic indications where interneuron excitability is impaired. Xenon intends to build upon this promising work and continue to advance potential Nav1.1 potentiators in pre-clinical development.

About the BioMarin Scientific Exhibit: "Genetic Epilepsies – Updates in the Science and Diagnosis"
Xenon, in collaboration with Invitae and Stoke Therapeutics, is participating in the BioMarin Scientific Exhibit entitled "Genetic Epilepsies – Updates in the Science and Diagnosis" on Sunday, December 8, 2019 from 8:00 am ET to 5:00 pm ET in the Convention Center, Room 318-319 on Level 300 at the AES 2019 Annual Meeting.

About Xenon Pharmaceuticals Inc.

We are a clinical stage biopharmaceutical company committed to developing innovative therapeutics to improve the lives of patients with neurological disorders, including rare central nervous system (CNS) conditions. 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 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 and supporting assumptions are not based on historical fact, and include statements regarding the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN496, XEN901, XEN1101 and our other product candidates; the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN496, XEN901, XEN1101 and our other product candidates; the anticipated timing of IND, or IND-equivalent, submissions and the initiation of future clinical trials for XEN496, XEN1101 and our other product candidates; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in the XEN496, XEN901, XEN1101 and other development programs, either alone or with our collaborators; the timing and results of our interactions with regulators; the potential to advance certain of our product candidates directly into Phase 2 or later stage clinical trials; anticipated enrollment in our clinical trials; the progress and potential of our other ongoing development programs; the potential receipt of milestone payments and royalties from our collaborators and partners; and the timing of potential publication or presentation of future clinical data. 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 ongoing discovery and pre-clinical efforts may not yield additional 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; regulatory agencies may not permit certain of our product candidates to advance directly into a Phase 2 or later clinical trials, may impose additional requirements or delay the initiation of clinical trials; 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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