Xenon Pharmaceuticals Outlines Key Milestone Opportunities and Planned Leadership Transition in 2021

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Simon Pimstone to Assume New Role as Executive Chair and Ian Mortimer to be Named Chief Executive Officer at Annual Meeting of Shareholders in June 2021

Topline Data from XEN1101 Phase 2b X-TOLE Clinical Trial in Adult Focal Epilepsy on Track for Third Quarter of 2021

Phase 3 XEN496 "EPIK" Clinical Trial Initiated in Patients with KCNQ2-DEE, a Rare Orphan Pediatric Disease

BURNABY, British Columbia, Jan. 14, 2021 (GLOBE NEWSWIRE) -- Xenon Pharmaceuticals Inc. (Nasdaq:XENE), a neurology-focused biopharmaceutical company, today outlined its key milestone opportunities and plans for a leadership transition in 2021, with all changes anticipated to take effect in June 2021 at the time of the Company's annual meeting of shareholders. As part of the leadership transition, Dr. Simon Pimstone, Xenon's co-founder and Chief Executive Officer, will step down from his current role as Chief Executive Officer and assume the new role of Executive Chair of the Board of Directors, replacing Mr. Michael Tarnow, current Chair of the Board, who will not be standing for re-election at the 2021 annual meeting of shareholders. Mr. Ian Mortimer, who currently serves as President and Chief Financial Officer, will be appointed as President and Chief Executive Officer and will also be nominated for election as a director at the 2021 annual meeting of shareholders. Concurrent with these appointments, Ms. Sherry Aulin, Xenon's current Vice President, Finance, will be appointed Chief Financial Officer, and Ms. Dawn Svoronos will be appointed Lead Independent Director of the Board.

Dr. Simon Pimstone, Xenon's Chief Executive Officer, stated, "As co-founder of Xenon, I am proud of Xenon's immense progress over the years, resulting in one of the most robust and novel neurology-focused therapeutic pipelines in our industry. I have forged a strong partnership with Ian, who has been integral to Xenon's growth and a key strategic partner in building our company and pipeline, as well as our strong balance sheet. Xenon is in excellent shape and, as a founder and long-time CEO, this is a natural leadership transition that will allow me to focus on a strategic role while continuing to work closely with Ian and the rest of the leadership team as we execute on Xenon's plans for the continued advancement of our pipeline programs. In addition, I want to extend my deep gratitude to Michael Tarnow for his more than 20 years of service as a member of Xenon's Board since the company's inception. We have all benefitted immensely from Michael's guidance, leadership and mentorship as Board Chair."

Mr. Ian Mortimer, Xenon's President and Chief Financial Officer said, "It is Simon's vision and drive that has helped position Xenon today as a premier neuroscience company focused on developing and delivering innovative medicines to improve the health of patients with epilepsy and other neurological disorders. We have attracted top talent across our business while building a strong leadership team, and I am excited to take on this new role as we work together to advance our therapeutic programs into later-stage development."

Dr. Pimstone and Mr. Mortimer jointly stated, "Looking ahead to 2021, we anticipate a number of key milestone events. Importantly, we expect a topline read-out in the third quarter from our XEN1101 Phase 2b X-TOLE study. Given its unique mechanism of action and other key pharmaceutical attributes, we believe XEN1101 has the opportunity to be an important new therapeutic choice in the adult focal epilepsy space. In addition, we have now initiated our Phase 3 EPIK clinical trial studying XEN496 in pediatric patients with KCNQ2-DEE and continue to work with the KCNQ2 community to develop a therapeutic that could address this rare, pediatric disorder. By mid-year, we expect additional data from a physician-led study examining the use of XEN007 to treat childhood absence epilepsy. We also anticipate a number of important milestone events from our partnered programs, including the initiation of a Phase 2 clinical trial with NBI-921352, related to our collaboration with Neurocrine Biosciences focused on developing treatments for epilepsy. Coming out of our partnered program with Flexion Therapeutics, we expect clinical development to start in 2021, examining the use of FX301 for the treatment of post-operative pain."

Highlights and Anticipated Milestones

Proprietary Programs

- XEN1101 is a differentiated Kv7 potassium channel modulator being developed for the treatment of epilepsy and potentially other neurological disorders. Designed as a randomized, double-blind, placebo-controlled, multicenter study, Xenon's "X-TOLE" study is an ongoing Phase 2b clinical trial 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. Xenon anticipates that patient randomization will be completed in the first half of 2021, with topline data anticipated in the third quarter of 2021, dependent upon ongoing patient enrollment rates. In addition, Xenon expects to support the initiation of a Phase 2 proof-of-concept clinical trial examining XEN1101 in a non-epilepsy indication within the first half of 2021.

- XEN496, a Kv7 potassium channel modulator, is a proprietary pediatric formulation of the active ingredient ezogabine being developed for the treatment of KCNQ2 developmental and epileptic encephalopathy (KCNQ2-DEE). Xenon has received Fast Track designation and Orphan Drug Designation for XEN496 for the treatment of seizures associated with KCNQ2-DEE from the U.S. Food and Drug Administration (FDA), as well as an orphan medicinal product designation in Europe. Xenon has initiated a Phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter clinical trial, called the "EPIK" study, evaluating the efficacy, safety, and tolerability of XEN496 administered as adjunctive treatment in approximately 40 pediatric patients aged one month to less than 6 years with KCNQ2-DEE.

- XEN007 (active ingredient flunarizine) is a CNS-acting Cav2.1 and T-type calcium channel modulator that is being studied in treatment-resistant childhood absence epilepsy (CAE) and potentially other neurological disorders. A physician-led, Phase 2 proof-of-concept study is ongoing to examine the potential clinical efficacy, safety, and tolerability of XEN007 as an adjunctive treatment in pediatric patients diagnosed with treatment-resistant CAE. A presentation of promising interim data collected from a small number of patients was presented at the virtual annual meeting of the American Epilepsy Society in December 2020. Xenon continues to work with its collaborators and expects that topline results from a larger data set will be available by the middle of 2021. Depending on the final results, CAE may represent a potential orphan indication for future development of XEN007.

Partnered Programs

- Xenon has an ongoing collaboration with Neurocrine Biosciences to develop treatments for epilepsy. Neurocrine Biosciences has an exclusive license to XEN901, now known as NBI-921352, a clinical stage selective Nav1.6 sodium channel inhibitor with potential in SCN8A developmental and epileptic encephalopathy (SCN8A-DEE) and other forms of epilepsy. The FDA has provided feedback on an Investigational New Drug (IND) application submitted by Neurocrine Biosciences in support of a Phase 2 clinical trial in SCN8A-DEE patients. Based on this feedback, Neurocrine Biosciences anticipates initiating a Phase 2 clinical trial in adolescent patients (aged 12 years and older) with SCN8A-DEE in the third quarter of 2021, and the trial protocol will be amended to include younger pediatric patients (aged 2-11 years) with SCN8A-DEE as soon as the FDA has reviewed and approved additional non-clinical information. In parallel, Neurocrine Biosciences is advancing clinical plans to develop NBI-921352 for the treatment of adult focal epilepsy and expects to initiate a Phase 2 clinical trial in 2021. Upon IND or equivalent regulatory acceptance for NBI-921352 in adult focal epilepsy, Xenon is eligible to receive a $10.0 million milestone payment; upon FDA acceptance of a protocol amendment for NBI-921352 in pediatric patients (aged 2-11 years) with SCN8A-DEE, Xenon is eligible to receive a $25.0 million milestone payment, or a $15.0 million milestone payment if the IND acceptance for adult focal epilepsy occurs first. Both milestone payments are in the form of 45% cash and a 55% equity investment in Xenon at a 15% premium to Xenon's 30-day trailing volume weighted average price at that time.

- Flexion Therapeutics, Inc. acquired the global rights to develop and commercialize XEN402, a Nav1.7 inhibitor also known as funapide. Flexion's pre-clinical FX301 consists of XEN402 formulated for extended release from a thermosensitive hydrogel. The initial development of FX301 is intended to support administration as a peripheral nerve block for control of post-operative pain. Flexion anticipates filing an IND application in the first half of 2021 to support a proof-of-concept clinical trial of popliteal fossa block with FX301 in patients undergoing bunionectomy. Results from that trial could potentially be available in late 2021. Pursuant to the terms of the agreement, Xenon is eligible to receive up to an additional $8.0 million in milestone payments through initiation of a Phase 2 clinical trial.

Corporate Highlights

- In addition to the planned leadership transition described above, the Board appointed Mr. Patrick Machado to the Audit Committee of the Board on January 12, 2021, effective immediately.

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. 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, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, 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 impact of anticipated leadership changes; the timing of and results from clinical trials and pre-clinical development activities, including those related to XEN496, XEN1101, XEN007, and other proprietary products, and those related to NBI-921352, FX301, and other partnered product candidates; the potential efficacy, safety profile, future development plans, addressable market, regulatory success and commercial potential of XEN496, XEN1101, XEN007 and other proprietary and partnered product candidates; the anticipated timing of IND, or IND-equivalent, submissions and the initiation of future clinical trials for XEN496, XEN1101, XEN007, and other proprietary products, and those related to NBI-921352, FX301, and other partnered candidates; the efficacy of our clinical trial designs; our ability to successfully develop and achieve milestones in the XEN496, XEN1101, XEN007 and other proprietary development programs; 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 and the timing thereof; the progress and potential of our other ongoing development programs; the potential receipt of milestone payments and royalties from our collaborators; 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: the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; our assumptions regarding our planned expenditures and sufficiency of our cash to fund operations may be incorrect; our ongoing discovery and pre-clinical efforts may not yield additional product candidates; promising results from trials involving a small number of patients may not be replicated in subsequent, larger trials; 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 impose additional requirements or delay the initiation of clinical trials; regulatory agencies may be delayed in reviewing, commenting on or approving any of our or our collaborators' clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; impact of new or changing laws and regulations; 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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