



## Teva and Xenon Provide Update on TV-45070 Phase 2b Study in Osteoarthritis Pain

July 1, 2015

- *TV-45070 4% and 8% did not demonstrate statistically significant difference from placebo in efficacy endpoints in Phase 2b study in pain due to osteoarthritis of the knee.*
- *TV-45070 demonstrated a favorable safety and tolerability profile, with no drug-related serious adverse events.*
- *Low drug plasma levels coupled with the favorable tolerability profile support the topical application rationale and continued development in neuropathic pain.*
- *Teva and Xenon remain fully committed to the development of TV-45070 for neuropathic pain indications and await the results from the ongoing PHN Phase 2b study, expected in the second half of 2016.*

JERUSALEM and BURNABY, British Columbia, July 1, 2015 (GLOBE NEWSWIRE) -- Teva Pharmaceutical Industries Ltd. (NYSE:TEVA) (TASE:TEVA) and Xenon Pharmaceuticals Inc. (Nasdaq:XENE) reported today top line results from the double-blind, placebo-controlled Phase 2b study designed to evaluate the safety and efficacy of topically applied TV-45070 (4% and 8% w/w ointment) in patients with chronic pain due to osteoarthritis (OA) of the knee.

TV-45070 is a small molecule inhibitor of the sodium channel Nav1.7 and other sodium channels, including those that are expressed in the pain-sensing peripheral nervous system. Results from this trial showed that TV-45070 4% and 8% did not demonstrate statistically significant difference from placebo in efficacy endpoints of reductions in pain due to OA.

TV-45070 did demonstrate a favorable safety and tolerability profile, with no drug-related serious adverse events. This is important given the ongoing Phase 2b study of TV-45070 in post-herpetic neuralgia (PHN). The most common adverse events were application site dermal skin reactions which were mostly mild and less frequent than seen with other topical analgesics. There were no cardiac or CNS safety issues.

"The rationale for development of TV-45070 in OA has unfortunately not been confirmed with these results. However, neuropathic pain represents a distinct mechanism of chronic pain to OA and, as such, the potential for positive study results in PHN is not impacted by these data," said Richard Malamut M.D. Teva's Vice President and Head of Pain Therapeutic Development. "Given the favorable safety and tolerability profile demonstrated, we remain hopeful that TV-45070 can offer a new and valuable option to patients with neuropathic pain."

"While we are disappointed that the Phase 2b trial top-line results did not indicate efficacy in OA, Teva and Xenon have always been committed to a broad development plan for TV-45070 in both nociceptive and neuropathic pain," said Dr. Simon Pimstone, Xenon's President and Chief Executive Officer. "The Phase 2b trial in PHN being conducted by Teva is progressing as planned, and we look forward to seeing top-line results from that trial in the second half of 2016. In addition, Xenon will continue to focus on advancing our partnered and proprietary pipeline programs, and leveraging the potential of our Extreme Genetics platform and expertise in ion channel target discovery. We look forward to other near-term milestone opportunities across our diverse product candidate pipeline."

### About TV-45070

TV-45070 (formerly XEN402) is a topically applied small-molecule inhibitor of the sodium channel Nav1.7 and other sodium channels, including those that are expressed in the pain-sensing peripheral nervous system. Applied topically, TV-45070 acts locally to inhibit Nav1.7 in the skin and underlying tissue, mitigating systemic absorption and the potential risks of side-effects that accompany systemic drug metabolism. The pain target Nav1.7 was identified by Xenon using its Extreme Genetics discovery platform. Xenon developed TV-45070 through early clinical development and partnered with Teva through a collaborative development and license agreement established in 2012, providing Teva with an exclusive worldwide license to develop and commercialize TV-45070. A Phase 2b trial in PHN is currently underway, with results expected in the second half of 2016.

### About the TV-45070 Osteoarthritis Phase 2b Trial

The Phase 2b osteoarthritis trial of TV-45070 was a randomized, double-blind, placebo-controlled study conducted at approximately 40 clinical sites across the US. There were three arms in the study and a total of 389 patients were randomized on a 1:1:1 basis: experimental TV-45070 4% administered twice per day; experimental TV-45070 8% administered twice per day; and placebo comparator (matched ointment without TV-45070) administered twice per day. Patients were eligible to participate in the trial if they were 40-85 years of age, had primary OA in a single knee (target knee), and met pre-specified visual analog scale (VAS) pain scores and were otherwise medically healthy. The primary endpoint of the Phase 2b trial was to evaluate the efficacy of four weeks of topical administration of TV-45070 (4% and 8% ointment) compared with placebo for the relief of symptoms of primary OA of the target knee as assessed by the change from baseline to the last five days of treatment in average evening pain score upon walking on a flat surface using Question 1 of the Western Ontario and McMaster Universities Arthritis Index

(WOMAC) on a 0-100 mm visual analog scale. The efficacy endpoints were analyzed on a full analysis set defined as all patients having received at least one dose of study drug and having at least one post baseline efficacy assessment. Key secondary objectives of the trial included changes in WOMAC pain subscale scores, responder rates, and patient-reported outcome assessments.

### **About Teva**

Teva Pharmaceutical Industries Ltd. (NYSE:TEVA) (TASE:TEVA) is a leading global pharmaceutical company that delivers high-quality, patient-centric healthcare solutions to millions of patients every day. Headquartered in Israel, Teva is the world's largest generic medicines producer, leveraging its portfolio of more than 1,000 molecules to produce a wide range of generic products in nearly every therapeutic area. In specialty medicines, Teva has a world-leading position in innovative treatments for disorders of the central nervous system, including pain, as well as a strong portfolio of respiratory products. Teva integrates its generics and specialty capabilities in its global research and development division to create new ways of addressing unmet patient needs by combining drug development capabilities with devices, services and technologies. Teva's net revenues in 2014 amounted to \$20.3 billion. For more information, visit [www.tevapharm.com](http://www.tevapharm.com).

### **About Xenon Pharmaceuticals Inc.**

Xenon is a clinical-stage biopharmaceutical company discovering and developing a pipeline of differentiated therapeutics for orphan indications that it intends to commercialize on its own and for larger market indications that the company intends to partner with global pharmaceutical companies. Xenon has built a core enabling discovery platform, referred to as Extreme Genetics®, for the discovery of validated drug targets by studying rare human diseases with extreme traits, including diseases caused by mutations in ion channels, known as channelopathies. Xenon's Extreme Genetics® platform has yielded the first approved gene therapy product in the European Union and a broad development pipeline and multiple pharmaceutical partnerships, including with Teva and Genentech. For more information, please visit [www.xenon-pharma.com](http://www.xenon-pharma.com).

### **Teva's Safe Harbor Statement under the U. S. Private Securities Litigation Reform Act of 1995:**

*This release contains forward-looking statements, which are based on management's current beliefs and expectations and involve a number of known and unknown risks and uncertainties that could cause our future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to: our ability to develop and commercialize additional pharmaceutical products; competition for our innovative products, especially Copaxone® (including competition from orally-administered alternatives, as well as from potential purported generic equivalents) and our ability to migrate users to our 40 mg/mL version; the possibility of material fines, penalties and other sanctions and other adverse consequences arising out of our ongoing FCPA investigations and related matters; our ability to achieve expected results from the research and development efforts invested in our pipeline of specialty and other products; our ability to reduce operating expenses to the extent and during the timeframe intended by our cost reduction program; our ability to identify and successfully bid for suitable acquisition targets or licensing opportunities, or to consummate and integrate acquisitions; the extent to which any manufacturing or quality control problems damage our reputation for quality production and require costly remediation; increased government scrutiny in both the U.S. and Europe of our patent settlement agreements; our exposure to currency fluctuations and restrictions as well as credit risks; the effectiveness of our patents, confidentiality agreements and other measures to protect the intellectual property rights of our specialty medicines; the effects of reforms in healthcare regulation and pharmaceutical pricing, reimbursement and coverage; governmental investigations into sales and marketing practices, particularly for our specialty pharmaceutical products; adverse effects of political or economic instability, major hostilities or acts of terrorism on our significant worldwide operations; interruptions in our supply chain or problems with internal or third-party information technology systems that adversely affect our complex manufacturing processes; significant disruptions of our information technology systems or breaches of our data security; competition for our generic products, both from other pharmaceutical companies and as a result of increased governmental pricing pressures; competition for our specialty pharmaceutical businesses from companies with greater resources and capabilities; the impact of continuing consolidation of our distributors and customers; decreased opportunities to obtain U.S. market exclusivity for significant new generic products; potential liability in the U.S., Europe and other markets for sales of generic products prior to a final resolution of outstanding patent litigation; our potential exposure to product liability claims that are not covered by insurance; any failure to recruit or retain key personnel, or to attract additional executive and managerial talent; any failures to comply with complex Medicare and Medicaid reporting and payment obligations; significant impairment charges relating to intangible assets, goodwill and property, plant and equipment; the effects of increased leverage and our resulting reliance on access to the capital markets; potentially significant increases in tax liabilities; the effect on our overall effective tax rate of the termination or expiration of governmental programs or tax benefits, or of a change in our business; variations in patent laws that may adversely affect our ability to manufacture our products in the most efficient manner; environmental risks; and other factors that are discussed in our Annual Report on Form 20-F for the year ended December 31, 2014 and in our other filings with the U.S. Securities and Exchange Commission. Forward-looking statements speak only as of the date on which they are made and we assume no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.*

### **Xenon 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 potential*

*efficacy, future development plans and commercial potential of TV-45070 and our other product candidates; the importance of the observed safety and tolerability profile of TV-45070 in the current trial and the ability to replicate these observed results in the ongoing clinical trial of TV-45070 in PHN; the timing of the completion of and results from additional clinical trials of TV-45070 in other indications and our other product candidates; the plans of our collaboration partners and their interactions with regulatory agencies; the results of research and development efforts; the effect of regulation by the FDA and other agencies and the potential impact of competitive products, product development, commercialization and technological difficulties. 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: ongoing or additional clinical trials of TV-45070 or our other product candidates may not demonstrate safety and efficacy; our Extreme Genetics discovery platform may not yield additional product candidates; any of our or our collaborators' product candidates, including TV-45070, 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 pursuant to our collaboration agreements; 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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