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Tonix Pharmaceuticals Announces Initiation of the Phase 3 RELIEF Study of TNX-102 SL for the Management of Fibromyalgia

First Patient Expected to be Dosed Before Year-End 2019

NEW YORK, Nov. 21, 2019 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that, having successfully closed an underwritten public equity offering for $9.0 million, it has initiated the Phase 3 RELIEF study (TNX-CY-F304). RELIEF is a potential pivotal study of TNX-102 SL* (cyclobenzaprine HCl sublingual tablets), a non-opioid, centrally-acting analgesic taken daily at bedtime, for the management of fibromyalgia.

“We are in the process of activating approximately 40 U.S. sites to start enrolling patients, and we expect to dose the first patient by year end 2019,” said Seth Lederman, M.D., President and Chief Executive Officer. “Initiating a new Phase 3 trial for TNX-102 SL in fibromyalgia is an important milestone for Tonix, physicians, and most importantly for the estimated 9 million U.S. adults suffering from this chronic, frequently debilitating central pain condition. Dr. Lederman continued, “Approximately one-third of those diagnosed with fibromyalgia in the U.S. are reported to receive chronic prescription opiates, which is part of the opiate crisis, since opiates are not believed to be effective for central pain. TNX-102 SL is a potential new, non-opioid, non-addictive analgesic that has been shown to have activity at a syndromal level, improving a broad array of fibromyalgia symptoms in prior Phase 2 and Phase 3 studies at the 2.8 mg dose.”

In a March 2019 Clinical Guidance meeting with the U.S. Food and Drug Administration (FDA), Tonix received guidance from the FDA to advance the development of TNX-102 SL 5.6 mg for the management of fibromyalgia. The Phase 3 study design features were discussed and agreed upon to test the safety and efficacy of TNX-102 SL at a dosage of 5.6 mg in a pivotal study to support the fibromyalgia indication with targeted enrollment of approximately 470 patients.

A lower dose of TNX-102 SL (2.8 mg) taken daily at bedtime was studied previously in fibromyalgia in a Phase 2 study and a Phase 3 study. In both studies, the 2.8 mg dose missed the primary endpoint of reduction in daily pain at Week 12. However, both studies showed broad clinical activity, evidenced by reduction of daily pain by other standard analytic approaches (30% responder analysis and mean pain, respectively) and improvements on the Fibromyalgia Impact Questionnaire – Revised, Patient Global Impression of Change, and measures of sleep quality. In Tonix’s posttraumatic stress disorder (PTSD) program, TNX-

102 SL 5.6 mg (2 x 2.8 mg tablets) demonstrated acceptable tolerability in PTSD patients. Furthermore TNX-102 SL 5.6 mg showed activity in reducing pain in PTSD patients with baseline chronic pain. In the clinical studies of TNX-102 SL in both the PTSD and fibromyalgia program, there were no serious and unexpected adverse events reported at the 2.8 mg or 5.6 mg doses; the most common adverse events were primarily related to local administration site reactions, such as transient oral hypoaesthesia (numbness) or paresthesia (tingling) or abnormal product taste after dosing.

Supported by the previous safety and efficacy findings of TNX-102 SL in fibromyalgia and PTSD, Tonix believes that increasing the dose of TNX-102 SL from the 2.8 mg to 5.6 mg in the new RELIEF Phase 3 fibromyalgia study has the potential to provide clinical evidence to support the efficacy and safety of TNX-102 SL for the management of fibromyalgia. The registration of TNX-102 SL 5.6 mg for the fibromyalgia indication will be supported by the long-term safety exposure data from the PTSD program.

About the Phase 3 RELIEF Study

The RELIEF study is a double-blind, randomized, placebo-controlled trial designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets). The two-arm, adaptive design trial is expected to enroll approximately 470 patients across approximately 40 U.S. sites. For the first two weeks of treatment, there will be a run-in period in which patients will start on TNX-102 SL 2.8 mg (1 tablet) or placebo. After the first two weeks, all patients will have the dose increased to TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) or two placebo tablets for 12 weeks. The primary endpoint is daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline (using the weekly averages of the daily numerical rating scale scores), analyzed by mixed model repeated measures with multiple imputation.

The RELIEF study is expected to have one unblinded interim analysis when the study has results from approximately the first 50% of efficacy-evaluable patients, pending agreement with the FDA. Additional details about the RELIEF study are available at www.theRELIEFstudy.com.

About Fibromyalgia

Fibromyalgia is a chronic pain disorder that is thought to result from amplified sensory and pain signaling. Fibromyalgia afflicts an estimated 6-12 million adults in the U.S, and physicians and patients report widespread dissatisfaction with currently marketed products. Common symptoms of fibromyalgia include chronic widespread pain, nonrestorative sleep, fatigue, and morning stiffness. Other associated symptoms include cognitive dysfunction and mood disturbances, including anxiety and depression. Individuals suffering from fibromyalgia struggle with their daily activities, have impaired quality of life, and frequently are disabled.

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering and developing small molecules and biologics to treat psychiatric, pain and addiction conditions. Tonix's lead product candidate, TNX-102 SL, is in development for posttraumatic stress disorder (PTSD), fibromyalgia, agitation in Alzheimer's disease and alcohol use disorder (AUD). TNX-102 SL is in Phase 3 development as a bedtime treatment for PTSD (trade name Tonmya**) and

fibromyalgia. The Phase 3 RECOVERY trial (P302) in PTSD is currently enrolling and results from an interim analysis are expected in the first quarter of 2020 and topline data are expected in the second quarter of 2020 if the sample size remains the same. The Company has initiated the Phase 3 RELIEF trial in fibromyalgia and expects to enroll the first patient by year-end 2019. The agitation in Alzheimer's disease program is Phase 2 ready and the development for AUD is in the pre-Investigational New Drug (IND) application stage. Tonix is advancing two other PTSD therapeutic programs in the pre-IND stage, with different mechanisms than TNX-102 SL and designed for daytime dosing: TNX-601 CR (tianeptine oxalate controlled-release tablets) and TNX-1600 (a triple reuptake inhibitor). TNX-601 CR is in clinical formulation testing outside of the U.S and is expected to be IND-ready in 2020. Tonix's programs for treating addiction conditions also include TNX-1300*** (double-mutant cocaine esterase), which is in Phase 2 development for the treatment of cocaine intoxication. Tonix's preclinical pipeline includes TNX-1500 (anti-CD154), a monoclonal antibody being developed to prevent and treat organ transplant rejection and autoimmune conditions, and TNX-1700 (rTFF2), a biologic being developed to treat gastric and pancreatic cancers. Finally, TNX-801 (live virus vaccine for percutaneous [scarification] administration) to potentially prevent smallpox and TNX-701 (undisclosed small molecule) to prevent radiation effects are being advanced as medical countermeasures to improve biodefense.

*TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication.

**Tonmya has been conditionally accepted by the U.S. Food and Drug Administration (FDA) as the proposed trade name for TNX-102 SL for the treatment of PTSD.

***TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication.

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward-Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2018, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2019, and periodic reports

on Form 10-Q filed with the SEC on or after the date thereof. Tonix does not undertake any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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