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Tonix Pharmaceuticals Presents Positive Results from Phase 3 RELIEF Study of TNX-102 SL for the Management of Fibromyalgia at the American College of Rheumatology Convergence 2021

CHATHAM, N.J., Nov. 08, 2021 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced an oral presentation of positive results from its Phase 3 clinical study, RELIEF, of TNX-102 SL for the management of fibromyalgia. A copy of the presentation is available under the IR Events tab of the Investors section of the Tonix website at www.tonixpharma.com.

The presentation, titled, "*TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia in the RELIEF Study: Positive Results of a Phase 3 Randomized, Double-Blind, Placebo-Controlled Multicenter Efficacy and Safety Trial*" by Dr. Gregory Sullivan, Chief Medical Officer of Tonix, reports that TNX-102 SL met its pre-specified primary endpoint in the Phase 3 RELIEF trial, significantly reducing daily pain compared to placebo ($p=0.01$) in participants with fibromyalgia. Also, when the primary endpoint was analyzed as a $\geq 30\%$ pain responder analysis, there was a higher rate of responders to TNX-102 SL (47%) than to placebo (35%; $p=0.006$). TNX-102 SL at 5.6 mg also showed activity in key secondary endpoints demonstrating improvements in sleep quality, mitigation of fatigue, and fibromyalgia-specific functional recovery.

Early discontinuation rates were similar for TNX-102 SL and placebo (16.5% and 17.7%, respectively). In addition, TNX-102 SL was well tolerated with the most common adverse event from active treatment being oral hypoaesthesia, a sensory administration site reaction that is typically transient, was never rated as severe, and only lead to one discontinuation.

"Results of the Phase 3 RELIEF trial demonstrated that TNX-102 SL had broad syndromal effects across core fibromyalgia symptoms of widespread pain, fatigue, memory and sleep disturbance," said Seth Lederman, M.D., President and Chief Executive Officer. "The positive Phase 3 RELIEF study achieved statistical significance on the primary endpoint in December, 2020. We had started a second Phase 3 study, RALLY in September 2020. Based on disappointing efficacy results at the interim analysis of RALLY in July 2021, we stopped enrolling new participants. Topline results from RALLY are expected before year end. The Company will determine the next steps in this program based on analysis of the RALLY data, which will include pharmacogenomic analyses of RALLY and RELIEF."

About Fibromyalgia

Fibromyalgia is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system. Fibromyalgia afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women. 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. Physicians and patients report common dissatisfaction with currently marketed products.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which provides rapid transmucosal absorption and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. As a multifunctional agent with potent binding and antagonist activities at the serotonin_{2A}, α_1 -adrenergic, histaminergic-H₁, and muscarinic-M₁ receptors, TNX-102 SL is in clinical development as a daily bedtime treatment for fibromyalgia, PTSD, alcohol use disorder and agitation in Alzheimer's disease. The U.S. Patent and Trademark Office (USPTO) has issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in these patents are important elements of Tonix's proprietary TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.

About the Phase 3 RELIEF Study

The RELIEF study has been completed and TNX-102 SL achieved a statistically significant benefit as measured by the primary, pre-specified endpoint of improvement over placebo in daily pain. The RELIEF study was a double-blind, randomized, placebo-controlled Phase 3 trial designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the management of fibromyalgia. The two-arm trial targeted enrollment of 470 participants, at approximately 40 U.S. sites. RELIEF completed final enrollment of 503 participants. The first two weeks of treatment were a run-in period in which participants start on TNX-102 SL 2.8 mg (1 tablet) or placebo. After the first two weeks, all participants had 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 was 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.

Additional details about the completed RELIEF study are available at [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04172831) (NCT04172831).

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics and diagnostics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is primarily composed of immunology and central nervous system (CNS) product candidates. Tonix's immunology portfolio includes COVID-

19-related product candidates to prevent and treat COVID-19, to treat Long COVID as well as to detect functional T cell immunity to SARS-CoV-2. The Company's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL¹ (cyclobenzaprine HCl sublingual tablets), is in mid-Phase 3 development for the management of fibromyalgia. TNX-1300² is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial before year end. Tonix's lead vaccine candidate for COVID-19, TNX-1800³, is a live replicating vaccine based on Tonix's recombinant pox vaccine (RPV) platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects to start a Phase 1 study in humans in the second half of 2022. Tonix is developing TNX-2100⁴, an *in vivo* diagnostic to measure the presence of functional T cell immunity to SARS-CoV-2 and intends to initiate a first-in-human clinical study in the fourth quarter of 2021, pending IND clearance. TNX-3500⁵ (sangivamycin) is a small molecule antiviral drug to treat acute COVID-19 and is in the pre-IND stage of development. Finally, TNX-102 SL is a small molecule drug being developed to treat Long COVID, a chronic post-COVID condition, and is also in the pre-IND stage. Tonix expects to conduct a Phase 2 study in Long COVID in the first half of 2022. Tonix's immunology portfolio also includes biologics to address immunosuppression, cancer, and autoimmune diseases.

¹*TNX-102 SL is an investigational new drug and has not been approved for any indication.*

²*TNX-1300 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication.*

³*TNX-1800 is an investigational new biologic and has not been approved for any indication. TNX-1800 is based on TNX-801, live horsepox virus vaccine for percutaneous administration, which is in development to protect against smallpox and monkeypox. TNX-801 is an investigational new biologic and has not been approved for any indication.*

⁴*TNX-2100 is an investigational new biologic and has not been approved for any indication*

⁵*TNX-3500 is an investigational new drug at the pre-IND stage of development 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; delays and uncertainties caused by the global COVID-19 pandemic; 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. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the Securities and Exchange Commission (the “SEC”) on March 15, 2021, and periodic reports filed with the SEC on or after the date thereof. All Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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