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Tonix Pharmaceuticals Announces Publication of Results from Phase 3 RELIEF Trial of TNX-102 SL for the Management of Fibromyalgia

Previously Disclosed Data Demonstrated that TNX-102 SL Achieved Statistically Significant Pain Reduction Over Placebo at Week 14 (Primary Endpoint, p=0.01) and Was Generally Safe and Well Tolerated

Topline Data from RESILIENT, a Potentially Confirmatory Registration-Enabling Phase 3 Fibromyalgia Trial of TNX-102 SL, Expected Fourth Quarter 2023

CHATHAM, N.J., June 15, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, today announced that previously disclosed results from the Phase 3 RELIEF study of TNX-102 SL for the management of fibromyalgia have been published in the peer-reviewed journal *Arthritis Care & Research*, an official journal of the American College of Rheumatology. In RELIEF, treatment with TNX-102 SL was associated with significant reductions in daily pain and was generally safe and well tolerated in patients with fibromyalgia. Secondary results also suggest that treatment with TNX-102 SL can improve sleep and reduce fatigue, which together with pain are recognized as core fibromyalgia symptoms. TNX-102 SL is a novel, non-opioid, centrally-acting analgesic, intended to be taken once daily at bedtime. The paper can be accessed online at https://pubmed.ncbi.nlm.nih.gov/37165930/.

“There continues to be a pressing need for novel, safe and more tolerable drugs to treat patients with fibromyalgia, a debilitating chronic disease that afflicts an estimated 6 to 12 million adults in the United States, with symptoms including multisite pain and disturbed sleep,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “Current fibromyalgia therapies have limited efficacy in alleviating symptoms of sleep disturbance and fatigue. These Phase 3 RELIEF data suggest that treatment with TNX-102 SL may improve sleep quality and fatigue in patients with fibromyalgia, in addition to reducing pain.”

The paper, titled, “*Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results From the Randomized, Placebo Controlled RELIEF Trial,”* includes data demonstrating 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, in an exploratory analysis, when the primary endpoint was analyzed as a ≥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 global symptomatic and functional recovery.

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

Tonix is currently enrolling in a potentially confirmatory, registration-enabling Phase 3 study (RESILIENT). Topline results are expected in the fourth quarter of this year.

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 5-HT2A-serotonergic, α1-adrenergic, H1-histaminergic, and M1-muscarinic receptors, TNX-102 SL is in development as a daily bedtime treatment for fibromyalgia, Long COVID (formally known as post-acute sequelae of COVID-19 [PASC]), alcohol use disorder and agitation in Alzheimer's disease. The United States Patent and Trademark Office (USPTO) 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 the patent 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 RESILIENT Study

The RESILIENT study is a double-blind, randomized, placebo-controlled trial designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) in the management of fibromyalgia. The two-arm trial is expected to enroll approximately 470 participants in the U.S. The first two weeks of treatment consist of a run-in period in which participants start on TNX-102 SL 2.8 mg (1 tablet) or placebo. Thereafter, all participants increase their dose to TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) or two placebo tablets for the remaining 12 weeks. The primary endpoint is the daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline to Week 14 (using the weekly averages of

the daily numerical rating scale scores), analyzed by mixed model repeated measures with multiple imputation.

For more information, see ClinicalTrials.gov Identifier: NCT05273749.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 study has been completed, and topline results are expected in the third quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), in development for chronic migraine, is currently enrolling with topline data expected in the fourth quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets), a once-daily formulation being developed as a treatment for major depressive disorder (MDD), is also currently enrolling with interim data expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is a small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the third quarter of 2023. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox, for which a Phase 1 study is expected to be initiated in the first quarter of 2024. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease portfolio also includes TNX-3900 and TNX-4000, classes of broad-spectrum small molecule oral antivirals.

**All of Tonix's product candidates are investigational new drugs or biologics and have 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 the 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, 2022, as filed with the Securities and Exchange Commission (the "SEC") on March 13, 2023, and periodic reports filed with the SEC on or after the date thereof. All of 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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