January 9, 2024

Tonix Pharmaceuticals Presents Additional Data Highlighting the Favorable Tolerability and Differentiated Side Effect Profile of TNX-102 SL in Second Positive Phase 3 Clinical Trial for the Management of Fibromyalgia

As previously announced, Phase 3 RESILIENT study of TNX-102 SL met its primary endpoint (p=0.00005) with statistically significant and clinically meaningful daily pain reduction over placebo

Results demonstrated a favorable tolerability and side effect profile, including improvement in female sexual function and no increases in weight or blood pressure – three treatment-limiting side effects often observed with currently approved medicines for fibromyalgia

Overall results from two positive Phase 3 trials point to TNX-102 SL's potential as a new first-line medicine fit for long term use in managing fibromyalgia, a chronic, often debilitating condition suffered by 6-12 million adults in the U.S.

New Drug Application (NDA) submission to the FDA planned for second half of 2024 under the 505(b)(2) regulatory pathway

CHATHAM, N.J., Jan. 09, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced the presentation of additional safety and tolerability data from RESILIENT, the second positive Phase 3 study evaluating TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the management of fibromyalgia, at Biotech Showcase™ 2024 in San Francisco, January 8-10.

As previously announced, RESILIENT met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.00005) in participants with fibromyalgia. Statistically significant and clinically meaningful results were also seen in all key secondary endpoints related to improving sleep quality, reducing fatigue, and improving overall fibromyalgia symptoms and function. Tonix plans to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in the second half of 2024 for TNX-102 SL for the management of fibromyalgia.

RELIEF, the first Phase 3 trial of TNX-102 SL 5.6 mg in fibromyalgia, was completed in December 2020. It met its pre-specified primary endpoint of daily pain reduction compared to

placebo (p=0.010) and showed activity in key secondary endpoints.

In presenting more detailed data from the RESILIENT study, Seth Lederman, M.D., President and Chief Executive Officer of Tonix, said, “The results showed that TNX-102 SL treatment was not associated with increases in systolic or diastolic blood pressure or body weight, nor were there any reported sexual side effects. In fact, when systematically investigated using the Changes in Sexual Functioning Questionnaire short form (CSFQ-14), women who received study drug had a higher CSFQ-14 score relative to those who received placebo consistent with improved sexual function. These are important tolerability factors for fibromyalgia patients on long-term therapies, particularly since weight gain is associated with gabapentinoids, negative sexual side effects are associated with serotonin-reuptake inhibiting medications, and increased blood pressure is associated with potent noradrenergic-reuptake inhibiting medications.”

Dr. Lederman added, “We believe that the data from our two positive Phase 3 studies, with clinically meaningful separation from placebo on pain, sleep, and fatigue, show that fibromyalgia can be successfully treated by TNX-102 SL 5.6 mg and may provide the opportunity for Tonix to launch the first FDA-approved drug for fibromyalgia in more than a decade.”

“An estimated 6 million to 12 million adults in the U.S. are living with fibromyalgia, the majority of whom are women. We believe that these safety and efficacy results will be important to fibromyalgia patients who struggle not only with pain, but also multiple other symptoms and potential side effects from the currently approved pharmacotherapies,” said Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. “Because fibromyalgia is a chronic condition with treatments intended to be used on a long-term basis, favorable tolerability and side effect profiles are integral to managing this debilitating condition and enhancing the quality of life for those suffering. We are now another important step closer to bringing a new first-line treatment to fibromyalgia patients that offers broad symptom relief with favorable tolerability attributes for chronic use and adherence.”

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 randomized 457 participants in the U.S. across 33 sites. 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.

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 million to 12 million adults in the U.S., the majority 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 cholinergic receptors, TNX-102 SL is in development as a daily bedtime treatment for fibromyalgia, fibromyalgia-type 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. In addition, Tonix has pending but not issued U.S. patent applications directed to the transmucosal absorption of CBP-HCl, with U.S. market exclusivity expected until 2033, for treating depressive symptoms in fibromyalgia, with U.S. market exclusivity expected until 2032, and for treating pain in fibromyalgia with U.S. market exclusivity expected until 2041.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's development portfolio is focused on central nervous system disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA for TNX-102 SL (cyclobenzaprine HCl sublingual tablet), which has completed two positive Phase 3 studies for the management of fibromyalgia. Tonix intends to meet with the FDA in the first half of 2024 and submit an NDA for the approval of TNX-102 SL for the management of fibromyalgia in the second half of 2024. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition, and topline results from a proof-of-concept study were reported in the third quarter of 2023. 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 first quarter of 2024. Tonix's rare disease development portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome (PWS). TNX-2900 has been granted Orphan Drug designation by the FDA and an investigational new drug (IND) application has been cleared to support a Phase 2 study in PWS patients. Tonix's immunology development 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 was initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases, including TNX-

1800, in development as a vaccine to protect against COVID-19. During the fourth quarter of 2023, TNX-1800 was selected by the U.S. National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID) Project NextGen for inclusion in Phase 1 clinical trials. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults.

*Tonix's product development 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; risks related to the failure to successfully market any of our products; 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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