November 18, 2024

Tonix Pharmaceuticals Presented Data and Analyses of TNX-102 SL Treatment Effects on Fibromyalgia at the American College of Rheumatology (ACR) Convergence 2024 Annual Meeting

Poster presentation highlighted results from confirmatory Phase 3 RESILIENT study of TNX-102 SL (sublingual cyclobenzaprine HCl) treatment demonstrating statistically significant improvement in primary endpoint of fibromyalgia nociplastic pain and in all six key secondary endpoints, including sleep quality

New Drug Application (NDA) submitted to FDA in October 2024; Fast Track designation previously granted by FDA; FDA decision on approval expected 2025

TNX-102 SL is a potential non-opioid analgesic targeting non-restorative sleep

If approved by FDA, TNX-102 SL would be the first member of a new class of analgesic drugs for fibromyalgia and the first new drug for treating fibromyalgia in more than 15 years

CHATHAM, N.J., Nov. 18, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, presented data in a poster presentation at the ACR Convergence 2024 Annual Meeting, held November 14-19, 2024, in Washington, D.C. A copy of the Company's presentation, titled "*Randomized, Double-Blind, Placebo-Controlled Confirmatory Phase 3 Trial of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) in Fibromyalgia*" is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

In the Phase 3 RESILIENT study, TNX-102 SL met the pre-specified primary endpoint of significantly reducing daily pain compared to placebo (p-value=0.00005) in participants with fibromyalgia. In the RESILIENT study, TNX-102 SL demonstrated a broad spectrum of benefits with statistically significant improvement in all six pre-specified key secondary endpoints including those related to improved sleep quality, reduced fatigue, and improved patient global ratings and overall fibromyalgia symptoms and function. TNX-102 SL was generally well tolerated with an adverse event profile comparable to prior studies and no new safety signals observed.

"Fibromyalgia is the prototypic nociplastic syndrome and one of the chronic overlapping pain conditions (COPCs)[1,2,3]," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "TNX-102 SL, designed as a bedtime treatment to target non-restorative

sleep, has shown a statistically significant improvement in pain in two phase 3 studies. We believe TNX-102 SL has the potential to be the first new drug treatment option for fibromyalgia patients in 15 years."

Tonix submitted a new drug application (NDA) to the U.S. Food and Drug Administration (FDA) in October 2024 for TNX-102 SL for the management of fibromyalgia. The FDA typically has a 60-day filing review period to determine whether the submitted NDA is complete and accepted for review. If the FDA accepts the NDA for review, the Company expects a 2025 date for a FDA decision on approval, based on the Prescription Drug User Fee Act (PDUFA).

[1]*Fitzcharles MA, et al. Lancet. 2021;397(10289):2098-2110.*

[2]*Clauw DJ. Ann Rheum Dis. 2024;83(11):1421-1427.*

[3]*Kaplan CM, et al. Nat Rev Neurol. 2024;20(6):347-363.*

About Fibromyalgia

Fibromyalgia is a common chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system, called central sensitization. Brain imaging studies have localized the functional disorder to the brain's insular and anterior cingulate cortex. Fibromyalgia afflicts more than 10 million adults in the U.S., the majority of whom are women. Symptoms of fibromyalgia include chronic widespread pain, non-restorative sleep, fatigue, and brain fog (or cognitive dysfunction). Other associated symptoms include mood disturbances, including depression, anxiety, headaches, and abdominal pain or cramps. Individuals suffering from fibromyalgia often struggle with their daily activities, have impaired quality of life, and frequently are disabled. Physicians and patients report common dissatisfaction with currently marketed products. Fibromyalgia is now recognized as the prototypic nociplastic syndrome. Nociplastic pain is the third primary type of pain in addition to nociceptive pain and neuropathic pain. Many patients present with pain syndromes that are combinations of the three primary types of pain. Nociplastic syndromes can involve components of both central and peripheral sensitization. Fibromyalgia can occur without any identifiable precipitating event. However, many fibromyalgia cases follow one or more precipitating event(s) including: chronic nociceptive or neuropathic pain states; recovery from an infectious illness; a cancer diagnosis or cancer treatment; a metabolic or endocrine stress; or a traumatic event. In the cases of recovery from an infectious illness, fibromyalgia is considered an Infection-Associated Chronic Condition. In addition to fibromyalgia cases associated with other conditions or stressors, the U.S. National Academies of Sciences, Engineering, and Medicine, has concluded that fibromyalgia is a diagnosable condition that occurs after recovery from COVID-19 in the context of Long COVID. Fibromyalgia is also recognized as a Chronic Overlapping Pain Condition, due to shared symptoms with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), irritable bowel syndrome, endometriosis, low back pain, post-concussive syndrome (also known as mild traumatic brain injury), chronic Lyme Disease, chronic diabetic neuropathy and chronic post-herpetic neuralgia.

About TNX-102 SL

TNX-102 SL is a centrally acting, non-opioid bedtime investigational drug, designed for

chronic use. The tablet is a patented sublingual formulation of cyclobenzaprine hydrochloride developed for bedtime dosing for the management of fibromyalgia. Cyclobenzaprine interacts as an antagonist at four different receptors in the brain: serotonergic-5-HT_{2A}, adrenergic-α_1, histaminergic-H_1, and muscarinic-M_1-cholinergic receptors. Together, these interactions are believed to target the non-restorative sleep characteristic of fibromyalgia that was identified by Professor Harvey Moldofsky in 1975. Approved oral cyclobenzaprine products are not associated with risk of addiction or dependence. The TNX-102 SL tablet is based on a eutectic formation of cyclobenzaprine HCl and mannitol that provides a stable product which dissolves rapidly and efficiently delivers cyclobenzaprine by the transmucosal route into the bloodstream. The eutectic protects cyclobenzaprine HCl from interacting with the basifying agent that is also part of the formulation and required for efficient transmucosal absorption. Patents based on TNX-102 SL's eutectic composition and its properties have issued in the U.S., E.U., Japan, China and many other jurisdictions around the world and provide market protection into 2034. The European Patent Office's Opposition Division maintained Tonix's European Patent EP 2 968 992 in unamended form after an Opposition was filed against it by a Sandoz subsidiary, Hexal AG. Hexal AG did not appeal that decision. The formulation of TNX-102 SL was designed specifically for sublingual administration and transmucosal absorption for bedtime dosing to target disturbed sleep, while reducing the risk of daytime somnolence. Clinical pharmacokinetic studies indicated that the addition of a basifying agent was necessary for efficient transmucosal absorption which results in higher levels of exposure during the first 2 hours after dosing and in deceased levels of the long-lived active metabolite, norcyclobenzaprine, relative to cyclobenzaprine, consistent with bypassing first pass hepatic metabolism.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on transforming therapies for pain management and vaccines for public health challenges. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to advance TNX-102 SL, a product candidate for the management of fibromyalgia, for which an NDA was submitted based on two statistically significant Phase 3 studies for the management of fibromyalgia. The FDA has granted Fast Track designation to TNX-102 SL for the management of fibromyalgia. We expect an FDA decision on the acceptance of the NDA for review and an assigned PDUFA date in December and if accepted, a decision on NDA approval in 2025. TNX-102 SL is also being developed to treat acute stress reaction and acute stress disorder under a Physician-Initiated IND at the University of North Carolina in the OASIS study funded by the U.S. Department of Defense (DoD). Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic in Phase 2 development designed to treat cocaine intoxication that has FDA Breakthrough Therapy designation and its development is supported by a grant from the U.S. National Institute on Drug Abuse. Tonix's immunology development portfolio consists of biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is an Fc-modified humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. Tonix also has product candidates in development in the areas of rare disease, including TNX-2900 for Prader-Willi syndrome, and infectious disease, including a vaccine for mpox, TNX-801. Tonix recently announced a contract with the U.S. DoD's Defense Threat Reduction Agency (DTRA) for up to $34 million over five years to develop TNX-4200, small molecule broad-

spectrum antiviral agents targeting CD45 for the prevention or treatment of infections to improve the medical readiness of military personnel in biological threat environments. Tonix owns and operates a state-of-the art infectious disease research facility in Frederick, MD. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

* Tonix's product development candidates are investigational new drugs or biologics; their efficacy and safety have not been established and have not been approved for any indication.

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. All other marks are property of their respective owners.

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, 2023, as filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, 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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