October 16, 2024

Tonix Pharmaceuticals Announces Submission of the TNX-102 SL New Drug Application (NDA) for Fibromyalgia to the U.S. Food and Drug Administration (FDA)

NDA based on two Phase 3 studies of TNX-102 SL in fibromyalgia with statistically significant results on the primary endpoint of reducing widespread pain; generally well tolerated

TNX-102 SL is a non-opioid, centrally acting analgesic, granted Fast Track designation by FDA

Fibromyalgia affects more than 10 million adults in the U.S. who are mostly women

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., Oct. 16, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), today announced the submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg, a non-opioid, centrally-acting analgesic that showed statistically significant reduction in the chronic, widespread pain associated with fibromyalgia in two Phase 3 studies and was generally well tolerated. TNX-102 SL was granted Fast Track designation for fibromyalgia by the FDA in July of 2024. Fast Track is designed to expedite FDA review of important new drugs to treat serious conditions and fill an unmet medical need.

“With the submission of this NDA, Tonix has achieved a critical milestone in potentially bringing a new first-line treatment option to the large and dissatisfied fibromyalgia population that has not had a new pharmacotherapy in over 15 years,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “TNX-102 SL would be the first member of a new class of medicines for treating fibromyalgia. TNX-102 SL was designed and developed as a bedtime treatment to be taken daily on a chronic basis. Tonix believes bedtime TNX-102 SL relieves fibromyalgia pain by targeting the non-restorative sleep that is characteristic of fibromyalgia.”

The NDA submission is supported by data from two 14-week double-blind, randomized, placebo-controlled Phase 3 clinical trials evaluating the safety and efficacy of TNX-102 SL 5.6 mg as a bedtime treatment for fibromyalgia. The prior Phase 3 RELIEF trial of TNX-102 SL in fibromyalgia, completed in December 2020, met its pre-specified primary endpoint of significantly reducing daily pain compared to placebo (p=0.010). In the confirmatory Phase 3

RESILIENT study in fibromyalgia, completed in December 2023, TNX-102 SL met the pre-specified primary endpoint of significantly reducing daily pain compared to placebo (p =0.00005). In both trials, TNX-102 SL was generally well tolerated with an adverse event profile comparable to prior studies and with no new safety signals observed. In both pivotal studies, the most common treatment-emergent adverse event was tongue or mouth numbness at the administration site, which was temporally related to dosing, self-limited, never rated as severe, and rarely led to study discontinuation (one participant in each study). Therefore, Tonix believes the submitted dossier contains the requisite safety and efficacy data from two adequate and well-controlled studies to support NDA submission.

“Despite three FDA-approved medications, representing two different classes of medicines, there remains a need for new treatment options for fibromyalgia patients,” commented Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. “If approved by FDA, TNX-102 SL would be the first of a new tricyclic class of medicines for treating fibromyalgia. The existing FDA-approved drugs for fibromyalgia include the gabapentinoid class, represented by Pfizer’s Lyrica® (pregabalin) approved in 2008, and the SNRI class, represented by Lilly’s Cymbalta® (duloxetine) and AbbVie’s Savella® (milnacipran) approved in 2007 and 2009, respectively. The TNX-102 SL tablet is based on a proprietary eutectic formulation of cyclobenzaprine HCl and mannitol that provides a stable product which dissolves rapidly and efficiently delivers cyclobenzaprine by the transmucosal route into the bloodstream. I would like to thank all the participants in our clinical trials, as well as the trial investigators and staff, who worked together over many years to help make this important milestone possible.”

The FDA typically has a 60-day filing review period to determine whether the submitted NDA is complete and accepted for review. If FDA accepts the NDA for review, the Company expects a 2025 date for an FDA decision on approval, based on the Prescription Drug User Fee Act (PDUFA).

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 a spectrum of mixtures of the three primary types of pain. Nociplastic syndromes are associated with 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. Cyclobenzaprine is 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 delivers cyclobenzaprine by the transmucosal route efficiently 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 in both single dose and multiple dose studies, consistent with bypassing first pass hepatic metabolism. At steady state after 20 days of dosing TNX-102 SL, the dynamic peak level of cyclobenzaprine is higher than the background level of norcyclobenzaprine. In contrast, after 20 days of dosing oral cyclobenzaprine, the simulated peak level of cyclobenzaprine is lower than the simulated background level of norcyclobenzaprine.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully integrated biopharmaceutical company focused on transforming therapies for pain management and modernizing solutions for public health challenges. Tonix's development portfolio is focused on central nervous system (CNS) disorders, and its priority is to progress TNX-102 SL, a product candidate 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.

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 of Drug Abuse and Addiction. 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.

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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