August 12, 2024

Tonix Pharmaceuticals Presented Data and Analyses of TNX-102 SL Treatment Effects on Fibromyalgia, the Prototypic Nociplastic Pain Syndrome, at the IASP 2024 World Congress on Pain

Bedtime TNX-102 SL (sublingual cyclobenzaprine HCl) treatment in the Phase 3 RESILIENT study resulted in statistically significant improvement in the primary endpoint of fibromyalgia nociplastic pain and in all six key secondary endpoints, including sleep quality

Post hoc analyses highlight the strong correlations between improvements in nociplastic pain and sleep quality

Nociplastic pain originates from altered pain perception in the brain and is the type of pain that manifests in fibromyalgia and other chronic overlapping pain conditions (COPCs)

FDA granted TNX-102 SL Fast Track designation for the management of fibromyalgia; NDA submission on track for second half 2024

CHATHAM, N.J., Aug. 12, 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 International Association for the Study of Pain (IASP) 2024 World Congress on Pain, held August 5-9, 2024 in Amsterdam, the Netherlands. A copy of the Company's poster presentation titled, "*Targeting Fibromyalgia Non-Restorative Sleep with Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl): Results of the Positive Phase 3 RESILIENT Trial Consistent with Syndromal Improvement*", is available under the Scientific Presentations tab of the Tonix website atwww.tonixpharma.com.

TNX-102 SL met the pre-specified primary endpoint in the Phase 3 RESILIENT study, significantly reducing daily pain compared to placebo (p-value=0.00005) in participants with fibromyalgia. TNX-102 SL also demonstrated broad syndromal benefits with statistically significant improvement in all six pre-specified key secondary endpoints including those related to improving sleep quality, reducing fatigue, and improving patient global ratings and overall fibromyalgia symptoms and function. A new *post hoc* analysis showed correlations between improvements in pain and sleep quality at Week 14, supporting the concept that targeting sleep quality has the potential to achieve syndromal improvement in fibromyalgia. TNX-102 SL was well tolerated with an adverse event profile comparable to prior studies and no new safety signals observed.

“Approximately 50 years ago, the central role of nonrestorative sleep in the pathogenesis and persistence of fibromyalgia was recognized by Dr. Harvey Moldofsky[1,2]”, said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “TNX-102 SL was designed as a bedtime treatment to target non-restorative sleep and improve sleep quality. The statistically significant results of TNX-102 SL in two positive Phase 3 studies provide evidence of the activity and tolerability of TNX-102 SL in fibromyalgia and also support the critical role of sleep quality in the pathogenesis, persistence and exacerbations of fibromyalgia originally proposed by Dr. Moldofsky.”

Greg Sullivan, M.D., Chief Medical Officer, added, “Today, fibromyalgia is recognized as the prototypic ‘nociplastic syndrome’. Understanding nociplastic syndromes is crucial for developing effective treatment strategies for chronic overlapping pain conditions (COPCs)[3,4,5]. Traditional analgesics like NSAIDs or opioids often prove ineffective if not deleterious in these conditions. In contrast, TNX-102 SL provided broad-spectrum symptom relief in the RESILIENT study. We believe TNX-102 SL has the potential to be the first new treatment option for fibromyalgia patients in 15 years.”

TNX-102 SL was recently granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for the management of fibromyalgia. Tonix remains on track to submit an NDA to the FDA in the second half of 2024 for TNX-102 SL for the management of fibromyalgia.

[1]Moldofsky H, et al. *Psychosom Med.* 1975;37:341-51

[2]Moldofsky H, Scarisbrick P. *Psychosom Med*. 1976;38:35-44

[3]Fitzcharles MA, et al. *Lancet.* 2021;397:2098-110

[4]Clauw DJ. *Ann Rheum Dis.* Published Online First: 2024

[5]Kaplan CM, et al. *Nat Rev Neurol*. 2024;20, 347–363

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 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 anxiety and depression, headaches, and abdominal pain or cramps. 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. According to the recent report from the U.S. National Academies of Sciences, fibromyalgia is a diagnosable condition that may also occur in the context of Long COVID

About TNX-102 SL

TNX-102 SL is a centrally acting, non-opioid, non-addictive, bedtime investigational drug. The tablet is a patented sublingual formulation of cyclobenzaprine hydrochloride developed

for the management of fibromyalgia. In December 2023, the company announced highly statistically significant and clinically meaningful topline results in RESILIENT, the second pivotal Phase 3 clinical trial of TNX-102 SL for the management of fibromyalgia. In the study, TNX-102 SL 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 six key secondary endpoints related to improving sleep quality, reducing fatigue and improving overall fibromyalgia symptoms and function. RELIEF, the first statistically significant Phase 3 trial of TNX-102 SL 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 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). TNX-102 SL was recently granted Fast Track Designation by the FDA for the management of fibromyalgia and remains on track to submit an NDA to the U.S. Food and Drug Administration in the second half of 2024.

About Nociplastic Pain

Nociplastic pain is the third category of pain distinct from nociceptive pain and neuropathic pain. Nociplastic pain is characterized by pain arising from altered nociception despite no evidence of actual or threatened tissue damage causing activation of peripheral nociceptors or somatosensory system disease or lesion. Its underlying pathophysiology involves altered pain processing by the central nervous system (CNS). Nociplastic syndromes, officially recognized by the International Association for the Study of Pain (IASP) in 2017, also include several other chronic overlapping pain conditions: myalgic encephalomyelitis/chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorders, forms of chronic back pain and chronic headache. The pathophysiology of nociplastic pain involves central sensitization (CS), where neurons of the CNS become hyperexcitable, amplifying pain signals. CS can be triggered by peripheral pain stimuli, emotional stress, or other factors, leading to persistent pain despite no peripheral nociceptive input.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for TNX-102 SL, a product candidate for which two statistically significant Phase 3 studies have been completed 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. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic designed to treat cocaine intoxication that has Breakthrough Therapy designation. Tonix's immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease. 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 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.

Investor Contact

Jessica Morris
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(862) 904-8182

Peter Vozzo
ICR Westwicke
peter.vozzo@westwicke.com
(443) 213-0505

Media Contact

Katie Dodge
LaVoieHealthScience
kdodge@lavoiehealthscience.com
(978) 360-3151

Source: Tonix Pharmaceuticals Holding Corp.