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Tonix Pharmaceuticals Announces Potential Positive Impact of the U.S. National Academies (NASEM) New Definition of Long COVID on the Size of the Fibromyalgia Market for Tonmya™

Fibromyalgia is a "diagnosable condition" in people suffering from Long COVID according to NASEM[1]

Diagnosing fibromyalgia in Long COVID patients is expected to expand the potential addressable market for Tonmya relative to pre-COVID-19 pandemic estimates[2]

Tonmya is a potential new first-line non-opioid analgesic under development for the management of fibromyalgia with Fast Track designation: NDA submission target is second half of 2024, with potential for FDA approval in 2025

CHATHAM, N.J., July 31, 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, today provided an update on the potential impact on the size of the fibromyalgia market for its development candidate Tonmya (TNX-102 SL or cyclobenzaprine HCl sublingual tablets), based on the new definition of Long COVID by the U.S. National Academies of Sciences, Engineering and Medicine (NASEM) announced on June 11, 2024[1].

"The consensus report from the NASEM concludes that fibromyalgia is a 'diagnosable condition' in people suffering from Long COVID," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "It has long been recognized that fibromyalgia can arise after a viral illness and is considered an infection-associated chronic condition.[2,3] The NASEM definition confirms that fibromyalgia occurs after infection with the SARS-CoV-2 virus in some patients with Long COVID. Tonix is planning to file a New Drug Application (NDA) for Tonmya in the second half of this year for the indication of fibromyalgia with the U.S. Food and Drug Administration (FDA). We believe that diagnosing fibromyalgia in Long COVID patients will increase the potential market for Tonmya following approval as compared to market estimates from before the COVID-19 pandemic."

Dr. Lederman continued, "Prior to the COVID-19 pandemic, the prevalence of fibromyalgia was estimated to be more than 10 million adults in the U.S.[4] The U.S. Census Bureau, the National Center for Health Statistics Household Pulse Survey and the Centers for Disease Control and Prevention (CDC) estimate that approximately 5.3% of U.S. adults suffer from

Long COVID, or 14 million people.[5] Fibromyalgia is commonly diagnosed in Long COVID patients[6-8]. Although it is unknown how many Long COVID patients meet the diagnostic criteria for fibromyalgia, the National Institutes of Health (NIH)-sponsored RECOVER study found many Long COVID patients suffer from pain at multiple sites[9]. The Company has previously presented its analysis of real-world evidence from the TriNetX claims database suggesting that over 40% of Long COVID patients present with a constellation of symptoms that overlap with fibromyalgia.[10,11] The Company completed a proof-of-concept study in Long COVID patients who presented with multisite pain and found a nominal benefit in fatigue with TNX-102 SL treatment with no new safety signals. We hope this new definition of Long COVID will allow patients suffering from chronic pain and other debilitating symptoms to access the care they need."

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, 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.

About Tonmya* (also known as TNX-102 SL)

Tonmya™ (cyclobenzaprine HCl sublingual tablets) is a centrally acting, non-opioid, non-addictive, investigational drug being developed as a daily bedtime medication for the management of fibromyalgia, alcohol use disorder and agitation in Alzheimer's disease. The tablet is a patented sublingual formulation of cyclobenzaprine hydrochloride TNX-102 SL 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. 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 December 2023, the company announced highly statistically significant and clinically meaningful topline results in RESILIENT, the second pivotal Phase 3 clinical trial of Tonmya for the management of fibromyalgia. In the study, Tonmya 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 Tonmya 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). Tonix has recently announced receipt of the formal minutes from both recent pre-New Drug Application (NDA) meetings with the U.S. Food and Drug Administration (FDA) for Tonmya for the management of fibromyalgia. At these meetings, the Company and the FDA agreed on the proposed content and timing of an NDA submission. The Company reaffirmed its guidance to submit the NDA for Tonmya to the FDA in the second half of 2024 which would allow for a potential FDA approval in 2025. Tonmya for the management of fibromyalgia has been granted FDA Fast Track designation.

About the Phase 2 PREVAIL Study

The Phase 2 PREVAIL study was a 14-week double-blind, randomized, multicenter, placebo-controlled study to evaluate the efficacy and safety of TNX-102 SL taken daily at bedtime in patients with multi-site pain associated with Long COVID. The trial was conducted at approximately 30 sites in the U.S. The study was not significant on the primary efficacy endpoint of the change from baseline in the weekly average of daily self-reported worst pain intensity scores at the Week 14 endpoint. Nominal activity of TNX-102 SL was shown in fatigue.

For more information, see ClinicalTrials.gov Identifier: NCT05472090.

About Long COVID

Long COVID is an infection-associated chronic condition (IACC) that occurs after SARS-CoV-2 infection and is present for at least 3 months as a continuous, relapsing and remitting, or progressive disease state that affects one or more organ systems. Long COVID is the term widely recognized for the post-COVID syndrome formerly known as Post-acute sequelae of COVID-19, or PASC. Although most people recover from COVID-19 within weeks of the acute illness, a substantial portion develops Long COVID. These individuals experience a constellation of disabling symptoms long past the time of recovery from acute COVID-19. Most Long COVID patients who have been studied appear to have cleared the SARS-CoV-2 infection from their systems.

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 Tonmya, a product candidate for which two statistically significant Phase 3 studies have been completed 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.

*Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration as the tradename for TNX-102 SL for the management of fibromyalgia. Tonmya has not been approved for any indication.

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

[1]U.S. National Academies of Sciences, Engineering, and Medicine. 2024. *A Long COVID Definition: A chronic, systemic disease state with profound consequences.* Washington, DC: The National Academies Press. https://doi.org/10.17226/27768. http://www.nationalacademies.org/long-covid-definition.

[2]Clauw DJ, et al. *Pain*. 2020 161(8):1694–7.

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[4]Vincent A, et al. *Arthritis Care Res (Hoboken)*. 2013 65(5):786-92. doi: 10.1002

[5]National Center for Health Statistics. U.S. Census Bureau, Household Pulse Survey, 2022–2024. Long COVID. Generated interactively: July 22, 2024 from https://www.cdc.gov/nchs/covid19/pulse/long-covid.htm

[6]Gavrilova, N, et al. 2022. *Pathophysiology* 29(1):24-29. https://doi.org/10.3390/pathophysiology29010003.

[7]Clauw, DJ, and L Calabrese. 2024. *Annals of the Rheumatic Diseases* 83:136-138

[8]Savin, E., et al. 2023. *PLoS One* 18(2):e0281593. https://doi.org/10.1371/journal.pone.0281593.

[9]Thaweethai T, et al. *JAMA*. 2023 329(22):1934-1946.

[10]Feb 22, 2023 Tonix Pharmaceuticals Press Release. URL: https://ir.tonixpharma.com/news-events/press-releases/detail/1369/tonix-pharmaceuticals-describes-emerging-research-on-the

[11]September 21, 2022, Tonix Pharmaceuticals Poster at the IASP, "Retrospective observational database study of patients with Long COVID with multi-site pain, fatigue and insomnia". URL: www.tonixpharma.com/wp-content/uploads/2022/09/Retrospective-Observational-Database-Study-of-Patients-with-Long-COVID-with-Multi-Site-Pain-Fatigue-and-Insomnia_A-Real-World-Analysis-of-Symptomatology-and-Opioid-Use.pdf

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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