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Tonix Pharmaceuticals Announces FDA IND Clearance for DoD Funded Trial of TNX-102 SL for the Reduction of Acute Stress Reaction and Prevention of PTSD

Bedtime TNX-102 SL improves sleep quality in PTSD and is also being developed for the management of fibromyalgia for which NDA preparation is ongoing

Investigator-Initiated OASIS Trial at UNC is a Phase 2180-patient, randomized, placebo-controlled trial in acute trauma patients following motor vehicle collisions

One-third of emergency department visits in the U.S. (40-50 million patients per year) involve evaluation after trauma exposures

CHATHAM, N.J., Feb. 12, 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 U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application for the Phase 2 investigator-initiated OASIS trial to evaluate TNX-102 SL[1] in reducing the severity of acute stress reaction (ASR) and the frequency of acute stress disorder (ASD) and posttraumatic stress disorder (PTSD). The trial is sponsored by The University of North Carolina (UNC) Institute for Trauma Recovery and supported by a $3 million grant from the U.S. Department of Defense (DoD).

“No medication is currently available at or near the point-of-care to treat patients suffering from traumatic events and support long-term health,” said Seth Lederman, M.D., Chief Executive Officer of Tonix. “There is an unmet need for treating ASR after traumatic events such as civilian motor vehicle collisions or warfighter experiences in forward bases or in theater. Previous trials of TNX-102 SL in PTSD suggested activity on sleep and stress related symptoms in the first several weeks of treatment.[2,3] The study is motivated by the observation that the symptoms of ASR and PTSD are similar and by the hypothesis that TNX-102 SL’s effect on sleep quality may reduce ASR symptoms.”

The Optimizing Acute Stress Reaction Interventions with TNX-102 SL (OASIS) trial will examine the safety and efficacy of TNX-102 SL to reduce adverse posttraumatic neuropsychiatric sequelae among patients presenting to the emergency department (ED) after a motor vehicle collision. The trial will enroll approximately 180 trauma survivors at ED study sites around the U.S. Participants will be randomized in the ED to receive a two-week course of either TNX-102 SL 5.6 mg or placebo.

The OASIS trial will build upon a foundation of knowledge and infrastructure developed through the UNC-led, $40 million AURORA initiative. AURORA is a major national research initiative to improve the understanding, prevention, and recovery of individuals who experience a traumatic event. AURORA is supported by funding from the National Institutes of Health (NIH), leading brain health nonprofit One Mind, private foundations, and partnerships with leading tech companies such as Mindstrong Health and Verily Life Sciences, the healthcare arm of Alphabet, the parent company of Google.

“This innovative clinical trial and partnership will help address the need for safe and effective therapies to treat acute trauma,” said Samuel McLean, M.D., Professor of Psychiatry and Emergency Medicine at the UNC School of Medicine at UNC, School of Medicine, and lead principal investigator of the proposed study. “ASR and posttraumatic stress symptoms are common among civilian motor vehicle collision survivors. The AURORA initiative, which has collected thousands of data points from motor vehicle collisions, has allowed us to better investigate the correlation between motor vehicle collisions and the emergence of acute stress disorder or PTSD symptoms. In OASIS, we will test a pharmacological intervention in the immediate aftermath of trauma that has potential for fast relief of stress symptoms, improvement in coping and functioning, and preclusion of escalation to more severe conditions, ASD in the short term and PTSD thereafter.”

Acute and chronic stress disorders can affect both civilian and military populations. According to the National Center for PTSD, in the U.S. about 60% of men and 50% of women experience at least one trauma in their lives.[4] In the U.S. alone, one-third of emergency department visits (40-50 million patients per year) involve evaluation after trauma exposures, and in a 2014 study involving 3,157 US veterans, 87% reported exposure to at least one potentially traumatic event during their service.[5] Moreover, as many as 500,000 U.S. troops who served in wars between 2001 and 2015 were diagnosed with PTSD.[6]

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

Tonmya is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which is designed for daily administration at bedtime with a proposed mechanism of improving sleep quality in fibromyalgia. Tonmya 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, Tonmya is in development as a daily bedtime treatment for fibromyalgia. TNX-102 SL is also in development for 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 Tonmya composition. These patents are expected to provide Tonmya, 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 cyclobenzaprine 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 Tonmya, 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 Tonmya for the management of fibromyalgia in the second half of 2024. TNX-102 SL is 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.

1. *TNX-102 SL (cyclobenzaprine HCl sublingual tablets)* has *not been approved for any indication; (Tonmya™ is conditionally approved by FDA for the management of fibromyalgia)*
2. *Sullivan GM, et al. Randomized clinical trial of bedtime sublingual cyclobenzaprine (TNX-102 SL) in military-related PTSD and the role of sleep quality in treatment response. Psychiatry Res. 2021 Jul;301:113974.*
3. *Parmenter ME, et al. A phase 3, randomized, placebo-controlled, trial to evaluate the efficacy and safety of bedtime sublingual cyclobenzaprine (TNX-102 SL) in military-*

related posttraumatic stress disorder. Psychiatry Res. 2024 (In Press). https://doi.org/10.1016/j.psychres.2024.115764
4. *Goldstein RB, et al. Soc Psychiatry Psychiatr Epidemiol. 2016. 51(8):1137-48*
5. *Wisco BE, et al. J Clin Psychiatry. 2014. 75(12):1338-46*
6. *Thompson M. Time. 2015;185(12):40-3*

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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