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Tonix Pharmaceuticals Completes Clinical Phase of PREVAIL Proof-of-Concept Study of TNX-102 SL for the Treatment of Fibromyalgia-Type Long COVID

Topline Results Expected Third Quarter 2023

Long COVID Afflicts Approximately 19% of Patients Following COVID-19[1], and is Expected to be a Global Health Burden

Fibromyalgia-Type Long COVID with Multi-Site Pain Affects Approximately 40% of Long COVID Patients

CHATHAM, N.J., Aug. 07, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company, today announced the completion of the clinical phase of the Phase 2 proof-of-concept PREVAIL study of TNX-102 SL as a potential treatment for fibromyalgia-type Long COVID. Topline results for the PREVAIL study are expected in the third quarter of 2023.

“Approximately 40% of U.S. Long COVID patients have fibromyalgia-like multi-site pain symptoms based on our observational studies of Long COVID patients from the TriNetX claims database,”[2,3] said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “In addition to multi-site pain, these individuals often suffer from one or more other symptoms typically associated with fibromyalgia such as fatigue, sleep disturbance, and brain fog. We have termed this subgroup, ‘Fibromyalgia-type Long COVID.’ Given our encouraging results with TNX-102 SL as a potential treatment for fibromyalgia[4], we are testing TNX-102 SL as a bedtime medicine for the management of Fibromyalgia-type Long COVID. In completing this clinical milestone, marked by the last enrolled patient finishing their final visit, we can now begin to look forward to topline results from the 63-patient PREVAIL study later this quarter.”

Dr. Lederman continued, “TNX-102 SL improves sleep quality in fibromyalgia, and we believe this is the mechanism by which TNX-102 SL improves other symptoms, like multi-site pain.[5] Recently, the U.S. National Institutes of Health (NIH) has identified improving sleep quality as a target for potential therapeutics for Long COVID[6,7,8], consistent with the proposed mechanism of TNX-102 SL.

“Common symptoms of Long COVID, including multi-site pain, fatigue, unrefreshing sleep, and cognitive dysfunction, or ‘brain fog,’ are also hallmarks of conditions like fibromyalgia and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME),”[9] said Herbert Harris,

M.D., Ph.D., Executive Vice President and Head of Translational Medicine of Tonix Pharmaceuticals. “Defining subgroups of Long COVID patients that overlap with fibromyalgia and CFS/ME is expected to facilitate the development of new treatments.[4] It can be challenging to distinguish fibromyalgia and CFS/ME clinically, given the high level of symptom overlap between them. Each of these conditions is defined by a constellation of symptoms, and there is no widely recognized diagnostic laboratory test that distinguishes them.”

Dr. Harris continued, “The recent identification of Long COVID subgroups in the National Institutes of Allergy and Infectious Diseases (NIAID)-sponsored RECOVER study[10] was an important step. In their recent publication, cluster analysis of the symptom frequencies in the RECOVER study identified four subgroups of Long COVID patients. Cluster #4 represented approximately one-quarter of the population (28%) and reported the highest frequencies of pain (back pain (58%), joint pain (64%) or muscle pain (60%)), high frequencies of fatigue (94%) and ’Brain Fog,’ (94%) and a high level of impairment of Quality of Life. We believe Cluster #4 is a subgroup of Long COVID that shares many clinical features with fibromyalgia and may involve common disease mechanisms. We also believe that Cluster #3, representing another approximately 29% of the RECOVER cohort, includes many patients with fibromyalgia-type Long COVID because 100% of that group suffer from ‘Brain Fog’, 94% experience fatigue and approximately one-third experience pain (back pain (32%), joint pain (36%) or muscle pain (34%)).”

Dr. Harris concluded, “With no FDA approved treatment for Long COVID, we understand the need to better understand long COVID and to develop treatments for subgroups of this unserved population of patients. Fibromyalgia has been recognized by the U.S. Food and Drug Administration (FDA) with three approved medicines. Consequently, measuring daily pain is a validated endpoint for FDA registrational studies in fibromyalgia. We believe that daily pain has the potential to be an endpoint for registrational studies in fibromyalgia-like long COVID.”

About the Phase 2 PREVAIL Study

The Phase 2 PREVAIL study is 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 post-acute sequelae of SARS-CoV-2 infection (PASC). The trial is being conducted at approximately 30 sites in the U.S. The primary efficacy endpoint will be the change from baseline in the weekly average of daily self-reported worst pain intensity scores at the Week 14 endpoint. Key secondary efficacy endpoints include change from baseline in self-reported scores for sleep disturbance, fatigue, and cognitive function. Topline results are expected in the third quarter of 2023.

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

About Long COVID or Post-Acute Sequelae of COVID-19 (PASC)

Post-acute sequelae of COVID-19, or PASC is the formal name for a condition now widely known as Long COVID. Although most people recover from COVID-19 within weeks of the acute illness, a substantial portion develops a chronic syndrome called Long COVID.[11] 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. The symptoms of Long COVID can include fatigue, sleep disorders, multi-site pain, fevers, shortness of breath, cognitive impairment described as “brain fog” or memory disturbance, gastrointestinal symptoms, anxiety, and depression. According to the Centers for Disease Control and Prevention (CDC), 1 in 13 adults in the U.S. (7.5%) have Long COVID symptoms.[1] Long COVID is typically associated with moderate or severe COVID-19, but can occur after mild COVID-19 or even after asymptomatic SARS-CoV-2 infection. More than 40% of adults in the United States reported having COVID-19 in the past, and nearly one in five of those (19%) are currently still having symptoms of Long COVID.[1] Long COVID is a chronic disabling condition that is expected to result in a significant global health and economic burden.[12-15] In response to the urgent need for therapies that address Long COVID, Congress awarded $1.15 billion to the National Institutes of Health to study Long COVID in December 2020[16] The U.S. Department of Health and Human Services *National Research Action Plan on Long COVID*[17], released in August 2022, addresses the overlap of Long COVID with CFS/ME, which, like fibromyalgia, is one of the overlapping chronic pain syndromes with central and peripheral sensitization.[18] A published survey[19] found comparable pain, fatigue, and functional impairment between Long COVID, fibromyalgia, and CFS/ME. This symptom overlap between these conditions has suggested that altered neurologic function is one of the leading hypotheses to explain them.[20] While the vaccines available in the U.S., through either FDA approval or under Emergency Use Authorization, have been shown to prevent acute COVID, their ability to prevent Long COVID is unknown. There is currently no approved drug for the treatment of Long COVID. Fibromyalgia-type Long COVID, like fibromyalgia and CFS/ME, appears to be one of several chronic overlapping pain conditions that have in common the neurological process called central and peripheral sensitization, which is increasingly known by the term nociplastic pain.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which 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, TNX-102 SL is in development as a daily bedtime treatment for fibromyalgia, 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 TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.

*TNX-102 SL is an investigational new drug and is not approved for any indication

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17. Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID, 200 Independence Ave SW, Washington, DC 20201. www.covid.gov/assets/files/National-Research-Action-Plan-on-Long-COVID-08012022.pdf
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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 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 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 development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS development portfolio includes both small molecules and biologics

to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment of a potentially confirmatory Phase 3 study in the third quarter of 2023, with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 proof-of-concept study has been completed, and topline results are expected in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the μ-opioid receptor while maintaining activity in the rat Novel Object Recognition test *in vivo* and the ability to activate PPAR-β/δ and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment in a Phase 2 proof-of-concept study with topline data expected in the fourth quarter of 2023. TNX-1900 is also being studied in binge eating disorder, pediatric obesity and social anxiety disorder by academic collaborators under investigator-initiated INDs. 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 third quarter of 2023. Tonix's rare disease development portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. 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 is expected to be 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. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals.

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

Tonix Medicines has contracted to acquire the Zembrace SymTouch and Tosymra registered trademarks. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc.

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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