August 24, 2021

Tonix Pharmaceuticals Announces Results of Pre-IND Meeting with FDA for TNX-102 SL as a Potential Treatment for Long COVID Syndrome, Also Known as Post-Acute Sequelae of COVID-19 (PASC)

Company Plans to Submit an IND to Support a Phase 2 Clinical Trial of TNX-102 SL for the Treatment of Long COVID

Long COVID Symptoms of Pain, Sleep Disturbance, Fatigue and Brain Fog Overlap with Symptoms of Fibromyalgia, for which TNX-102 SL is in Mid-Phase 3 Development

Long COVID Afflicts More Than 30% of Patients Following Infection with SARS-CoV-2, the Virus that Causes COVID-19, and is Expected to be a Global Health Burden

CHATHAM, N.J., Aug. 24, 2021 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that it received the official minutes from a Type B pre-Investigational New Drug Application (IND) meeting with the U.S. Food and Drug Administration (FDA) to develop TNX-102 SL[1] (cyclobenzaprine HCl sublingual tablets) as a potential treatment for Long COVID Syndrome (Long COVID), which is now known officially as Post-Acute Sequelae of COVID-19 (PASC[2]). Tonix believes the minutes provide a path to agreement on the design of a Phase 2 study and the overall clinical development plan to qualify TNX-102 SL as an indicated treatment for a subset of patients affected by Long COVID. Based on the minutes, the Company is planning to submit the IND in the fourth quarter of 2021 to support a Phase 2 study for the management of a subset of Long COVID patients whose symptoms overlap with fibromyalgia.

Seth Lederman, M.D., President and Chief Executive Officer of Tonix, stated, “Long COVID is a new, complex and heterogeneous disorder. Long COVID is a protracted syndrome experienced by many people following SARS-CoV-2 infection that can include a number of persistent disabling symptoms, including fatigue, widespread pain, sleep disturbance, brain fog or difficulty concentrating, arthralgias, diffuse myalgia, olfactory dysfunction, and headache.[3] Our Phase 2 study will focus on Long COVID patients whose primary symptoms overlap with fibromyalgia, and, therefore, our Long COVID program leverages what we have learned about the pharmacodynamic activity of TNX-102 SL from more than 1,000 participants who have been or are enrolled in our fibromyalgia trials to date. Long COVID has been compared to fibromyalgia because of the common symptoms of sleep disturbance, persistent widespread pain, fatigue, and brain fog.[4] Additionally, Long COVID,

like fibromyalgia, is experienced by women at a rate approximately four times that of men.[5] The 2003 SARS outbreak, due to an earlier coronavirus, was also described as causing a post-SARS syndrome similar to fibromyalgia.[6]"

Gregory Sullivan, M.D., Chief Medical Officer of Tonix, commented, "Based on our positive fibromyalgia Phase 3 RELIEF study in which TNX-102 SL showed activity in addressing persistent pain, sleep disturbance, memory, fatigue and energy, we are hopeful that TNX-102 SL might provide a unique treatment opportunity for the symptoms of Long COVID in patients whose symptoms overlap with those of fibromyalgia. We believe the core symptoms of Long COVID, including fatigue, sleep disturbances, persistent pain and diffuse myalgia share an underlying pathogenesis with fibromyalgia."

Dr. Lederman added, "TNX-102 SL is in mid-Phase 3 development for the treatment of fibromyalgia. The proposed mechanism of TNX-102 SL is to improve sleep quality. Since disturbed sleep is linked to exacerbation and chronicity of a number of pain, neuropsychiatric and addictive disorders, we plan to conduct clinical trials to determine whether TNX-102 SL improves sleep in certain of these other disorders in addition to Long COVID and fibromyalgia."

About Long COVID or Post-Acute Sequelae of SARS-CoV-2 (PASC)

Although most people recover from COVID-19 within weeks of the acute illness, a substantial portion develop a chronic syndrome called Long COVID. These individuals experience a constellation of 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 virus from their systems. The symptoms of Long COVID can include fatigue, sleep disorders, pain, fevers, shortness of breath, cognitive impairment described as "brain fog" or memory disturbance, gastrointestinal symptoms, anxiety, and depression. Long COVID can persist for months and can range in severity from mild to incapacitating. Several cohort studies have reported that persistence of symptoms following SARS-CoV-2 infection occurs in more than 30% of patients.[3] While typically associated with moderate or severe COVID-19, Long COVID can occur after mild COVID-19 or even after asymptomatic SARS-CoV-2 infection. Patients with Long COVID are sometimes referred to as "long-haulers". Long COVID is a chronic disabling condition that is expected to result in a significant global health and economic burden.[7] 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 last December.[8] While the vaccines available in the U.S. 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."

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 serotonin$_{2A}$, α_1-adrenergic, histaminergic-H_1, and muscarinic-M_1 receptors, TNX-102 SL is in clinical development as a daily bedtime treatment for fibromyalgia, PTSD, alcohol use disorder and agitation in Alzheimer's disease. The U.S. Patent and Trademark Office (USPTO) has

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 these patents 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.

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing small molecules and biologics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is primarily composed of central nervous system (CNS) and immunology product candidates. The Company's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL[1], is in mid-Phase 3 development for the management of fibromyalgia. Tonix's immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer, and autoimmune diseases. Tonix's lead vaccine candidate, TNX-1800[9], is a live replicating vaccine based on the horsepox viral vector platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix reported positive efficacy data from animal studies of TNX-1800 in the first quarter of 2021. TNX-801[9], live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox. TNX-3500[10] (sangivamycin) is a small molecule antiviral drug for COVID-19 in the pre-IND stage of development.

[1]TNX-102 SL is an investigational new drug and has not been approved for any indication.

[2]Feb. 24, 2021 - White House COVID-19 Response Team press briefing; Feb 25, 2021 - policy brief from the World Health Organization on long COVID.

[3]Nalbandian, Ani, et al. "Post-acute COVID-19 syndrome." Nature Medicine (2021): 1-15.

[4]Clauw DJ, Häuser W, Cohen SP, Fitzcharles M-A. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. Pain. 2020 Aug; 161(8): 1694–1697.

[5]Cox, D. "Why are women more prone to long Covid?" The Guardian.13 Jun 2021 https://www.theguardian.com/society/2021/jun/13/why-are-women-more-prone-to-long-covid

[6]Moldofsky H, Patcai J. Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. BMC Neurol 2011;11:37.

[7]Briggs, Andrew, and Anna Vassall. "Count the cost of disability caused by COVID-19." (2021): 502-505.

[8]The NIH provision of Title III Health and Human Services, Division M--Coronavirus Response and Relief Supplemental Appropriations Act, 2021, of H.R. 133, The Consolidated Appropriations Act of 2021. The bill was enacted into law on 27 December 2020, becoming Public Law 116-260.

[9]TNX-1800 and TNX-801 are investigational new biologics at the pre-IND stage of development and have not been approved for any indication.

[10]TNX-3500 is an investigational new drug at the pre-IND stage of development and has 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, the risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; 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, 2020, as filed with the Securities and Exchange Commission (the “SEC”) on March 15, 2021, and periodic reports filed with the SEC on or after the date thereof. All 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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