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

Phase 2 Clinical Trial of TNX-102 SL for the Treatment of Long COVID Expected to Start Second Quarter 2022

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., April 06, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to support a Phase 2 clinical trial with TNX-102 SL[1] as a potential treatment for a subset of patients with Long COVID Syndrome (Long COVID) whose symptoms overlap with fibromyalgia. Long COVID is now known officially as Post-Acute Sequelae of COVID-19 (PASC[2]).

“We are excited to have received the FDA’s IND clearance to begin clinical trials of TNX-102 SL for the treatment of Long COVID,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “Over 30% of people who recover from COVID-19 continue to experience a constellation of symptoms long past the time that they have recovered from acute COVID-19 illness[3-4]. The symptoms of Long COVID, which can include fatigue, multi-site pain, sleep disturbances, fevers, shortness of breath, cognitive impairment, gastrointestinal symptoms, anxiety, and depression, can persist for many months and can range from mild to incapacitating[5]. Our study will focus on testing TNX-102 SL in the treatment of patients with multi-site pain associated with Long COVID. This group of patients have symptoms that overlap with other chronic pain conditions, which as a group have been termed, ‘chronic overlapping pain conditions.’[6,7] This type of pain syndrome is increasingly recognized as nociplastic pain,[8] and the underlying mechanism as ‘central sensitization.’[9] Fibromyalgia is considered one of the chronic overlapping pain conditions and our experience with TNX-102 SL in fibromyalgia is the motivation for undertaking the development of TNX-102 SL in patients with Long COVID whose symptoms overlap with fibromyalgia.”

About the Phase 2 Study

This Phase 2 study will be a double-blind randomized, placebo-controlled 14-week trial to evaluate the safety and efficacy of sublingual TNX-102 SL 5.6 mg daily at bedtime in the treatment of patients with multi-site pain associated with Long COVID. The trial will be conducted at approximately 30 sites to enroll approximately 470 patients (235 per arm) who will be randomized in a 1:1 ratio to treatment with TNX-102 SL or placebo tablets. The primary efficacy endpoint will be Change from Baseline in the weekly average of daily self-reported worst pain intensity scores at the Week 14 endpoint. An interim analysis is expected to be completed after the first 50% of enrolled patients have completed the study for the purpose of possible sample size re-estimation.

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 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. Long COVID can persist for many 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.[3-5] 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.[10-13] 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.[14] 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.

[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] *Logue JK, et al. (2021) “Sequelae in Adults at 6 Months After COVID-19 Infection”. JAMA Netw Open. ;4(2):e210830. doi:10.1001/jamanetworkopen.2021.0830*

[4] *Carfì, A et al.. (2020) "Persistent symptoms in patients after acute COVID-19." JAMA 324.6: 603-605.*

[5] *Nalbandian, Ani, et al. (2021) "Post-acute COVID-19 syndrome." Nature Medicine27(4): 601-615.*

[6] *Maixner W, et al.. (2016) “Overlapping Chronic Pain Conditions: Implications for Diagnosis and Classification”. J Pain. 17(9 Suppl):T93-T107.*

[7] *Veasley C, et al. (2015): Impact of chronic overlapping pain conditions on public health and the urgent need for safe and effective treatment: 2015 analysis and policy recommendations. Chronic Pain Research Alliance. http://www.chronicpainresearch.org/public/CPRA_WhitePaper_2015-FINAL-Digital.pdf. Accessed July 26, 2021.*

[8] *Trouvin AP, Perrot S. (2019) "New concepts of pain". Best Pract Res Clin Rheumatol. 33(3):101415.*

[9] *Nijs J, George SZ, Clauw DJ, et al. (2021) "Central sensitisation in chronic pain conditions: latest discoveries and their potential for precision medicine". The Lancet Rheumatology. 3(5):e383-e392. doi:10.1016/s2665-9913(21)00032-1*

[10] *Briggs, A, and Vassall, A. (2021) "Count the cost of disability caused by COVID-19." Nature 593(7860): 502-505.*

[11] *Nittas V, et al. (2022) "Long COVID Through a Public Health Lens: An Umbrella Review." Public Health Rev. 43:1604501. Published 2022 Mar 15. doi:10.3389/phrs.2022.1604501*

[12] *Davis, HE., et al. (2021) "Characterizing long COVID in an international cohort: 7 months of symptoms and their impact." EClinicalMedicine 38: 101019.*

[13] *Martin C, et al. (2021) "A model framework for projecting the prevalence and impact of Long-COVID in the UK." PLoS One. 16(12):e0260843. Published 2021 Dec 2. doi:10.1371/journal.pone.0260843*

[14] *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.*

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-5-HT_{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 Long COVID, 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 therapeutics and diagnostics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of immunology, rare disease, infectious disease, and central nervous system (CNS) product candidates. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500[1] which is a humanized monoclonal antibody targeting CD40-ligand being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second half of 2022. Tonix's rare disease portfolio includes TNX-2900[2] for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan-Drug Designation by the FDA.

Tonix's infectious disease pipeline includes a vaccine in development to prevent smallpox and monkeypox called TNX-801[3], next-generation vaccines to prevent COVID-19, and an antiviral to treat COVID-19. Tonix's lead vaccine candidates for COVID-19 are TNX-1840 and TNX-1850[4], which are live virus vaccines based on Tonix's recombinant pox vaccine (RPV) platform. TNX-3500[5] (sangivamycin, *i.v.* solution) is a small molecule antiviral drug to treat acute COVID-19 and is in the pre-IND stage of development. TNX-102 SL, (cyclobenzaprine HCl sublingual tablets), is a small molecule drug being developed to treat Long COVID that overlaps with fibromyalgia, a chronic post-COVID condition. Tonix expects to initiate a Phase 2 study in Long COVID in the second quarter of 2022. 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, is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study expected to start in the second quarter of 2022. Finally, TNX-1300[6] is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial in the second quarter of 2022.

[1] *TNX-1500 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication.*

[2] *TNX-2900 is an investigational new drug at the pre-IND stage of development and has not been approved for any indication.*

[3] *TNX-801 is a live horsepox virus vaccine for percutaneous administration in development to protect against smallpox and monkeypox. TNX-801 is an investigational new biologic and has not been approved for any indication.*

[4] *TNX-1840 and TNX-1850 are live horsepox virus vaccines for percutaneous administration, in development to protect against COVID-19. TNX-1840 and TNX-1850 are designed to express the SARS-CoV-2 spike protein from the omicron and BA.2 variants, respectively. TNX-1840 and TNX-1850 are investigational new biologics at the pre-IND stage of development and have not been approved for any indication.*

[5] *TNX-3500 is an investigational new drug at the pre-IND stage of development and has not been approved for any indication.*

[6] *TNX-1300 is an investigational new biologic 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, risks related to the development of TNX-102 SL, 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, 2021, as filed with the Securities and Exchange Commission (the “SEC”) on March 14, 2022, 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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