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Tonix Pharmaceuticals Presents Phase 1 Formulation Development Data for TNX-601 CR in a Poster Presentation at CNS Summit 2021

Phase 2 Trial of TNX-601 CR for the Treatment of Major Depressive Disorder Expected to Start First Half 2022

CHATHAM, N.J., Nov. 09, 2021 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced a poster presentation of results from its open-label, Phase 1 clinical study of TNX-601 CR (tianeptine oxalate and naloxone controlled-release tablets). Tonix is developing TNX-601 CR as a potential treatment for major depressive disorder (MDD) as well as post-traumatic stress disorder and neurocognitive dysfunction associated with corticosteroid use. A copy of the poster is available under the IR Events tab of the Investors section of the Tonix website at www.tonixpharma.com. CNS Summit 2021 is taking place November 7th – 10th in Boston, Mass. The poster presentations by Greg Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals, took place on November 8th and will also be presented on November 9th from 5:00 pm – 7:00 pm ET.

The poster, titled, "*TNX-601 CR*: a Once-Daily Formulation of Tianeptine in Development for the Treatment of Major Depressive Disorder"* provides data related to the Phase 1 pharmacokinetic study in healthy subjects that assessed several novel modified-release (MR) prototype formulations of tianeptine oxalate. The study showed that the selected TNX-601 MR1 demonstrated pharmacokinetics appropriate for once-daily dosing with minimal food effect, which is a potential treatment adherence advantage over three times per day dosing of immediate release tianeptine sodium. This MR prototype was selected in the development of the final formulation of TNX-601 CR as a once-daily treatment for MDD.

"We believe that these Phase 1 findings support our upcoming Phase 2 study of once-daily TNX-601 CR for MDD that we expect to initiate in the first half of 2022," said Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals. "Tianeptine products have been approved in Europe and other countries around the world and marketed as prescription drugs for the treatment of depression for more than three decades. Based on our Phase 1 results, we believe that with respect to plasma tianeptine and its primary metabolite, TNX-601 CR would meet the bioequivalence standard for daily dosing of these immediate release products. No tianeptine-containing product has been approved by the U.S. Food and Drug Administration (FDA). TNX-601 CR's proposed mechanism of action is distinct from any antidepressant approved in the U.S for chronic or

long-term use."

Tonix previously completed a Phase 1 clinical trial for formulation development outside of the U.S. Based on this study, the final formulation of TNX-601 CR to be used in Phase 2 testing will be 39.4 mg tianeptine oxalate and 1 mg naloxone for once daily treatment of MDD. Naloxone is included in the formulation to mitigate the potential for high dose parenteral abuse. Tianeptine has weak off-target activity at the μ-opioid receptor that presents the potential for parenteral abuse with doses on the order of eight to 80 times the therapeutic daily dose for depression. The Phase 2 study design is expected to be a randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of TNX-601 CR monotherapy compared to placebo in MDD. Treatment duration will be six weeks, preceded by up to five weeks in screening and followed by a two-week safety follow-up period (total up to 13 weeks of participation). We plan to randomize approximately 260 individuals with MDD at a 1:1 ratio to two arms of 130 each for drug and placebo at approximately 25-30 U.S. sites. The primary efficacy endpoint will be the change from baseline to Week 6 in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score. Enrollment is estimated to start in the first half of 2022, pending clearance of the Investigational New Drug application.

**TNX-601 CR is an investigational new drug and has not been approved for any indication.*

About Depression

According to the National Institute of Mental Health, approximately 17 million adults in the U.S.[1] have had at least one major depressive episode. Depression is a condition characterized by symptoms such as a depressed mood or loss of interest or pleasure in daily activities most of the time for two weeks or more, accompanied by appetite changes, sleep disturbances, motor restlessness or retardation, loss of energy, feelings of worthlessness or excessive guilt, poor concentration, and suicidal thoughts and behaviors. These symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. The majority of people who suffer from depression do not respond adequately to initial antidepressant therapy.[2]

[1]National Institute of Mental Health. (2017). Major Depression. Retrieved from http://www.nimh.nih.gov/health/statistics/major-depression.shtml
*[2]\Rush AJ, et al. (2007) Am J. Psychiatry 163:11, pp. 1905-1917 (STAR*D Study).*

About TNX-601 CR

TNX-601 CR is a novel oral formulation of tianeptine oxalate designed for once-daily daytime dosing that is in development for the treatment of MDD. Tianeptine sodium (amorphous) immediate release was first marketed for depression in France in 1989 and has been available for decades in Europe, Russia, Asia, and Latin America for the treatment of depression. Tianeptine sodium has an established safety profile from decades of use in these jurisdictions. Currently there is no tianeptine-containing product approved in the U.S. and no controlled-release tianeptine product approved in any jurisdiction. Tonix discovered a novel oxalate salt of tianeptine that may provide improved stability, consistency, and manufacturability compared to known forms of tianeptine. Tianeptine is believed to work in depression as a modulator of the glutamatergic system. Tianeptine modulates the

glutamatergic system indirectly since it does not directly bind to NMDA, AMPA or kainate receptors. In animals, tianeptine has been shown to reverse the adverse neuroplastic changes that are observed during periods of stress and elevated corticosteroid exposure. Tianeptine and its MC5 metabolite are weak μ-opioid receptor agonists. Tonix has added naloxone to the TNX-601 CR tablet to mitigate potential for parenteral abuse as tianeptine has been linked to illicit misuse at higher doses than the reported therapeutic dose in the treatment of MDD. Neither tianeptine nor MC5 have been shown to bind other neurotransmitter receptors. Tianeptine's reported pro-cognitive and anxiolytic effects as well as its ability to attenuate the neuropathological effects of excessive stress responses suggest that it may also be used to treat post-traumatic stress disorder by a different mechanism of action than TNX-102 SL.

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 primarily composed of immunology and central nervous system (CNS) product candidates. Tonix's immunology portfolio includes COVID-19-related product candidates to prevent and treat COVID-19, to treat Long COVID as well as to detect functional T cell immunity to SARS-CoV-2. 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] (cyclobenzaprine HCl sublingual tablets), is in mid-Phase 3 development for the management of fibromyalgia. TNX-1300[2] is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial before year end. Tonix's lead vaccine candidate for COVID-19, TNX-1800[3], is a live replicating vaccine based on Tonix's recombinant pox vaccine (RPV) platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects to start a Phase 1 study in humans in the second half of 2022. Tonix is developing TNX-2100[4], an *in vivo* diagnostic to measure the presence of functional T cell immunity to SARS-CoV-2 and intends to initiate a first-in-human clinical study in the fourth quarter of 2021, pending IND clearance. TNX-3500[5] (sangivamycin) is a small molecule antiviral drug to treat acute COVID-19 and is in the pre-IND stage of development. Finally, TNX-102 SL is a small molecule drug being developed to treat Long COVID, a chronic post-COVID condition, and is also in the pre-IND stage. Tonix expects to conduct a Phase 2 study in Long COVID in the first half of 2022. Tonix's immunology portfolio also includes biologics to address immunosuppression, cancer, and autoimmune diseases.

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

[2]TNX-1300 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication.

[3]TNX-1800 is an investigational new biologic and has not been approved for any indication. TNX-1800 is based on TNX-801, live horsepox virus vaccine for percutaneous administration, which is 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-2100 is an investigational new biologic and has 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.

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 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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