UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): March 16, 2023

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Main Street, Chatham, New Jersey 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company □

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. □

Item 7.01 Regulation FD Disclosure.

On March 16, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that the first participant was enrolled in the Phase 2 'UPLIFT' study for its TNX-601 ER (tianeptine hemioxalate extended-release tablets) product candidate for the treatment of major depressive disorder ("MDD"). A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference.

The information in the Presentation, and this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.01, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

On March 16, 2023, the Company announced that the first participant was enrolled in the Phase 2 UPLIFT study for TNX-601 ER for the treatment of MDD. The Phase 2 UPLIFT study, TNX-TI-M201, is a double-blind, randomized, multicenter, placebo-controlled study to evaluate the efficacy and safety of TNX-601 ER taken by mouth once-daily for 6 weeks for the treatment of MDD. It is a parallel design study with two arms, a TNX-601 ER 39.4 mg arm and a placebo arm. A total of 300 participants will be randomized in a 1:1 ratio into the two arms across approximately 30 U.S. sites, enrolling adult patients 18-65 years old with a DSM-5 diagnosis of depression and a duration for the current major depressive episode of at least 12 weeks. The primary efficacy endpoint is mean change from baseline in the Montgomery-Åsberg Depression Rating Scale total score at Week 6. Key secondary efficacy endpoints include the Clinical Global Impression of Severity Scale and the Sheehan Disability Scale. An interim analysis is expected to be completed after the first 50% of enrolled patients have completed the study for the purpose of potential sample size re-estimation, currently anticipated in the fourth quarter of 2023. A 24-week open-label extension study, TNX-TI-M202, is planned to receive patients completing the UPLIFT study

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press release of the Company, dated March 16, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: March 16, 2023

By: /s/ Bradley Saenger
Bradley Saenger
Chief Financial Officer

Exhibit 99.01

Tonix Pharmaceuticals Initiates Enrollment in Phase 2 'UPLIFT' Study of TNX-601 ER (Tianeptine Hemioxalate Extended-Release Tablets) for the Treatment of Major Depressive Disorder (MDD)

Results from Planned Interim Analysis Expected Fourth Quarter 2023

Approximately 21 Million Adults in U.S. Suffer From a Major Depressive Episode Each Year

TNX-601 ER is a Once-Daily Tablet that is Bioequivalent to Three-Times-Daily Tianeptine Sodium Immediate Release (IR) that has been available in Europe, Asia and Latin America for More than Three Decades

Tianeptine IR is Associated with Low Incidences of Sexual Dysfunction, Sleep Disruption, Sedation, Weight Gain, and Cognitive Impairment Compared with Traditional Monoaminergic Antidepressants

TNX-601 ER is a New Chemical Entity in the U.S. and Represents a Potential Innovative Approach to Addressing Depression: Restoration of Neuroplasticity and Neurogenesis Rather than Modulation of Neurotransmitter Levels and Activity

CHATHAM, N.J., Mar. 16, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that the first participant was enrolled in the Phase 2 'UPLIFT' study of TNX-601 ER[1] (tianeptine hemioxalate extended-release tablets) for the treatment of major depressive disorder (MDD). The double-blind, placebo-controlled registrational-quality study has a target enrollment of 300 participants at approximately 30 sites across the U.S. Results from a planned interim analysis are expected to be released in the fourth quarter of 2023.

The proprietary once-daily formulation of TNX-601 ER was designed to be bioequivalent to the three-times-a-day formulation of tianeptine sodium (amorphous) immediate release (IR) tablets. IR tianeptine sodium has been available in Europe and many countries in Asia and Latin America for the treatment of MDD for more than three decades since being first marketed in France in 1989. No tianeptine-containing product has been approved by the U.S. Food and Drug Administration (FDA).

"Despite the availability of several classes of MDD treatments in the U.S. that directly modulate neurotransmitters and their synaptic receptors, there remains an unmet need for novel approaches," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "In animal studies, TNX-601 ER has a unique mechanism of action that restores brain neuroplasticity by exerting biological effects on neurons and glial cells that increase arborization of dendrites in critical hippocampal circuits.[2] In animal models, tianeptine also reverses stress-induced impairments in synaptic glutamate neurotransmission, and it restores hippocampal neurogenesis.[2]"

Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals said, "After a decade of development of our proprietary once-daily tianeptine formulation, it is very gratifying to enter the next stage of clinical testing required to make TNX-601 ER available to those suffering from MDD in the U.S.

TNX-601 ER not only has the potential to relieve depressive symptoms, but also to improve the quality of life and resiliency for the millions of MDD sufferers. The short and long-term safety of tianeptine sodium IR has been well-established based on its clinical use outside the US."

Dr. Sullivan added, "The efficacy of tianeptine sodium IR has repeatedly been shown to be comparable with that of either selective serotonin reuptake inhibitor (SSRI) or tricyclic antidepressants[3,4] while being associated with a lower incidence of sexual dysfunction, derangement of sleep architecture, sedation, weight gain, or cognitive impairment.[5-7] Given tianeptine's metabolic pathway, which is independent of the hepatic cytochrome P450 system, we believe that TNX-601 ER has a reduced risk of drug-drug interactions compared to antidepressants marketed in the U.S.[7]

"MDD is a seriously disabling condition that is also often associated with suicidal behavior. Extensive animal studies have taught us that tianeptine restores the stress-induced deficits in neuroplasticity and neurogenesis. The dramatic impact of tianeptine on a brain experiencing many types of stress is best illustrated by the effects it has in restoring dendritic arborization and spine synapse remodeling of pyramidal neurons in the CA3 region of hippocampus, as well as new neuron formation and their microglia-mediated integration into neuronal networks of the hippocampal formation. With an estimated 21 million individuals suffering from a major depressive episode each year in the U.S., it's exciting to move beyond neurotransmitter modulation and begin an era where MDD may be treated by enhancing a resilient biological phenotype of neurons and glial cells under stress."

[1]TNX-601 ER is in the Phase 2 stage of development and is not approved for any indication

[2]McEwen, B. S., et al. *Mol. Psychiatry* **2010**, *15* (3), 237–249.

[3]Jeon, H. J., et al. .*J. Clin. Psychopharmacol.* **2014**, *34* (2), 218–225.

[4]Emsley, R., et al. *J. Clin. Psychiatry* **2018**, *79* (4)

[5]Bonierbale M, et al. *Curr Med Res Opin* **2003**, *19*(2):114-124.

[6]Costa e Silva, J. A., et al. *Neuropsychobiology* **1997**, *35* (1), 24–29.

[7]Wagstaff, A. J. et al. *CNS Drugs* **2001**, *15* (3), 231–259.

About the Phase 2 UPLIFT Study

The Phase 2 UPLIFT study, TNX-TI-M201, is a double-blind, randomized, multicenter, placebo-controlled study to evaluate the efficacy and safety of TNX-601 ER taken by mouth once-daily for 6 weeks **for the treatment of MDD. It is a parallel design study with two arms, a** TNX-601 ER 39.4 mg arm **and a placebo arm. A total of 300 participants will be randomized in a 1:1 ratio into the two arms across approximately 30 U.S. sites, enrolling adult patients 18-65 years old with a DSM-5 diagnosis of depression and a** duration for the current major depressive episode (MDE) of at least 12 weeks. **The primary efficacy endpoint is mean** change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at Week 6. **Key secondary efficacy endpoints include** the Clinical Global Impression of Severity Scale (CGI-S) and the Sheehan Disability Scale (SDS). **An interim analysis is expected to be completed after the first 50% of enrolled patients have completed the study for the purpose of potential sample size re-estimation, currently anticipated in the fourth quarter of 2023. A 24-week open-label extension study, TNX-TI-M202, is planned to receive patients completing the UPLIFT study.**

For more information, see ClinicalTrials.gov Identifier: NCT05686408

About Major Depressive Disorder (Depression)

According to the National Institute of Mental Health, an estimated 21 million adults in the U.S. in 2020 experienced at least one major depressive episode[1], with highest prevalence among individuals aged 18-25 at a rate of 17.0%. 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 behavior. 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] The current FDA approved drugs for long term monotherapy treatment of MDD include selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and Auvelity® (dextromethorphan HBr-bupropion HCl). Dextromethorphan is a direct antagonist of the NMDA-type glutamate receptor.

[1]Data Courtesy of SAMHSA on Past Year Prevalence of Major Depressive Episode Among U.S. Adults (2020). 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 ER

TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a novel oral formulation of tianeptine hemioxalate designed for once-daily daytime dosing in development as a candidate for the treatment for MDD, posttraumatic stress disorder, and neurocognitive dysfunction associated with corticosteroid use. Tianeptine sodium (amorphous) immediate release (dosed 3 times daily) 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 extended-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 salt forms of tianeptine. Tianeptine is believed to work in depression as an indirect modulator of the glutamatergic system, without direct binding NMDA, AMPA or kainate receptors. Tianeptine reverses stress induced increases in AMPA receptor trafficking, restores hippocampal long-term potentiation and neurogenesis, and reverses the negative neuroplastic changes from stress and corticosteroid exposure. In contrast with the modulation of neurotransmitter levels and activity at synaptic receptors like traditional antidepressants, in animal models tianeptine restores dendritic arborization of pyramidal neurons in the CA3 region of hippocampus and in the dentate gyrus region promotes new neuron formation and integration into hippocampal networks.[1] *Tianeptine's enhancement of neuroplasticity in animal models of stress implies a mechanism of action involving indirect glutamatergic modulation, which makes TNX-601 ER's properties distinct from traditional monoaminergic antidepressants in the U.S. and contributes to its potential for clinical indications beyond MDD and stress disorders.* Tianeptine and its MC5 metabolite are also weak mu-opioid receptor (MOR) agonists that present a potential abuse liability if illicitly misused in large quantities (typically abused at 8-80 times the therapeutic dose on a daily basis[2]). In patients who were prescribed tianeptine for depression, the French Transparency Committee found an incidence of misuse of approximately 1 case per 1,000 patients treated[3] suggesting low abuse liability when used at the antidepressant dose in patients prescribed tianeptine for depression. Clinical trials have

shown that cessation of a therapeutic course of tianeptine does not appear to result in dependence or withdrawal symptoms following 6-weeks[4-8], 3-months[9], or 12-months[10] of treatment. The ER formulation of TNX-601 includes several potentially abuse deterrent ingredients include gel forming polymers which impede extraction. In addition, the tablet's hardness makes it difficult to crush, cut or grind to fine particle size, which potentially hinders efforts to misuse by insufflation or intravenous routes. 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 posttraumatic stress disorder (PTSD), and neurocognitive dysfunction associated with corticosteroid use. TNX-601 ER is expected to have patent protection through 2037.

[1]McEwen, B. S., et al. *Mol. Psychiatry* **2010**, *15* (3), 237–249.

[2]Lauhan, R., et al. *Psychosomatics* **2018**, *59* (6), 547–53.

[3]Haute Authorite de Sante; Transparency Committee Opinion. Stablon 12.5 Mg, Coated Tablet, Re- Assessment of Actual Benefit at the Request of the Transparency Committee. December 5, 2012.

[4]Emsley, R., et al. *J. Clin. Psychiatry* **2018**, *79* (4)

[5]Bonierbale M, et al. *Curr Med Res Opin* **2003**, *19*(2):114-124.

[6]Guelfi, J. D., et al. *Neuropsychobiology* **1989**, *22* (1), 41–48.

[7]Invernizzi, G. et al., *Neuropsychobiology* **1994**, *30* (2–3), 85–93.

[8]Lepine, J. P., et al. *Hum. Psychopharmacol.* **2001**, *16* (3), 219–227.

[9]Guelfi, J. D. et al., *Neuropsychobiology* **1992**, *25* (3), 140–148.

[10]Lôo, H. et al., *Br. J. Psychiatry. Suppl.* **1992**, No. 15, 61–65.

About Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix'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 (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with interim data expected in the second quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition, for which a Phase 2 study was initiated in the third quarter of 2022. TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is currently enrolling with interim data expected in the fourth quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets), a once-daily formulation of tianeptine being developed as a treatment for major depressive disorder (MDD), is also currently enrolling with interim data expected in the fourth 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 second quarter of 2023. Tonix's rare disease 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 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 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 quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox, for which a Phase 1 study is expected to be initiated in the second half of 2023. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease portfolio also includes TNX-3900, a class of broad-spectrum small molecule oral antivirals.

*All of Tonix's product candidates are investigational new drugs or biologics and have 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 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, 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.

Contacts

Jessica Morris (corporate)

Tonix Pharmaceuticals

investor.relations@tonixpharma.com

(862) 904-8182

Olipriya Das, Ph.D. (media)

Russo Partners

Olipriya.Das@russopartnersllc.com

(646) 942-5588

Peter Vozzo (investors)

ICR Westwicke

peter.vozzo@westwicke.com

(443) 213-0505