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): October 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 October 16, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced the completion of the clinical phase of the Phase 2 UPLIFT1 study of its TNX-601 ER2 (tianeptine hemioxalate extended-release tablets) product candidate as a potential treatment for 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 this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.01 attached hereto, 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 October 16, 2023, the Company announced the completion of the clinical phase of the Phase 2 UPLIFT1 study of TNX-601 ER2 as a potential treatment for MDD. Topline results from the intention-to-treat sample (N=132) are expected in early November 2023.

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 October 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: October 16, 2023

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

Exhibit 99.01

Tonix Pharmaceuticals Completes Clinical Stage of Phase 2 UPLIFT Study of TNX-601 ER for the Treatment of Major Depressive Disorder

Topline Results Expected Early November 2023

Tianeptine, the Active Ingredient in TNX-601 ER, is Not Associated with Sexual Dysfunction or Weight Gain Which are Treatment-Limiting Side Effects of Many Traditional Antidepressants

Tianeptine Acts by Directly Restoring Neuroplasticity and Neurogenesis and Limiting the Effects of Oxidative Stress in the Brain

CHATHAM, N.J., October 16, 2023 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, today announced the completion of the clinical phase of the Phase 2 potential registration-quality, double-blind, randomized, multicenter, placebo-controlled UPLIFT [1] study of TNX-601 ER[2] (tianeptine hemioxalate extended-release tablets) as a potential treatment for major depressive disorder (MDD). Topline results from the intention-to-treat (ITT) sample (N=132) are expected in early November 2023.

TNX-601 ER is being developed as a monotherapy and first-line treatment for MDD and works by a distinct mechanism of action as compared to traditional monoaminergic antidepressants. Tonix recently reported that tianeptine activates peroxisome proliferator-activated receptors PPAR-β/δ and PPAR-γ. These activities on intracellular molecular targets in neurons and glia in the brain are believed to relate to tianeptine's ability to restore connectivity between neurons that atrophy under conditions of stress, in animal models.[3,4] Tianeptine is the active ingredient of an antidepressant that has been marketed as a three-times-a-day medicine outside the U.S. for more than 30 years. Tonix has developed a novel, patented once-daily oral formulation.

"Because of its unique mechanism, tianeptine avoids some of the treatment-limiting side effects of traditional antidepressants, including sexual dysfunction and weight gain," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Tianeptine restores connectivity between neurons, or neuroplasticity, and limits the effects of oxidative stress in the brain in animal models of depression. In contrast to traditional antidepressants which alter the levels of neurotransmitters in the synapse, tianeptine directly induces mature neurons to sprout new connections and also induces formation of new neurons."

"With the last patient now treated, we look forward to analysis of the results of this registration-quality study, which will help to inform our plans as we discuss next steps with the U.S. Food and Drug Administration (FDA)," said Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. "We would like to thank the participants, their families, and all the investigators and researchers who have been an important part of this journey so far."

1. Clinical Trials.gov I.D. NCT05686408
2. TNX-601 ER is an investigational new drug and is not approved for any indication.
3. McEwen, B. S., et al. *Mol. Psychiatry* **2010**, *15* (3), 237–249
4. Sullivan, GM et al. June 1, 2023. Poster presentation at the American Society of Clinical Psychopharmacology, Miami, FL.https://www.tonixpharma.com/wp-content/uploads/2023/06/ASCP-Poster-2023-A-Randomized-Placebo-Controlled-Multicenter-Trial-of-Monotherapy-with-TNX-601-ER.pdf

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About the Phase 2 UPLIFT Study

The Phase 2 UPLIFT study, TNX-TI-M201, is a potential registration-quality, 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 moderate-to-severe 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 132 participants were randomized in a 1:1 ratio into the two arms across approximately 27 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 (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).

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%. For approximately 2.5 million adults in the U.S., adjunctive therapies are necessary for depression treatment.[2,3] 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.[4]

[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] IMS NSP, NPA, NDTI MAT-24-month data through Aug 2017.

[3] Kubitz N, et al. PLoS One 2013, 8 (10), e76882.

[4] Rush AJ, et al. Am J. Psychiatry 2007, 163 (11), 1905-1917.

About TNX-601 ER

TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a novel oral formulation of tianeptine designed for once-daily daytime dosing in development as a candidate for the treatment of 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 no tianeptine-containing product is approved in the U.S. and no extended-release tianeptine product is 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. 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 is believed to be mediated by activation of PPAR isoforms PPAR-β/δ and PPAR-γ, 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, such as 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, 15, 61–65.

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, LLC 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 late December 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 were reported 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 in the third quarter of 2023, with topline results expected in early November of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, a 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 mu-opioid receptor while maintaining activity and the ability to activate PPAR-β/δ and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development as a preventive treatment in chronic migraine, and enrollment has completed in a Phase 2 proof-of-concept study with topline data expected in early December 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 fourth 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 was 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.

This press release and further information about Tonix can be found atwww.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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