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): December 4, 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 December 4, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that the U.S. Food and Drug Administration ("FDA") cleared the Investigational New Drug ("IND") application to support the clinical development of its TNX-2900 (intranasal potentiated oxytocin) product candidate to treat Prader-Willi syndrome ("PWS") in children and adolescents. A copy of the press release that discusses this matter is filed as Exhibit 99.01 and hereto and incorporated herein by reference.

Data from two poster presentations (the "Presentations") concerning the Company's TNX-4300 (estianeptine) product candidate were presented at the American College of Neuropsychopharmacology 2023 annual meeting.

The Company updated its investor presentation, which is used to conduct meetings with investors, stockholders and analysts and at investor conferences, and which the Company intends to place on its website, which may contain nonpublic information. Copies of the Presentations and the investor presentation are furnished hereto as Exhibits 99.02, 99.03 and 99.04, 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 December 4, 2023, the Company ") announced that the FDA cleared the IND application to support the clinical development of TNX-2900 to treat PWS in children and adolescents. The Phase 2 study approved by the IND is a dose-finding study with approximately nine PWS patients per group across four groups (one placebo group and three groups with different dosage regimens of TNX-2900). The Company intends to seek a partner to advance TNX-2900 for PWS in clinical development.

Separately, combined product sales from the Company's marketed products, Zembrace® SymTouch® and Tosymra®, for the 12 months ended September 30, 2023, were approximately $27 million.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press Release, dated December 4, 2023
99.02	The Enantiomer (R)-Tianeptine, but not (S)-Tianeptine, is an Agonist on the μ-Opioid Receptor and Decreases Immobility in the Murine Forced Swim Test
99.03	Differential Effects of Enantiomers (S)- and (R)-Tianeptine on Neurite Outgrowth and Mitochondrial Activity in Cultured Glutamatergic Neurons
99.04	Corporate Presentation by the Company for November 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: December 4, 2023

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

Exhibit 99.01

Tonix Pharmaceuticals Announces IND Clearance by the FDA for Phase 2 Trial of TNX-2900 for the Treatment of Prader-Willi Syndrome, the Most Common Genetic Cause of Life-Threatening Childhood Obesity

TNX-2900 is a proprietary magnesium-potentiated formulation of intranasal oxytocin, a naturally occurring hormone that reduces appetite and eating

Preclinical data show magnesium-potentiation increases the potency of exogenous oxytocin

Formulations of intranasal oxytocin without magnesium have reported inconsistent results in clinical trials of Prader Willi Syndrome[1,2]

CHATHAM, N.J., December 4, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to support clinical development of TNX-2900 (intranasal potentiated oxytocin), a proprietary magnesium (Mg^{2+})-enhanced formulation of intranasal oxytocin, to treat Prader-Willi syndrome (PWS) in children and adolescents. TNX-2900 for the treatment of PWS was granted Orphan Drug designation by the FDA in 2022.

The Phase 2 study approved by the IND is a dose-finding study involving approximately 36 PWS patients divided into four groups with approximately nine PWS patients per group. One group will receive placebo and three groups will receive different dosage regimens of TNX-2900. Tonix intends to seek a partner to advance TNX-2900 for PWS in clinical development.

“We are pleased that TNX-2900 is cleared for clinical studies for the treatment of PWS in children and adolescents as there remains a significant need for new therapies, particularly for PWS hyperphagia, which currently has no approved treatments,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “PWS is the most common genetic cause of life-threatening childhood obesity.[3,4] We believe adding Mg^{2+} to the formulation has the potential to improve intranasal oxytocin’s therapeutic action.”

The IND application for TNX-2900 was supported by preclinical data demonstrating that Mg^{2+} enhances the potency of oxytocin. Oxytocin is a naturally-occurring hormone that reduces appetite and eating and regulates hunger, anxiety and prosocial behavior. PWS is a genetic disorder associated with abnormalities of the oxytocin system [5]. Several previous clinical studies in PWS of intranasal oxytocin without Mg^{2+}-potentiation have shown trends toward improvement, but the results have been inconsistent.[1,2] Tonix believes that Mg^{2+}-potentiation of intranasal oxytocin in PWS may improve consistency in clinical trials because in animal studies Mg^{2+}-potentiation appears to eliminate the high-dose suppression of oxytocin’s inverted “U”-shaped dose response.[6]

Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals added, “Recent reports show Mg^{2+} is necessary for oxytocin to fully activate the oxytocin receptor.[3,6] Oxytocin has potent effects in adult mice correcting behavioral characteristics of the*Magel2* knock-out mouse model for PWS and autism.[4] Oxytocin has many potential therapeutic roles in reducing appetite, eating, weight, migraine pain and autistic spectrum behaviors. Tonix recently completed enrollment in a Phase 2 study of TNX-1900, a related Mg^{2+}-potentiated intranasal oxytocin candidate, for the prevention of migraine headaches, and is also studying TNX-1900 through external collaborations for the treatment of obesity in adolescents, binge eating disorder, bone health in autism, and social anxiety disorder.”

About Prader-Willi Syndrome (PWS)

PWS is recognized as the most common genetic cause of life-threatening childhood obesity and affects males and females with equal frequency and all races and ethnicities. PWS results from the absence of expression of a group of genes on the paternally acquired chromosome 15. The hallmarks of PWS are lack of suckling in newborns and, in children and adolescents, severe hyperphagia, an overriding physiological drive to eat, leading to severe obesity and other complications associated with significant mortality. A systematic review of the morbidity and mortality as a consequence of hyperphagia in PWS found that the average age of death in PWS was 22.1 years.[7] There is no approved medication to treat poor feeding in newborns or hyperphagia in children and adolescents with PWS. Given these serious or life-threatening manifestations of these conditions, there is a critical need for effective treatments to decrease morbidity and mortality, improve quality of life, and increase life expectancy in people with PWS. Oxytocin has potent effects in adult mice correcting behavioral characteristics of the *Magel2* knock-out mouse model for PWS and autism.[4] In addition, oxytocin has potent effects in correcting behavioral characteristics of the neonatal *Magel2* knock-out mouse model for PWS and autism[8] and intriguing effects in a clinical trial of neonates with PWS.[9]

About TNX-2900 and Tonix’s Potentiated Oxytocin Platform

TNX-2900 is based on Tonix’s patented intranasal potentiated oxytocin formulation intended for use by adults and adolescents. Tonix’s patented potentiated oxytocin formulation is believed to increase specificity for oxytocin receptors relative to vasopressin receptors as well as to enhance the potency of oxytocin. Tonix is also developing a different intranasal formulation, designated TNX-1900, for prophylaxis of chronic migraine as well as for adolescent obesity, binge eating disorder, bone health in autism and social anxiety disorder. Oxytocin is a naturally occurring human hormone that acts as a neurotransmitter in the brain. Oxytocin is believed to be more than 600 million years old and is present in vertebrates including mammals, birds, reptiles, amphibians and fish.[10,11] It was originally approved by the U.S. Food and Drug Administration as Pitocin®*, an intravenous infusion or intramuscular injection drug, for use in pregnant women to induce labor. An intranasal formulation of oxytocin is marketed in some European countries to assist in the production of breast milk as Syntocinon®** (oxytocin nasal 40 units/ml). **Pitocin® is a trademark of Par Pharmaceutical, Inc.*

***Syntocinon® is a trademark of BGP Products Operations GmbH*

Citations

1. Shalma NM, et al. *Diabetes Metab Syndr.* 2023. 17(2):102711.
2. Rice LJ, et al. *Curr Opin Psychiatry.* 2018. 31(2):123-127.
3. Meyerowitz JG, et al. Nat Struct Mol Biol. 2022. 29(3):274-281.
4. Meziane H, et al. Biol Psychiatry. 2015. 78(2):85-94.
5. Correa-da-Silva F, et al. *J Neuroendocrinol.* 2021. 33(7):e12994.
6. Bharadwaj VN, et al. *Pharmaceutics.* 2022. 14(5):1105.
7. Bellis SA, et al. *Eur J Med Genet.* 2022. 65(1):104379.
8. Bertoni A, et al. *Mol Psychiatry.* 2021. 26(12):7582-7595.
9. Tauber M, et al. *Pediatrics.* 2017. 139(2):e20162976.
10. Oxytocin in Wikipedia https://en.wikipedia.org/wiki/Oxytocin (accessed 8-8-23)

11. Gruber CW. *Exp Physiol*. 2014. 99(1):55-61. doi: 10.1113/expphysiol.2013.072561.

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 the clinical phase of a potentially confirmatory Phase 3 study in the fourth 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, and topline results were reported in the third quarter of 2023. 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, including TNX-1800, in development as a vaccine to protect against COVID-19. During the fourth quarter of 2023, TNX-1800 was selected by the U.S. National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID) Project NextGen for inclusion in Phase 1 clinical trials. 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 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; 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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Exhibit 99.02

The Enantiomer *(R)*-Tianeptine, but not *(S)*-Tianeptine, is an Agonist on the μ-Opioid Receptor and Decreases Immobility in the Murine Forced Swim Test

www.tonixpharma.com

Darryl Rideout[1], David T. Hsu[1*], Luciana M. Leo[2], Sam R. J. Hoare[2], Alexis Zajicek[3], Taleen Hanania[3], Siobhan Fogarty[1], Bruce Daugherty[1], Seth Lederman[1], Gregory Sullivan[1]

[1]Tonix Pharmaceuticals Inc, [2]Montana Molecular LLC, [3]PsychoGenics Inc

Introduction

Tianeptine sodium (trade name Stablon®) is an approved antidepressant in Europe, Asia, and Latin America, but is not approved in the US for any indication. Tianeptine's antidepressant efficacy is well established, however its mechanism of action is not completely understood. Tianeptine was discovered to have weak agonist activity at the μ-opioid receptor (MOR) [1] and reduce immobility in the murine forced swim test (FST) [2], an animal model for behavioral "despair."

Tianeptine is a racemic drug composed of a 1:1 mixture of two enantiomers (mirror image isomers):

***(R)*-Tianeptine** ***(S)*-Tianeptine**

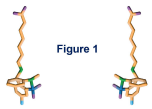

Figure 1

Previous studies have shown that both enantiomers are biologically active and may have differential effects [3,4], however those studies did not report their chiral purity, and did not examine their differential effects on the MOR or in an animal model of depression.

In the present study, we isolated and compared the activity of *(R)*- and *(S)*-tianeptine at the MOR using G-protein coupled receptor signaling *via* cAMP inhibition and β-arrestin recruitment and compared their effects of each on immobility in the FST.

Establishing differential activity of *(R)*- vs. *(S)*-tianeptine at the MOR may serve to elucidate and differentiate tianeptine's unique antidepressant mechanism from its potential abuse liability due to activity at the MOR.

Methods

Drugs

Racemic tianeptine sodium and hemioxalate were obtained from (Chemo Iberica, Madrid, Spain). Racemic tianeptine was separated into *(R)*- and *(S)*-tianeptine using chiral supercritical fluid chromatography (SFC) (X-Chem, Waltham, MA). Chiral purities for *in vitro* assays using *(R)*- and *(S)*-tianeptine are shown in Figs. 2 & 3. [D-Ala[2], NMe-Phe[4], Gly-ol[5]-enkephalin (DAMGO) (Cayman Chemical, Ann Arbor, MI) served as a positive control for the *in vitro* assays. Chiral purities for the behavioral studies were >99.9% enantiomeric excess (e.e.) for *(R)*-tianeptine sodium and >99.9% e.e. for *(S)*-tianeptine sodium. Sertraline (Sigma-Aldrich, St. Louis, MO) served as a positive control in the behavioral study.

MOR assays *in vitro*

MOR activation was assessed with fluorescent biosensors measuring cyclic adenosine 3,5-monophosphate (cAMP) inhibition and β-arrestin recruitment in HEK293T cells. Concentrations of the compounds ranged from 0.001 nM to 31620 nM. Concentration-response curves were generated and EC_{50} values were determined. Detailed information on the protocol for this assay can be obtained from Montana Molecular (https://montanamolecular.com/).

Forced Swim Test

Animals: Male BalbC/J mice (8 weeks of age; Jackson Laboratories, Bar Harbor, ME) were group-housed with chow and water provided *ad libitum* and maintained on a 12h/12h light/dark schedule. Mice were acclimated to the vivarium for 1 week prior to testing. Each mouse was randomly assigned to a treatment group (n = 10 per group) and testing was performed during the light phase. All behavioral studies were conducted at PsychoGenics, Inc. (Paramus, NJ). Protocols were approved by the Institutional Animal Care and Use Committee in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals.

Behavioral Testing: Following i.p. administration of drug, animals were placed in holding cages for 60 min for racemic, *(R)*-, and *(S)*-tianeptine sodium, or 30 min for sertraline, prior to the Forced Swim Test (FST). All drugs were dissolved in saline with a dose volume of 10 ml/kg. Each animal was placed in an opaque cylinder (1000 ml) containing fresh tap water 12 cm deep. Time immobile was recorded over one 6-min session by an observer unaware of treatment conditions. Between groups analysis of variance (ANOVA) was conducted followed by Dunnett's post-hoc test. An effect was considered significant at $P < 0.05$.

Summary & Conclusions

- ***In vitro*, *(R)*-tianeptine showed MOR agonism similar to that observed with racemic tianeptine, whereas *(S)*-tianeptine was devoid of MOR agonist activity.**
- **In the mouse FST, *(R)*-tianeptine significantly reduced immobility similar to that observed with racemic tianeptine, whereas *(S)*-tianeptine did not reduce immobility at any dose tested.**

The results suggest that *(R)*-tianeptine, and not *(S)*-tianeptine, is responsible for the MOR-mediated effects of racemic tianeptine, including reduced immobility in the FST in mice. It has been proposed that tianeptine's antidepressant mechanism is dependent its activity on the MOR [2,5], however the relatively high acute doses required for these effects (10 or 30 mg/kg) can induce hyperlocomotion [2,6], which could explain reduced immobility in the FST. Other MOR agonists, such as morphine, have also been shown to reduce immobility in the FST [7,8]. In addition, there are limitations for the use of i.p. tianeptine in mice as a model for p.o. tianeptine in humans. When administered i.p. in mice, <1% of peak tianeptine remains in plasma 1 hour after peak plasma concentration [2] compared to >70% for p.o. tianeptine in humans [9]. In the mouse, nearly all of the tianeptine was metabolized to MC5 by the time the FST studies began [2], suggesting that these mouse models are testing MC5 rather than tianeptine.

Results

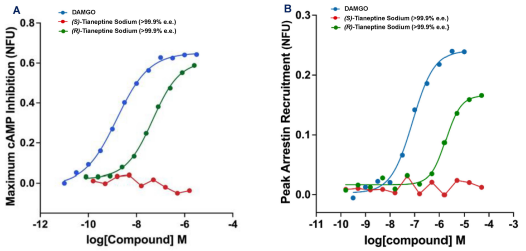

Figure 2. (A) G-protein coupled receptor signaling measured in HEK293T cells *via* cAMP inhibition. **(B)** MOR measured via arrestin recruitment.

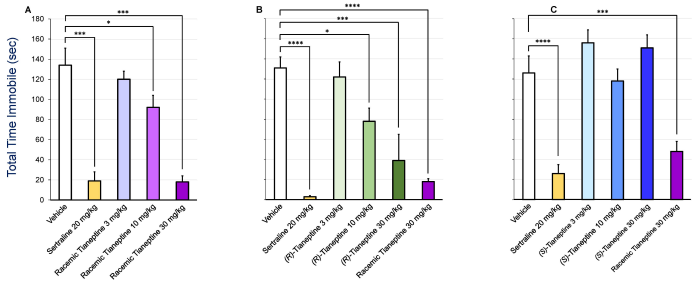

Figure 3. Dose response of **(A)** racemic, **(B)** *(R)*-tianeptine, and **(C)** *(S)*-tianeptine on immobility in the FST. Data are mean + s.e.m. for 10 mice/group. *$P < 0.05$; ***$P < 0.001$; ****$P < 0.0001$

Citations & Disclosures

1. Gassaway et al., 2014. The atypical antidepressant and neuroresilience agent tianeptine is a μ-opioid receptor agonist. *Transl Psychiatry*, 4:e411.
2. Samuels et al., 2017. The behavioral effects of the antidepressant tianeptine require the mu-opioid receptor. *Neuropsychopharmacol*, 42:2052-2063.
3. Gluyzmi et al., 1997. Effects of the (+) and (-) enantiomers of the antidepressant drug tianeptine on 5-HT-induced behavior. *Neuropharmacol*, 36:383–387.
4. Shalekoty et al., 2002. Overcoming the effects of stress on synaptic plasticity in the intact hippocampus: rapid actions of serotonergic and antidepressant agents. *J Neurosci*, 22:3636–3644.
5. Fee et al., 2022. Mu opioid receptors on hippocampal GABAergic interneurons are critical for the antidepressant effects of tianeptine. *Neuropsychopharmacol*, 47:1361–13
6. Allen et al., 2023. Chronic tianeptine induces tolerance in analgesia and hyperlocomotion via mu-opioid receptor activation in mice. *Front Psychiatry*, 14:1166397.
7. Zomkowski et al., 2005. Evidence for the involvement of the opioid system in the agmatine antidepressant-like effect in the forced swimming test. *Neurosci Lett*, 381:279–283.
8. Szumiec et al., 2023. The differential influence of PDYN21, a nonrewarding μ-opioid receptor agonist with Gi protein bias, on behavioural despair and fear response in mice. *Behav Brain Res*, 449:114460.
9. Royer et al., 1999. Tianeptine and its main metabolite pharmacokinetics in chronic alcoholism and cirrhosis. *Clin Pharmacokinet*, 16:186–191.

Disclosures D. Rideout, D.T. Hsu, S. Fogarty, B. Daugherty, S. Lederman, and G. Sullivan are employees of Tonix Pharmaceuticals, Inc., and own stock and/or stock options in the company. L.M. Leo and S.R.J. Hoare are employees of Montana Molecular, LLC. A. Zajicek and T. Hanania are employees of PsychoGenics, Inc.

Presented at American College of Neuropsychopharmacology (ACNP) 62nd Annual Meeting, Tampa, FL December 3-6, 2023; Poster Session 1, Poster M128, Monday, Dec 4th, 5:00 PM-7:00 PM EST

Exhibit 99.03

Differential Effects of Enantiomers *(S)*- and *(R)*-Tianeptine on Neurite Outgrowth and Mitochondrial Activity in Cultured Glutamatergic Neurons

www.tonixpharma.com

Authors^: Herbert Harris, David Hsu*, Bruce Daugherty, Siobhan Fogarty, Darryl Rideout, Sina Bavari, Annabelle Iserson, Seth Lederman, Gregory Sullivan

^Tonix Pharmaceuticals Inc, *Presenter

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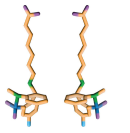
Introduction

- Tianeptine is an antidepressant marketed ex-US for over 30 years (Europe, Asia, Latin America)
- In animal models of stress to the brain, tianeptine has unique neuroprotective and neurorestorative effects, including restoration of neuroplasticity in key learning and memory regions such as hippocampus[1]
- Racemic tianeptine is a 50:50 mixture of *(S)*- and *(R)*-enantiomers
- We have previously reported that the *(S)*-isomer is a PPAR-β/δ agonist, whereas the *(R)*-isomer is a weak μ–opioid receptor agonist; both isomers have agonist activity at PPAR-γ[2]
- Tianeptine's neurorestorative and pro-cognitive effects are potentially explained by its activity on the PPAR system where it acts intracellularly, activating transcription factors
- The presented studies assessed the effects of the *(S)*- and *(R)*-isomers on *in vitro* plastogenic (i.e., connectivity-enhancing) activity in cultured human iPSC-derived glutamatergic neurons and *in vivo* in the rat Novel Object Recognition test



Methods

***In Vitro* Neurite Outgrowth Assay:** iCell Glutaneurons (Fujifilm CDI) were seeded, and on day 5 (D5) in culture, cells were treated with *(R)*- and *(S)*-tianeptine (0.1, 1, and 10 μM each), dexamethasone (0.001, 0.01, 0.1, 1, 10, and 100 μM), and matrixed concentrations of dexamethasone doses *(R)*- and *(S)*-tianeptine doses. Treatments refreshed on D7. On D9, plates treated for 24 hrs with staurosporine (0.02, 0.063, 0.2, and 0.63 μM), an inhibitor of ATP binding to protein kinases, and vincristine (0.2, 2, and 20 μM), a microtubule inhibitor. At 22 hours post-staurosporine and vincristine treatment, plates were treated with FCCP (6.2 and 62 μM), an uncoupler of oxidative phosphorylation, for 2 hrs. MitoTracker CMXRos (Thermo Fisher Scientific) added 45 min prior to end of treatment period; plates fixed at treatment endpoint. Cells stained with Hoechst (Thermo Fisher Scientific [TFS]) and CellMask Green (TFS). Image acquisition performed on Yokogawa CQ1. Image analysis performed using Neuronal Profiling protocol in HCS Studio Cellomics, v6.6.2.

***In Vivo* Novel Object Recognition (NOR) Test:** Adult male Long-Evans rats (275-299 g) assessed for recognition memory in an open-field arena (40 x 40 cm) under dimmed lighting. On Day 1 (D1) & D2, rats allowed to freely explore empty arena for 10-min habituation. On D3, rats (n=16/group) received intraperitoneal injections of saline (vehicle), galantamine (1 mg/kg) as a positive control, racemic, *(S)*- and *(R)*-tianeptine (3, 10, and 30 mg/kg). *(R)*- and *(S)*-tianeptine possessed a chiral purity of >99%. Test compounds administered 30 min prior to testing for saline and galantamine; 60 min prior for racemic, *(S)*- and *(R)*-tianeptine. Rats placed in test arena in presence of two identical objects, each placed facing same direction at same position. Time spent actively exploring objects during a 3-min training session (T1) video recorded. After 48 hrs, rats administered test compounds again and placed in test arena in presence of one familiar and one novel object. Time spent exploring each object recorded for 5 min in testing session (T2). T1 & T2 scored by an observer blind to treatments. Presentation order and object positions (left/right) in T2 randomized to prevent bias from order or place preference. Recognition Index (RI) was primary endpoint, defined as ratio of time spent exploring novel object divided by total time spent exploring both objects [(Novel / (Familiar + Novel)) × 100%] during the 5 min T2. RI value of 50% suggests no memory of familiar object. Data analyzed by one-way ANOVA followed by Dunnett's post hoc. Study approved by IACUC in accordance with National Institute for the Care and Use of Laboratory Animals.

Results

***In Vitro* Plastogenic Activity in Cultured Glutamatergic Neurons:**
***(S)*-Tianeptine Increased Neurite Outgrowth and Mitochondria, and Showed Additive Effects with Dexamethasone (DEX); *(R)*-tianeptine Without Activity on Neurites, Antagonized Trophic Effects of DEX, and Decreased Cell Body Mitochondria**

Morphometric image analysis of glutamatergic neurons cultured for 10 days demonstrated:

- *(S)*-tianeptine significantly increased all metrics of neurite outgrowth including neurite length (see **Fig 1A**), width, area, count, staining intensity and branching (p<0.05 in all cases); and *(S)*-tianeptine significantly increased mitochondrial (Mito) staining in neurite processes (p<0.05; see **Fig 1B**), and produced no changes in cell body Mito staining (data not shown)

Figure 1A

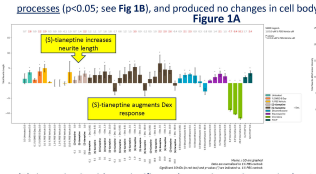
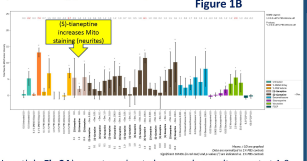


Figure 1B



- *(R)*-tianeptine is without significant changes in neurite metrics (ex. Length in **Fig 2A**) except moderate increase in neurite count at 1.0 μM concentration; and *(R)*-tianeptine without effect on Mito staining in neurite processes, and significantly decreased cell body Mito staining (see **Fig 2B**)

Figure 2A

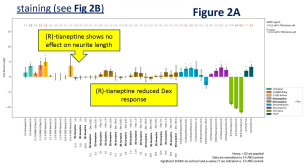
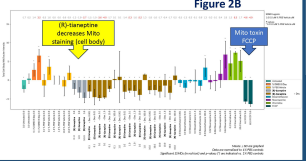


Figure 2B



Results

Dexamethasone effects in cultured glutamatergic neurons and effects of *(S)*- and *(R)*-tianeptine:

- Dexamethasone alone positively affected neurite outgrowth metrics (p<0.05; see **Fig 3B** for neurite length)
- Combined *(S)*-tianeptine and dexamethasone (Dex) results in larger effects on neurite outgrowth (see **Fig 3A**) and mitochondrial staining in neurites (see **Fig 1B**) than with either compound alone
- *(R)*-tianeptine in combination with Dex showed no evidence of additive effects and in fact reduced Dex response (see **Fig 3B**)

Figure 3A

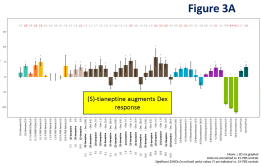
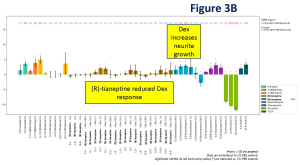


Figure 3B

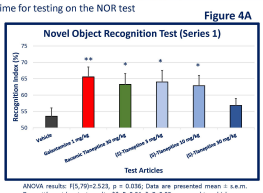


***In Vivo* Plastogenic Activity of *(S)*-Tianeptine on Memory in the Novel Object Recognition Test: a Model Relevant to Neurodegenerative Conditions Including Alzheimer's Disease**

Effects of Racemic Tianeptine, *(S)*-Tianeptine, and *(R)*-Tianeptine on the Rat Novel Object Recognition Test

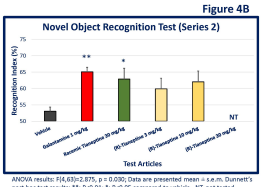
- Racemic tianeptine at 30 mg/kg significantly increased the Recognition Index in NOR test Series 1 (Fig 4A) and Series 2 (Fig 4B) by Dunnett's post hoc test by difference of means of 9.7% (p=0.024) and 9.8% (p=0.042), respectively
- *(S)*-tianeptine at 3 mg/kg and 10 mg/kg significantly increased the Recognition Index by 10.5% (p=0.015) and 9.3% (p=0.030), respectively; whereas 30 mg/kg showed a non-significant increase of 3.3% (Fig 4A)
- *(R)*-tianeptine at 3 and 10 mg/kg showed non-significant increases in Recognition Index of 6.8% and, at trend level, of 9.0% (p=*0.070*), respectively
- *(R)*-tianeptine at 30 mg/kg caused behavioral changes that did not allow testing of the group; within 5 minutes of injection, rats showed over sedation with majority in a catatonic-like state and complete immobility and rigidity; they lost righting reflexes and remained in whatever position placed until the effect wore off; they exhibited no blinking, with eyes wide open for remainder of response; as they did not respond to external stimuli or reflex tests, they could not be tested
- Some rats in *(R)*-tianeptine 10 mg/kg group showed a similar but much more minor adverse response, and they all recovered in time for testing on the NOR test

Figure 4A



ANOVA results: F(5,79)=2.523, p = 0.036; Data are presented mean +\- s.e.m. Dunnett's post hoc test results: **: P<0.01; *: P<0.05 compared to vehicle.

Figure 4B



ANOVA results: F(4,63)=2.875, p = 0.030; Data are presented mean +\- s.e.m. Dunnett's post hoc test results: **: P<0.01; *: P<0.05 compared to vehicle. NT, not tested

Conclusions

- *(S)*-tianeptine significantly stimulates all metrics of neurite outgrowth and mitochondrial staining in an *in vitro* assay of plastogenic effects in cultured human glutamatergic neuron; dexamethasone in this assay system is also stimulatory of neurite outgrowth and has additive or synergistic activity with *(S)*-tianeptine
- *(R)*-tianeptine, previously reported to be the enantiomer of tianeptine with all μ-opioid receptor activity, does not stimulate neurite outgrowth and reduces the stimulatory effects so dexamethasone, suggesting some level of anti-plastogenic activity
- *In vivo* exploration of plastogenic activity of the enantiomers in a test of memory relevant to pathology in Alzheimer's disease, the Novel Object Recognition (NOR) test, indicates *(S)*-tianeptine enhances learning and memory in the lower doses tested, 3 and 10 mg/kg, with a potential inverted-U shaped dose response suggested at 30 mg/kg
- In contrast, *(R)*-tianeptine did not significantly enhance memory on the NOR at 3 mg/kg, although the trend for an increase in the RI at 10 mg/kg may suggest minor activity in this system, possibly due to PPAR-γ effects
- The nature of the toxic effects on behaviors and reflexes at 30 mg/kg of *(R)*-tianeptine are potentially suggestive of an adverse impact resulting from its demonstrated activity on the μ-opioid receptor
- The robust *in vitro* and *in vivo* plastogenic effects of *(S)*-tianeptine suggest potential development of *(S)*-tianeptine as a new chemical entity for the treatment in neurodegenerative conditions such as Alzheimer's disease, Huntington's disease, and traumatic brain injury

Citations & Disclosures

[1] McEwen BS, et al. Mol Psychiatry. 2010 Mar;15(3):237-49.
[2] Sullivan GM, et al. American Society for Clinical Psychopharmacology Annual Meeting, Poster T41 presented 1 June 2023, Miami, FL

^ The authors are all employees of Tonix Pharmaceuticals and own stock and/or stock options in the company.

Presented at American College of Neuropsychopharmacology (ACNP) 62nd Annual Meeting, Tampa, FL December 3-6, 2023; Poster Session 3, Poster #W140, Wednesday, Dec 6th, 5:00 PM-7:00 PM EST

Exhibit 99.04

Cautionary Note on Forward-Looking Statements

Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are "forward-looking statements" as defined by 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" 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; 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. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by Tonix on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. 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 and current 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.

TONIX PHARMACEUTICALS

Who We Are

Tonix is committed to developing and marketing therapeutics to treat pain, neurologic, psychiatric and addiction conditions through our ***central nervous system portfolio*** and within other areas of ***high unmet need***, including immunology, infectious disease, and rare disease

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CNS-Focused Biopharma with Preclinical to Commercial Stage Products

Robust Development Pipeline
Topline data for two late-stage CNS programs expected by end of 2023

Internal Facilities
For R&D and clinical-scale manufacturing

Marketed Products
For the treatment of acute migraine

Strategic Partnerships
With government institutions, world-class academic & research organizations

Pipeline Development Strategy

Focusing on external collaborations with government agencies and academic institutions

- Validates Tonix's scientific expertise and technology
- Reduces internal spend on clinical trials and other R&D costs
- Increases number of trials studying Tonix's product candidates
- Helps to bring innovative therapeutics and vaccines to market faster
- Partnerships include grants, contracts and cost sharing or "in-kind" arrangements

Government partners providing direct funding, cost sharing or in-kind support include:

- National Institutes of Health (NIH)
- National Institute of Allergy and Infectious Disease (NIAID)
- National Institute on Drug Abuse (NIDA)
- Department of Defense (DoD)

Academic partners sponsoring clinical trials of Tonix's investigational drug products include:

- Massachusetts General Hospital (MGH)
- University of Washington
- University of North Carolina

TONIX PHARMACEUTICALS

Key Partnerships

TNX-1500: ALLOGRAFT REJECTION

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

TNX-1900: MIGRAINE & OTHER INDICATIONS

STANFORD UNIVERSITY

UNIVERSITÉ DE GENÈVE

UNIVERSITY of WASHINGTON

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

TNX-102 SL: ACUTE STRESS DISORDER

U.S. Department of Defense

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

TNX-1300: COCAINE INTOXICATION

NIH National Institute on Drug Abuse

COLUMBIA UNIVERSITY

TNX-1800: COVID-19 VACCINE

NIH National Institutes of Health

NIH National Institute of Allergy and Infectious Diseases

TNX-2900: PRADER-WILLI SYNDROME

Inserm transfert

CHU de Toulouse

Aix Marseille université

TONIX PHARMACEUTICALS

Clinical Portfolio: Tonix-Sponsored Programs

Molecule*	Indication	Phase 1	Phase 2	Phase 3	NDA Submission
TNX-102 SL Cyclobenzaprine Protectio® Sublingual Tablets	Fibromyalgia (FM)	*Phase 3 Topline Results Expected 4Q'23 (Late December)*			
TNX-1900 Intranasal Potentiated Oxytocin with Magnesium	Chronic Migraine	*Phase 2 Topline Results Expected 4Q'23 (Early December)*			
TNX-1300 Cocaine Esterase	Cocaine Intoxication	*Phase 2 Study Start Expected 4Q'23*			
TNX-1500 Anti-CD40L mAb	Organ Transplant Rejection and Autoimmune Conditions	*Phase 1 Study Ongoing*			

*All of Tonix's product candidates are investigational new drugs or biologics and none has been approved for any indication.

TONIX PHARMACEUTICALS

Two Marketed Proprietary Migraine Drugs
Non-oral Formulations of Sumatriptan

Zembrace® SymTouch®
(sumatriptan injection) 3 mg[1]

- Each indicated for the ***treatment of acute migraine with or without aura in adults***
- Sumatriptan remains the acute migraine 'gold standard' treatment for many patients and continues to represent the largest segment of the market in terms of unit sales[3]
- Each may provide migraine ***pain relief in as few as 10 minutes*** for some patients[1,2,4,5]
- Patents to 2036 (Zembrace) and 2031 (Tosymra)

Tosymra®
(sumatriptan nasal spray) 10 mg[2]

Acquired from Upsher-Smith Laboratories which has managed care contracts covering ~200 M lives

- Contract includes a transition period during which Tonix expects to secure its own contracts

Combined retail product sales of $27 million for the 12 months ended September 30, 2023[6]

Tonix is prepared to meet potential increased demand for Tosymra following GSK's planned discontinuation of Imitrex® (sumatriptan) nasal spray after January 2024

[1]Zembrace SymTouch [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: February 2021 - For more information, talk to your provider and read the Patient Information and Instructions for Use. – Important Safety Information is provided in the appendix
[2]Tosymra [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: Feb 2021. For more information, talk to your provider and read the Patient Information and Instructions for Use. – Important Safety Information is provided in the appendix
[3]Upsher-Smith Laboratories, LLC; Data On File, 2023
[4]Mathew NT, et al. Dose ranging efficacy and safety of subcutaneous sumatriptan in the acute treatment of migraine. US Sumatriptan Research Group. Arch Neurol. 1992;49(12):1271-1276.
[5]Wendt J, et al. A randomized, double-blind, placebo-controlled trial of the efficacy and tolerability of a 4-mg dose of subcutaneous sumatriptan for the treatment of acute migraine attacks in adults. Clinical Therapeutics. 2005;28(4):517-526.
[6]Symphony Health Solutions data as of November 2023

Zembrace and Tosymra Bypass the GI Tract

Bypassing gastrointestinal (GI) tract is *potential advantage for treating acute migraine*

- GI absorption may be inconsistent in migraineurs due to gastric stasis (also called "gastroparesis")[1-4]
- Nausea and vomiting are symptoms of migraine[5] which can complicate oral treatment

Existing intranasal products

- Imitrex® nasal spray (sumatriptan)
- Migranal® (dihydroergotamine) nasal spray – developed by Novartis, sold by Bausch Health

New intranasal products bringing attention to non-oral route

- Pfizer's Zavzpret® (zavegepant), FDA approved in March, 2023[1] is the first intranasal gepant
- Impel NeuroPharma's Trudhesa® (dihydroergotamine) FDA approved 2021[2]

[1]Pfizer Press Release March 10, 2023. – https://www.pfizer.com/news/press-release/press-release-detail/pfizers-zavzprettm-zavegepant-migraine-nasal-spray
[2]Impel Press Release September 3, 2021 - https://impelpharma.com/2021/09/03/impel-neuropharma-announces-u-s-fda-approval-of-trudhesa-dihydroergotamine-mesylate-nasal-spray-for-the-acute-treatment-of-migraine/

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-1900 for Chronic Migraine

Topline Results Expected – early December

Phase 2 Proof-of-Concept Study

TNX-102 SL for Fibromyalgia

Topline Results Expected – late December

Phase 3 Potential NDA Enabling Study

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TNX-102 SL

Cyclobenzaprine (Protectic®)

A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

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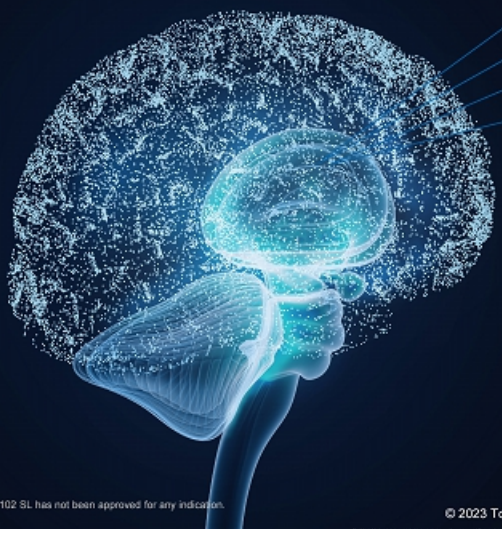
TNX-102 SL: Unique MOA Facilitates Restorative Sleep

Centrally Acting Analgesic

Potent binding and antagonist activities at four key receptors facilitate ***restorative sleep***



- *serotonergic-5-HT2A*
- *adrenergic-α1*
- *histaminergic-H1*
- *muscarinic-M1*

Key Differentiators

Relative to Oral Cyclobenzaprine

- Lower daytime exposure
- Avoids first-pass metabolism
- Reduces risk of pharmacological interference from major metabolite

Relative to Standard of Care

- Potential for better tolerability while maintaining efficacy
- Not scheduled nor with recognized abuse potential

*TNX-102 SL has not been approved for any indication.

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About Fibromyalgia

*Fibromyalgia (FM) is a **chronic pain disorder** resulting from amplified sensory and pain signaling within the CNS. Symptoms include chronic widespread pain, **nonrestorative sleep**, fatigue, and cognitive dysfunction*

6-12 million adults **Fibromyalgia afflicts an estimated 6-12 million adults in the US, predominantly women[1]**

Large unmet need:

- Patients struggle with daily activities, have impaired quality of life, and frequently are disabled
- Physicians and patients report common dissatisfaction with currently marketed products
  - Average patient has 20 physician office visits per year[2]

Current standard of care:

- FDA-approved products include Lyrica, Cymbalta, and Savella
- Fewer than half of those treated for fibromyalgia receive sustained benefit from the approved drugs[3]
  - Majority (60%) fail therapy due to lack of a response (25%) or poor tolerability (35%)[4]
  - Opioid usage is not uncommon

[1]American Chronic Pain Association (www.theacpa.org, 2019)
[2]Robinson et al, Pain Medicine 2013;14:1400
[3]The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[4]Market research by Frost & Sullivan, commissioned by Tonix

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Fibromyalgia Program Status

TNX-102 SL Cyclobenzaprine Protectio® Sublingual Tablets	**Fibromyalgia**	***Phase 3 Topline Results Expected 4Q'23 (Late December)***
	FM-Type Long COVID	*Phase 2 Topline Results Reported 3Q'23*

1) One **positive Phase 3 study (RELIEF) completed**[1]
2) Second Phase 3 study (RALLY) missed primary endpoint
   - Unexpected increase in adverse event-related discontinuations in both drug and placebo arms, potentially due to recruiting during COVID-19
3) Confirmatory Phase 3 study (RESILIENT) **enrollment complete**
   - Clinical stage complete as of November 15, 2023

Next Steps: ***Potentially confirmatory topline results expected 4Q 2023 (Late December)***

*TNX-102 SL has not been approved for any indication.
[1]Lederman et al., (2023) *Arthritis Care & Research* "Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results From the RELIEF Trial", doi: 10.1002/acr.25142. Epub ahead of print. PMID: 37165930.

TNX-102 SL: Phase 3 RESILIENT Study Design

RESILIENT Study

CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia
- U.S. sites only, ***completed enrollment of 457 patients***
- Clinical stage complete as of November 15, 2023
- Preliminary unaudited rate of adverse-event related discontinuations was 4.8%
  - Compares favorably with prior FM studies RELIEF, 6.0% and RALLY, 10.7%

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
  - Weekly averages of the daily numerical rating scale scores
- Threshold for potential NDA-enabling study is $p < 0.05$

Key Secondary Endpoints:

- Patient Global Impression of Change responder analysis
- Fibromyalgia Impact Questionnaire - Revised (FIQ-R) Symptom Domain score
- FIQ-R Function Domain score
- PROMIS Sleep Disturbance instrument
- PROMIS Fatigue instrument
- Weekly average of the daily diary assessment of sleep quality

*Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

ClinicalTrials.gov Identifier: NCT05273749
A Phase 3 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With Fibromyalgia (RESILIENT)

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About Fibromyalgia-Type Long COVID

CNS PORTFOLIO

Long COVID is broadly defined as signs, symptoms, and conditions that continue or develop after acute COVID-19 infection[1]

Many Long-COVID symptoms overlap with core symptoms of fibromyalgia

and are hallmarks of other chronic pain syndromes like myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

19% **Long COVID occurs in approximately 19% of recovered COVID-19 patients**[2]

40% **As many as 40% of Long COVID patients experience multi-site pain**[3,4]

[1]CDC - https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html#:~:text=Some%20people%20who%20have%20been,after%20acute%20COVID%2D19%20infection.
[2]CDC Press Release, June 22, 2022 - https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm
[3]Harris, H, et al. Tonix data on file. 2022
[4]TriNetX Analytics

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TNX-102 SL: Phase 2 PREVAIL Study Design

PREVAIL Study

CNS PORTFOLIO

Study characteristics:

- Randomized, double-blind, placebo-controlled study of TNX-102 SL in fibromyalgia-type Long COVID
- U.S. sites only, ***completed enrollment of 63 patients***

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
  - Weekly averages of the daily numerical rating scale scores

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

*Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

Placebo once-daily at bedtime

ClinicalTrials.gov Identifier: NCT05472090
"A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL in Patients With Multi-Site Pain Associated With Post-Acute Sequelae of SARS-CoV-2 Infection (PREVAIL)"

14 weeks

Next Steps: ***End of Phase 2 Meeting with FDA 1Q 2024***

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TNX-102 SL: Phase 2 PREVAIL Topline Results[1]

CNS PORTFOLIO

Did not meet the primary endpoint of multi-site pain reduction at Week 14

However, findings fulfill the objectives of proof-of-concept study, supporting the decision to advance the program based on a proposed primary endpoint using the PROMIS Fatigue scale

- TNX-102 SL showed robust effect size in improving fatigue and consistent activity across secondary measures of sleep quality, cognitive function, disability and Patient Global Impression of Change (PGIC)
- Was generally well tolerated with an adverse event (AE) profile comparable to prior studies with TNX-102 SL:
  - AE-related discontinuations were similar in drug and placebo arms
  - No new safety signals were observed

Fatigue is the signature symptom of Long COVID and has been identified as the dominant symptom contributing to disability[2]

- We observed numerical improvement in the PROMIS fatigue score (in RELIEF p=0.007 MMRM and in RALLY p=0.007 MMRM) in both prior Phase 3 studies of TNX-102 SL in fibromyalgia,
- We believe the results of PREVAIL, together with extensive data from studies in other chronic conditions[3-5], makes PROMIS Fatigue a solid candidate for the primary endpoint of future Long COVID registrational studies

[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z8FQHQ
[2]Walker S, *et al. BMJ Open* 2023;13:e069217. doi: 10.1136/ bmjopen-2022-069217
[3]Cook, K.F., *et al.* 2016. *Journal of Clinical Epidemiology*, 73, 89- 102
[4]Cella, D., et al. 2016. *Journal of Clinical Epidemiology*, 73, 128–134
[5]Lai, J.S., et al. 2011. *Archives of Physical Medicine and Rehabilitation*, 92(10 Supplement), S20-S27.

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Acute Stress Reaction (ASR)/ Acute Stress Disorder (ASD)

ASR/ASD are acute stress conditions resulting from trauma which can affect both civilian and military populations.

Large unmet need:

- According to National Center for PTSD, about 60% of men and 50% of women in the US are exposed least one traumatic experience in their lives[1]
- In the US alone, one-third of emergency department visits (40-50 million patients per year) are for evaluation after trauma exposures[2]

Current standard of care:

- No medications are currently available at or near the point of care to treat patients suffering from acute traumatic events and support long-term health

[1]National Center for PTSD. How Common is PTSD in Adults? https://www.ptsd.va.gov/understand/common/common_adults.asp
[2]Wisco et al. *J Clin Psychiatry*. 2014;75(12):1338-46

ASR/ASD Program Status

Status: Expect to start Phase 2 in 1Q 2024

Phase 2 Trial Funded by DoD grant to University of North Carolina (UNC)

- UNC Institute for Trauma Recovery awarded a $3M grant from the Department of Defense (DoD)
- OASIS trial will build upon infrastructure developed through the UNC-led, $40M AURORA initiative
  - AURORA study is a major national research initiative to improve the understanding, prevention, and recovery of individuals who have experienced a traumatic event
  - Supported in part by funding from the National Institutes of Health (NIH) and the health care arm of Google's parent company Alphabet
- Opportunity to investigate the correlation between motor vehicle collisions and the emergence of ASD and PTSD
- Supported by multiple clinical trials:
  - Phase 2 trial in military-related PTSD (AtEase or NCT02277704)
  - Phase 3 trial in military-related PTSD (HONOR or NCT03062540)
  - Phase 3 trial in primarily civilian PTSD (RECOVERY or NCT03841773)
- In each of these studies, early and sustained improvements in sleep were associated with TNX-102 SL treatment by the PROMIS sleep disturbance (SD) scale and the Clinician Administered PTSD Scale (CAPS-5) "sleep disturbance" item.

Together these studies provide preliminary evidence that TNX-102 SL is well-tolerated and may promote recovery from PTSD via a pharmacodynamic facilitation of sleep-dependent emotional memory processing

TNX-102 SL: Phase 2 OASIS Study Design

CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Acute Stress Reaction (ASR) / Acute Stress Disorder (ASD)
- The proposed Optimizing Acute Stress reaction Interventions with TNX-102 SL (OASIS) trial will examine the safety and efficacy of TNX-102 SL to reduce adverse posttraumatic neuropsychiatric sequelae among patients presenting to the emergency department after a motor vehicle collision (MVC)
- The trial will enroll approximately 180 individuals who acutely experienced trauma at study sites across the US
- Participants will be randomized in the emergency department to receive a two-week course of either TNX-102 SL or placebo
- Investigator-initiated IND

Objective:

- Investigate the potential of Tonix's TNX-102 SL (cyclobenzaprine HCl sublingual tablets) to reduce the frequency and severity of the adverse effects of traumatic exposure, including acute stress reaction (ASR), acute stress disorder (ASD), and posttraumatic stress disorder (PTSD).
- ASR refers to the body's immediate response to trauma, whereas ASD is the short-term effects of trauma (within 1 month), and PTSD is the long-term effects of trauma (beyond 1 month)

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

Placebo once-daily at bedtime

2 weeks

*First dose of TNX-102 SL 5.6 mg versus placebo taken in the emergency department, and then daily at bedtime to finish 2 weeks of treatment

A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With ASR/ ASD (OASIS)

- Primary outcome measure: Acute Stress Disorder Scale (ASDS) assessed at 7 and 21 days post MVC
- Posttraumatic stress symptom severity assessed at 6 and 12 weeks post MVC using the PTSD Checklist for DSM-5 (PCL-5)
- Standardized survey instruments of sleep disturbances, anxiety and depression symptoms, general physical and mental health, and clinical global improvement also employed
- Detailed and brief neurocognitive assessments are performed from baseline to 12 weeks after MVC at specific timepoints throughout study participation period

TONIX PHARMACEUTICALS

TNX-1900 and TNX-2900

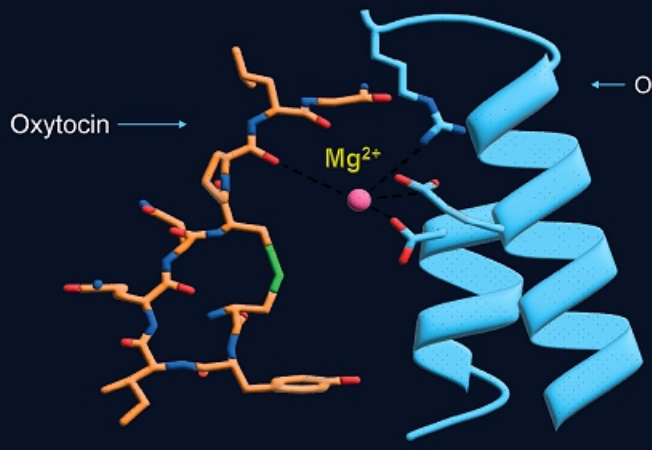
Intranasal Potentiated Oxytocin with Magnesium

A novel, non-CGRP antagonist approach to treatment

TONIX PHARMACEUTICALS

TNX-1900 & TNX-2900: Novel Formulation of Intranasal Oxytocin (OT) Potentiated with Magnesium

*Magnesium is known to **potentiate the binding of OT** to its receptor*[1,2]



Key Differentiators

- Targeted intranasal delivery
  - Low systemic exposure
- Blocks release of CGRP from trigeminal ganglia neurons
  - CGRP is a key peptide in the pathogenesis of migraine

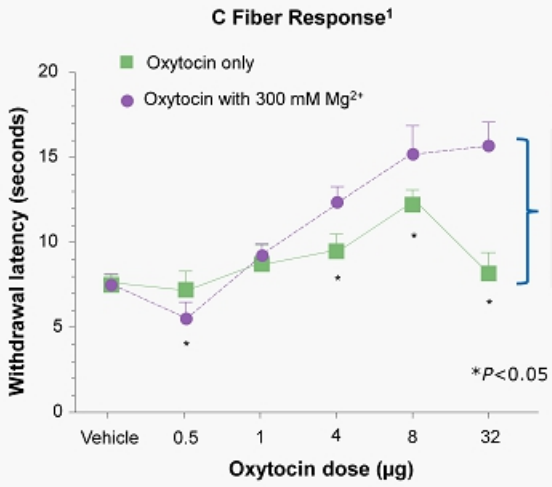
[1]Antoni et al., 1988. *Biochem J.* 257(2):611-4
[2]Meyerowitz et al., 2022. *Nat Struct Mol Biol.* (3):274-281
*TNX-1900 and TNX-2900 have not been approved for any indication.

TONIX PHARMACEUTICALS

Oxytocin Effects – Addressing the "Inverted U" Dose Response

Addition of Mg^{2+} Augments Oxytocin-Induced Analgesia in Animal Model

- A ***nonlinear dose response*** decreases efficacy at higher doses
- Addition of ***Mg^{2+} rescues the efficacy*** of oxytocin at high doses



[1]Adapted from: Bharadwaj VN, et al. *Pharmaceutics.* 2022;14(5):1105.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

About Chronic Migraine

Chronic migraine involves frequent (>15 days per month) or long-lasting episodes of headaches and migraines over the course of at least 3 months. Migraines can occur with or without an aura and are often ***debilitating for patients.***

3-7 *million adults*

Chronic migraine afflicts 3-7 million adults in the US[1]

Current standard of care:

- Anti-CGRP antibodies and Botox® (onabotulinumtoxinA) are specifically approved to prevent headaches in chronic migraine
- Nurtec® (Rimegepant), a gepant, is approved for both prevention of migraine and acute treatment

Large unmet need:

- Anti-CGRP antibodies and oral gepants involve systemic exposure
- Long term safety concerns with prolonged systemic blockade of CGRP receptor[2]

[1]Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[2]Robbins, At Stake: The Possible Long-Term Side Effects of CGRP Antagonists, https://www.practicalpainmanagement.com/pain/headache/stake-possible-long-term-side-effects-cgrp-antagonists, accessed November 8, 2020.

TNX-1900: Phase 2 PREVENTION Study Design

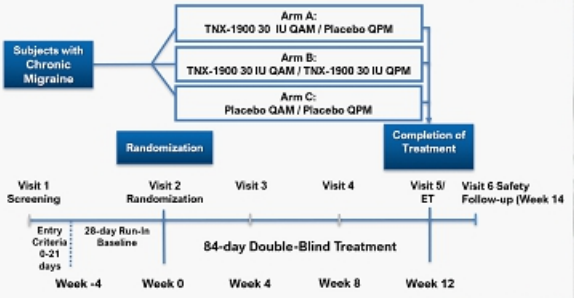
PREVENTION Study

General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms– two treatment regimens and one placebo) in chronic migraine
- U.S. sites only, ***completed enrollment with 88 patients***
- Clinical stage complete as of October 26, 2023

Primary Endpoint:

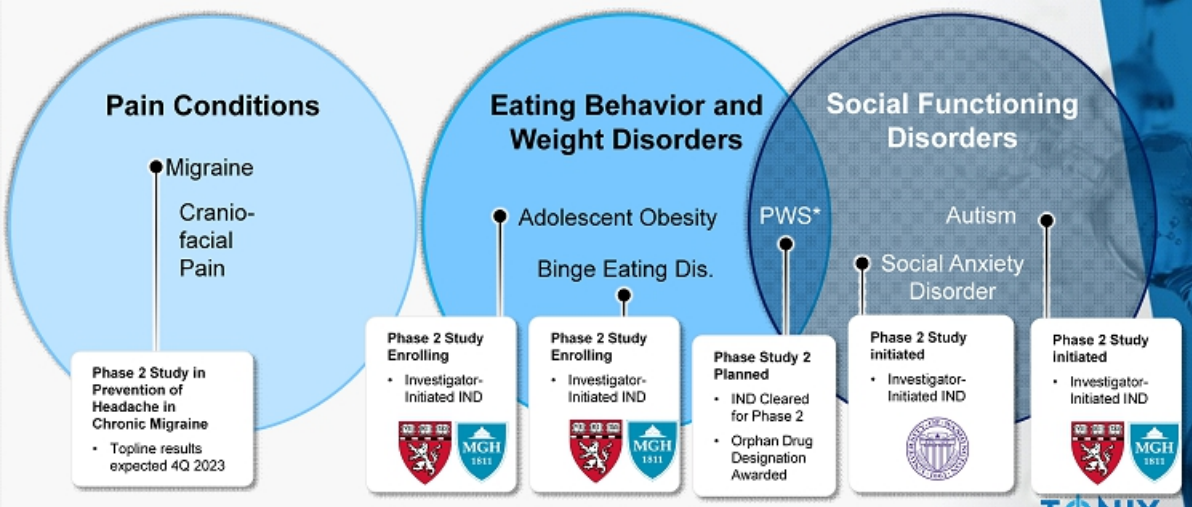
- Mean change in the number of migraine headache days between the 28-day Run-In phase and the last 28-days of the Treatment phase (TNX-1900 vs. placebo)
- Threshold for achieving positive proof-of-concept is Effect Size (ES) > 0.2



ClinicalTrials.gov Identifier: NCT05679908
A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)

Next Steps: ***Topline results expected 4Q 2023 (Early December)***

Potential Applications of TNX-1900 & TNX-2900: Investigator Led Studies



*Prader-Willi Syndrome

TNX-1900 – Studies in Collaboration with Academic Investigators

Pediatric Obesity[1]
- Phase 2 double-blind 'POWER' study testing TNX-1900 as a novel therapeutic agent to induce weight loss and improve indicators of cardiometabolic risk in adolescent patients with obesity
- Massachusetts General Hospital (MGH), Dr. Elizabeth Lawson, P.I.

Social Anxiety[2]
- Study effects of TNX-1900 on social safety learning in social anxiety disorder (SAD)
- Univ. of Washington, Dr. Angela Fang, P.I.

Binge Eating Disorder[3]
- Phase 2 double-blind 'STROBE' study testing TNX-1900 as a novel therapeutic agent to study effects of TNX-1900 on social safety learning
- Massachusetts General Hospital (MGH), Dr. Elizabeth Lawson, P.I.

Pediatric Autism[4]
- Phase 2 double-blind 'BOX' study testing TNX-1900 as a novel therapeutic agent to favorably impact bone formation and strength in children with autism
- Massachusetts General Hospital (MGH), Dr. Elizabeth Lawson, P.I.

[1]Tonix Press Release July 10 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1404/tonix-pharmaceuticals-announces-initiation-of-enrollment-in
[2]Tonix Press Release July 17, 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1405/tonix-pharmaceuticals-announces-agreement-and-initiation-o
[3]Tonix Press Release July 31, 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1410/tonix-pharmaceuticals-announces-enrollment-initiated-in-the
[4]Tonix Press Release November 13, 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1438/tonix-pharmaceuticals-announces-enrollment-initiated-in

TNX-2900 for Prader-Willi Syndrome

*Prader-Willi Syndrome (PWS) is the most common genetic cause of life-threatening childhood obesity. PWS causes unhealthy behaviors around food[1-4], consequences such as **obesity, type 2 diabetes, and cardiovascular disease**[1-5], and creates significant caretaker burden[1-4]*

10-20 *thousand individuals* **Rare genetic disease that afflicts 10-20 thousand individuals in the US**

Current standard of care:
- Human growth hormone treatment is FDA-approved for growth failure in PWS children

Large unmet need:
- Currently no cure, and no treatment for PWS-related hyperphagia
- Consequences can be life threatening - obesity and cardiovascular disease are leading cause of death

TNX-2900 has been granted FDA Orphan Drug Designation and received IND clearance by FDA for Phase 2 Trial

[1]Miller et al., 2011. *Am J Med Genet A.* 155A(5):1040-1049
[2]Butler et al., 2017. *Genet Med.* 19(6):635-642
[3]Butler MG. NORD. Updated 2018. Accessed May 25, 2022. https://rarediseases.org/rare-diseases/prader-willi-syndrome/
[4]Prader-Willi Syndrome Association USA. Accessed May 25, 2022. https://www.pwsausa.org/what-is-prader-willi-syndrome/
[5]Muscogiuri et al., 2021. *J Endocrinol Invest.* 44(10):2057-2070

TNX-1300
Cocaine Esterase

Fast acting antidote for life threatening cocaine intoxication

TNX-1300: Recombinant Protein Rapidly Degrades Cocaine in the Bloodstream

Drops plasma exposure by 90% in 2 minutes

FDA Breakthrough Therapy Designation

Awarded Cooperative Agreement Grant from ***National Institute on Drug Abuse (NIDA)***

Key Differentiators

- Rapidly metabolizes cocaine within matter of minutes
- No other product currently on the market for this indication

*TNX-1300 has not been approved for any indication.

TONIX PHARMACEUTICALS

About Cocaine Intoxication

Over 5 million Americans reported current cocaine use in 2020, which is almost 2% of the population[1]. In 2021, more than 24,900 individuals in the US died from drug overdose deaths involving cocaine[2]

500k **Over 500,000 emergency department visits for cocaine, annually[3,4]**

Current standard of care:

- Patients are currently managed only by supportive care for the adverse effects of cocaine intoxication on the cardiovascular and central nervous systems

Large unmet need:

- No other product currently on the market for this indication
- TNX-1300 could significantly reduce the time and resources required for other detox services
- Potentially reduces the risk of morbidity and mortality

CNS PORTFOLIO

[1]Substance Abuse and Mental Health Services Administration. (2021). Results from the 2020 National Survey on Drug Use and Health: Detailed Tables: Prevalence Estimates, Standard Errors, and Sample Sizes.
[2]Centers for Disease Control and Prevention (CDC) - https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

[3]Substance Mental Health Services Administration, Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.
[4] Drug Abuse Warning Network, 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits. Rockville, MD: Center for Behavioral Health Statistics and Quality, SAMHSA, 2013.

TONIX PHARMACEUTICALS

TNX-1500

Anti-CD40L Monoclonal Antibody

Next Generation mAb preserves efficacy without risk of thrombosis

TNX-1500: Next Generation anti-CD40L mAb

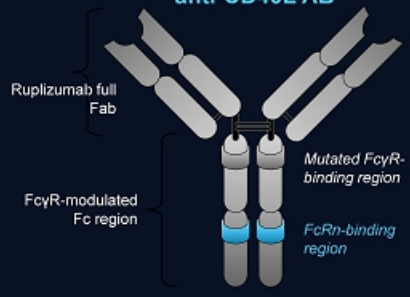
Re-engineered to better modulate the binding of FcγR and mitigate risk of thrombosis

Key Differentiators

Expected to deliver efficacy without compromising safety

- **First Generation:** Development halted due to thromboembolic (TE) complications—blood clots—traced to Fc gamma receptor (FcγR)
- **Second Generation:** Eliminated the FcγR TE complication but potency and half life was reduced, limiting utility
- **Third Generation (TNX-1500):** Re-engineered to better modulate the binding of FcγR.

Selectively Modified anti-CD40L AB



Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function

*TNX-1500 has not been approved for any indication.

TONIX PHARMACEUTICALS

TNX-1500 Strategy and Status

1 Proposed Initial Indication: Prevention of Allograft Rejection

Status: ***Phase 1 currently enrolling***

- Collaborations ongoing with Mass General Hospital on heart and kidney transplantation in non-human primates
- Collaboration with Boston Children's on bone marrow transplantation in non-human primates

Next Steps: Initiate Phase 2 study in Kidney Transplant Recipients

2 Second Indication: Hematopoetic Cell Transplant (Bone Marrow Transplant)

- Potential to reduce GvHD

3 Third Indication (and beyond): Autoimmune Diseases (e.g., Multiple Sclerosis, Sjögen's Syndrome, Systemic Lupus Erythematosus)

- These indications require large studies, but represent large target markets

Currently exploring strategic partnerships and out-licensing opportunities

IMMUNOLOGY PORTFOLIO

TONIX PHARMACEUTICALS

TNX-1500 Preclinical Data and Publications

Non-human Primate Kidney Allo-Transplantation

- TNX-1500 monotherapy consistently prevents kidney transplant rejection with no thrombosis observed
- April 2023 Publication: Lassiter, G., et al. (2023). TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Renal Allograft Survival. *American Journal of Transplantation*. www.sciencedirect.com/science/article/pii/S1600613523003714

Non-human Primate Heart Heterotopic Allo-Transplantation

- TNX-1500 monotherapy consistently prevents heart transplant rejection. Similar activity to chimeric hu5c8[2] during treatment phase in prior studies
- April 2023 Publication: Miura, S., et al. (2023) TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Cardiac Allograft Survival. *American Journal of Transplantation*. www.sciencedirect.com/science/article/pii/S1600613523003969

Non-Human Primate Kidney Xenograft Transplantation

- TNX-1500 therapy is part of a regiment to prevent rejection in kidney xenograft transplants
  - Anand, R.P., Layer, J.V., Heja, D. et al. (2023). Design and testing of a humanized porcine donor for xenotransplantation. *Nature*. https://www.nature.com/articles/s41586-023-06594-4
  - Kozlov, M. (2023). Monkey survives two years after gene-edited pig-kidney transplant. *Nature*. https://www.nature.com/articles/d41586-023-03176-2
  - Mohiuddin, M. (2023). Pig-to-primate organ transplants require genetic modifications of donor. *Nature*. https://www.nature.com/articles/d41586-023-02817-w

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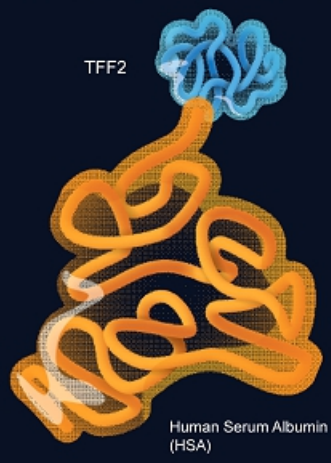
TNX-1700

Recombinant Trefoil Factor Family Member 2 (rTFF2-HSA) Fusion Protein

Targeting the toxic tumor micro-environment

TNX-1700: Fighting Cancer by Targeting the Tumor Micro-Environment

Suppresses myeloid-derived suppressor cells (MDSCs) and activates anti-cancer CD8+ T cells



Key Differentiators

- Different MOA than checkpoint inhibitors
- ***Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies***

Preclinical Evidence

- mTNX-1700 (mTFF2-MSA fusion protein) and anti-PD-1 monotherapy each was able to evoke anti-tumor immunity in the MC38 model of colorectal cancer[1]
- mTNX-1700 augmented the anti-tumor efficacy of anti-PD-1 therapy in both the MC38 and the CT26.wt models[1]

*TNX-1700 is in the pre-IND stage of development and has not been approved for any indication.
[1]Daugherty, B. et al. March 6, 2023 Keystone Poster. https://bit.ly/48nIRHM

TONIX PHARMACEUTICALS

About Gastric and Colorectal Cancer

Gastric and colorectal cancer are both leading cancers in the US. Colorectal cancer is the 3rd leading cause of cancer-related deaths in both men and women.[1]

>1.3M People living with colorectal cancer in the US[2]

>125k People living with gastric cancer in the US[3]

Current standard of care:

- PD-1 blockade
  - However, gastric and colorectal cancer are relatively unresponsive

Large unmet need:

- Gastric and colorectal cancer have a relative 5-year survival rate of 35.7% and 65%, respectively
  - Despite advances in the field, patients are still in need of life saving treatment

IMMUNOLOGY PORTFOLIO

[1]American Cancer Society, accessed September 2023 - https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html
[2]NIH, accessed September 2023 - https://seer.cancer.gov/statfacts/html/colorect.html
[3]NIH, accessed September 2023 - https://seer.cancer.gov/statfacts/html/stomach.html

TONIX PHARMACEUTICALS

Internal Development & Manufacturing Capabilities

R&D Center (RDC): Frederick, MD

- Research advancing CNS and immunology drugs
- Accelerated development of vaccines and antiviral drugs against infectious diseases
- ~48,000 square feet, BSL-2 with some areas designated BSL-3

Advanced Development Center (ADC): North Dartmouth, MA

- Development and clinical scale manufacturing of biologics
- ~45,000 square feet, BSL-2

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Broad-Spectrum Antiviral Discovery Programs

INFECTIOUS DISEASE PORTFOLIO

Host-directed antiviral discovery programs

CD45 targeted therapeutics

- Small molecule therapeutics that reduce endogenous levels of CD45, a protein tyrosine phosphatase
- Reduction in CD45 protects against many viruses including the Ebola virus

Cathepsin inhibitors

- Small molecule therapeutics that inhibit ***essential cathepsins*** which are required by viruses such as coronaviruses and filoviruses to infect cells
- Activity as monotherapy and in combination with other antivirals

Virus-directed antivirals discovery program

Viral glycan-targeted engineered biologics

- Bind to viral densely branched high-mannose (DBH) glycans
- ***Neutralize circulating virus*** and stop the entry of the progeny virus into cells
- Antiviral activity against a broad range of RNA viruses
- Activity as monotherapy and in combination with other antivirals

TONIX PHARMACEUTICALS

TNX-801

Live Virus Vaccine

Live virus vaccine platform with multitude of potential applications

TONIX PHARMACEUTICALS

TNX-801: Recombinant Pox Vaccine (RPV) Platform Using Live Virus Technology

Cloned version of horsepox[1] purified from cell culture

TNX-801*
scHPXV (Horsepox)
212,811 bp

Vaccinia → Horsepox

ANTIGEN CODING

- Mpox and Smallpox
- COVID-19
- Future Pandemics & New Infectious Diseases
- Biodefense
- Oncology

Key Differentiators

Live virus vaccines are the most established vaccine technology

- Prevents forward transmission
- Effective in eliciting durable or long-term immunity

Economical to manufacture at scale

- Low dose because replication amplifies dose *in vivo*
- Single administration

Standard refrigeration for shipping and storage

*TNX-801 is in the pre-IND stage of development and has not been approved for any indication.
[1]Noyce et al., 2018. *PLoS One*. 13(1):e0188453.

TONIX PHARMACEUTICALS

TNX-1800: Designed to Express the SARs-CoV-2 Spike Protein

TNX-1800 (recombinant horsepox virus) is a live virus vaccine based on Tonix's TNX-801 that is designed to express the spike protein of the SARS-CoV-2 virus and to elicit a predominant T cell response

- Immunogenic and well tolerated[1]
- Showed promise in protecting animals from challenge with SARS-CoV-2 delivered directly into the lungs[1]

Status: ***National Institute of Allergy and Infectious Diseases (NIAID) will conduct a Phase 1 clinical trial with TNX-1800***

- Expected to start in 2H 2024
- First vaccine candidate using Tonix's live virus recombinant pox virus (RPV) platform technology to enter clinical trials
- "Project NextGen" is an initiative by the U.S. Department of Health and Human Services (HHS) to advance a pipeline of new, innovative vaccines and therapeutics for COVID-19. NIAID will be conducting clinical trials to evaluate several early-stage vaccine candidates, including TNX-1800
- Phase 1 study is designed to assess safety and immunogenicity in approximately 60 healthy adult volunteers
- Upon completion of the trial, NIAID and Tonix will assess the results and determine the next steps for the development of TNX-1800

INFECTIOUS DISEASE PORTFOLIO

[1]Awasthi, M. et al. *Viruses*. 2023. 15(10):2131.
[2]Awasthi, M. et al. *BioRxiv*. 2023.

TONIX PHARMACEUTICALS

Management Team

Seth Lederman, MD
Co-Founder, CEO & Chairman

TARGENT · Fusilev (levoleucovorin) for injection · vela

Gregory Sullivan, MD
Chief Medical Officer

Columbia University Department of Psychiatry · New York State Psychiatric Institute

Bradley Saenger, CPA
Chief Financial Officer

Shire · VERTEX · Steward · pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank · svb SiliconValley Bank · American Capital

Summary of Upcoming Milestones

Clinical Trial Initiations

- **Phase 2 study of TNX-1300 for the treatment of cocaine intoxication – expected 4Q 2023**
- **Phase 1 study of TNX-1800 with NIAID – expected 2H 2024**

4th Quarter 2023 Data Readouts

- **Phase 2 PREVENTION study of TNX-1900 for chronic migraine – topline early December 2023**
  - Affects approximately 3-7 M adults in the U.S[1]
- **Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia – topline late December 2023**
  - Affects approximately 6-12 M adults in the U.S[2]

[1]Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalalgia, 2010, 30:599-609
[2]American Chronic Pain Association (www.theacpa.org, 2019)

TONIX PHARMACEUTICALS

Zembrace® Important Safety Information (1 of 2)

Zembrace SymTouch (Zembrace) can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop use and get emergency help if you have any signs of a heart attack:

- Discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back; severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw; pain or discomfort in your arms, back, neck, jaw or stomach; shortness of breath with or without chest discomfort; breaking out in a cold sweat; nausea or vomiting; feeling lightheaded

Zembrace is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam shows no problem.

Do not use Zembrace if you have:

- History of heart problems; narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease); uncontrolled high blood pressure; hemiplegic or basilar migraines. If you are not sure if you have these, ask your provider.
- Had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation; severe liver problems; taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, dihydroergotamine; are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- An allergy to sumatriptan or any of the components of Zembrace

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Zembrace can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

Zembrace® Important Safety Information (2 of 2)

Zembrace may cause serious side effects including:

- Changes in color or sensation in your fingers and toes; sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever; cramping and pain in your legs or hips; feeling of heaviness or tightness in your leg muscles; burning or aching pain in your feet or toes while resting; numbness, tingling, or weakness in your legs; cold feeling or color changes in one or both legs or feet; increased blood pressure including a sudden severe increase even if you have no history of high blood pressure; medication overuse headaches from using migraine medicine for 10 or more days each month. If your headaches get worse, call your provider.
- Serotonin syndrome, a rare but serious problem that can happen in people using Zembrace, especially when used with anti-depressant medicines called SSRIs or SNRIs. Call your provider right away if you have: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- Hives (itchy bumps); swelling of your tongue, mouth, or throat
- Seizures even in people who have never had seizures before

The most common side effects of Zembrace include: pain and redness at injection site; tingling or numbness in your fingers or toes; dizziness; warm, hot, burning feeling to your face (flushing); discomfort or stiffness in your neck; feeling weak, drowsy, or tired.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Zembrace. For more information, ask your provider.

This is the most important information to know about Zembrace but is not comprehensive. For more information, talk to your provider and read the Patient Information and Instructions for Use. You can also visit www.upsher-smith.com or call 1-888-650-3789. For full Prescribing Information, visit: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6e5b104f-2b9e-416e-92fb-ef1bdaea867d

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Zembrace is a prescription medicine used to treat acute migraine headaches with or without aura in adults who have been diagnosed with migraine.

Zembrace is not used to prevent migraines. It is not known if it is safe and effective in children under 18 years of age.

Tosymra® Important Safety Information (1 of 2)

Tosymra® can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop Tosymra and get emergency medical help if you have any signs of heart attack:

- Discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back; severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw; pain or discomfort in your arms, back, neck, jaw, or stomach; shortness of breath with or without chest discomfort; breaking out in a cold sweat; nausea or vomiting; feeling lightheaded

Tosymra is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam is done and shows no problem.

Do not use Tosymra if you have:

- History of heart problems; narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease); uncontrolled high blood pressure; severe liver problems; hemiplegic or basilar migraines. If you are not sure if you have these, ask your healthcare provider.
- Had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation; taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, or dihydroergotamine. Ask your provider if you are not sure if your medicine is listed above
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure
- An allergy to sumatriptan or any ingredient in Tosymra

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements. Tosymra can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

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Tosymra® Important Safety Information (2 of 2)

Tosymra may cause serious side effects including:

- Changes in color or sensation in your fingers and toes; sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever; cramping and pain in your legs or hips, feeling of heaviness or tightness in your leg muscles, burning or aching pain in your feet or toes while resting, numbness, tingling, or weakness in your legs, cold feeling or color changes in one or both legs or feet; increased blood pressure including a sudden severe increase even if you have no history of high blood pressure; medication overuse headaches from using migraine medicine for 10 or more days each month. **If your headaches get worse, call your provider**.
- Serotonin syndrome, a rare but serious problem that can happen in people using Tosymra, especially when used with anti-depressant medicines called SSRIs or SNRIs. **Call your provider right away if you have**: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- Seizures even in people who have never had seizures before

The most common side effects of Tosymra include: tingling, dizziness, feeling warm or hot, burning feeling, feeling of heaviness, feeling of pressure, flushing, feeling of tightness, numbness, application site (nasal) reactions, abnormal taste, and throat irritation.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Tosymra. For more information, ask your provider.

This is the most important information to know about Tosymra but is not comprehensive. For more information, talk to your provider and read the Patient Information and Instructions for Use. You can also visit www.upsher-smith.com or call 1-888-650-3789. For full Prescribing Information, visit: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=015a5cf9-f246-48bc-b91e-cd730a53d8aa

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Tosymra is a prescription medicine used to treat acute migraine headaches with or without aura in adults.

Tosymra is not used to treat other types of headaches such as hemiplegic or basilar migraines or cluster headaches.

Tosymra is not used to prevent migraines. It is not known if Tosymra is safe and effective in children under 18 years of age.

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