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): August 29, 2024

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 August 29, 2024, the Company presented clinical data on acute stress reaction and prevention of post-traumatic stress disorder ("PTSD") data of its TNX-102 SL product candidate in two poster presentations, and presented preclinical data demonstrating automated high-throughput assay enabling screening for therapeutics to accelerate wound healing in a third poster presentation, at the 2024 Military Health System Research Symposium held August 26, 2024 to August 29, 2024 ("MHSRS"). A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference. Copies of the posters 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 Exhibits 99.01, 99.02, 99.03 and 99.04 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 August 29, 2024, the Company presented clinical data on acute stress reaction and prevention of PTSD data of TNX-102 SL in two poster presentations titled "Two Clinical Trials of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) in Military-Related Posttraumatic Stress Disorder (PTSD) Provide Rationale to Study TNX-102 SL in the Aftermath of Trauma to Reduce Acute Stress Disorder (ASD) and Prevent PTSD" and "Development of the AURORA Platform Trial Network to Test Interventions to Reduce Acute Stress Reaction Symptoms, and Illustration of Use Testing Sublingual Cyclobenzaprine TNX-102 SL, at the MHSRS. the company also presented preclinical data demonstrating automated high-throughput assay enabling screening for therapeutics to accelerate wound healing in a third poster presentation entitled "Integrating Automated High-Throughput Scratch Assay and Cell Painting for Comprehensive Analysis of Cell Migration and Wound Healing".

The third poster, titled "*Integrating Automated High-Throughput Scratch Assay and Cell Painting for Comprehensive Analysis of Cell Migration and Wound Healing*", demonstrated optimization of a highly efficient scratch-wound assay development method. The scratch-wound assay, commonly used to study wound healing, has limitations that the study addresses by introducing an automated miniaturized high-throughput wound healing assay, enabling mass screening and identification of novel therapies for wound-healing. The screening technology was merged with cell-painting to allow discovery of morphological characteristics to identify mechanism of action of drugs for wound healing.

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, August 29, 2024
99.02	Two Clinical Trials of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) in Military-Related Posttraumatic Stress Disorder (PTSD) Provide Rationale to Study TNX-102 SL in the Aftermath of Trauma to Reduce Acute Stress Disorder (ASD) and Prevent PTSD
99.03	Development of the AURORA Platform Trial Network to Test Interventions to Reduce Acute Stress Reaction Symptoms, and Illustration of Use Testing Sublingual Cyclobenzaprine TNX-102 SL
99.04	Integrating Automated High-Throughput Scratch Assay and Cell Painting for Comprehensive Analysis of Cell Migration and Wound Healing
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: August 29, 2024

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

Exhibit 99.01

Tonix Pharmaceuticals Presented Data from Two Posters on TNX-102 SL for Reduction of Acute Stress Reaction and Prevention of PTSD and One Poster for Wound Healing at the 2024 Military Health System Research Symposium (MHSRS)

Investigator-initiated Phase 2 trial to evaluate TNX-102 SL's potential to reduce severity of acute stress reaction (ASR) and frequency of acute stress disorder (ASD) and posttraumatic stress disorder (PTSD) expected to begin third quarter 2024

Currently, no medication approved at or near point-of-care to treat patients suffering from traumatic events and support their long-term health

CHATHAM, N.J., August 29, 2024 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, presented clinical data on? acute stress reaction and prevention of PTSD data of TNX-102 SL in two poster presentations and presented preclinical data demonstrating automated high-throughput assay enabling screening for therapeutics to accelerate wound healing in a third poster presentation at the 2024 Military Health System Research Symposium (MHSRS), held August 26-29, 2024, in Kissimmee, Fla. Copies of the Company's posters, titled:

"*Two Clinical Trials of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) in Military-Related Posttraumatic Stress Disorder (PTSD) Provide Rationale to Study TNX-102 SL in the Aftermath of Trauma to Reduce Acute Stress Disorder (ASD) and Prevent PTSD*";

"*Development of the AURORA Platform Trial Network to Test Interventions to Reduce Acute Stress Reaction Symptoms, and Illustration of Use Testing Sublingual Cyclobenzaprine TNX-102 SL*";

"*Integrating Automated High-Throughput Scratch Assay and Cell Painting for Comprehensive Analysis of Cell Migration and Wound Healing"* , are available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

TNX-102 SL is being evaluated for the reduction in severity of acute stress reaction (ASR) and the frequency of acute stress disorder (ASD) and posttraumatic stress disorder (PTSD) when administered within 24 hours of trauma event. In two double-blind, randomized clinical trials of military-related PTSD, TNX-102 SL showed effects on sleep and PTSD symptoms in two and four weeks of treatment[1]. Supportive data on the effects of TNX-102 SL on reducing PTSD symptoms suggest early intervention immediately after trauma using TNX-102 SL has the potential to reduce ASR/ASD symptoms which are similar to those of PTSD[2,3]. TNX-102 SL has been well-tolerated with no recognized liability for tolerance or abuse. Data from these trials support testing of TNX-102 SL within 24 hours of index trauma for effects on acute stress reaction (ASR) symptoms and the incidence of PTSD. In the U.S. Department of Defense-funded Optimizing Acute Stress Reaction Interventions (OASIS) trial conducted by the University of North Carolina under an investigator-initiated investigational new drug (IND) application, 14 days of bedtime TNX-102 SL will be dosed and tested in the immediate aftermath of motor vehicle collision. The study will test the potential for TNX-102 SL to target trauma-related sleep disturbance and its ability to facilitate recovery from ASR and to prevent PTSD. The results may ultimately provide military personnel with a new treatment option that, when administered in the early aftermath of a traumatic event to individuals with ASR symptoms, improves warfighter function.

"In previous trials, TNX-102 SL has been shown to improve sleep quality in PTSD and increased activity on sleep and stress-related symptoms in the first several weeks of treatment after a trauma event", said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Since sleep disturbance plays a critical role in the development and maintenance of PTSD, sleep improvements may reorient the trajectory of posttraumatic pathology from acute trauma towards early recovery. The OASIS study is driven by the observation that the symptoms of ASR and PTSD are similar and by the hypothesis that TNX-102 SL's effect on sleep quality may reduce ASR symptoms, potentially providing military personnel, veterans, and civilians with a new treatment option that, when administered in the early aftermath of a traumatic event, improves recovery, job performance, and quality of life."

The investigator-initiated 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 (ED) after a motor vehicle collision. The trial plans to enroll approximately 180 trauma survivors at ED study sites around the U.S. Participants will be randomized in the ED to receive a two-week course of either TNX-102 SL 5.6 mg or placebo. The first participant for the OASIS trial is expected to enroll in the third quarter of 2024.

The OASIS trial will build upon a foundation of knowledge and infrastructure developed through the UNC-led, $40 million AURORA initiative. AURORA is a major national research initiative to improve the understanding, prevention and recovery of individuals who experience a traumatic event. AURORA is supported by funding from the National Institutes of Health (NIH), leading brain health nonprofit One Mind, private foundations, and partnerships with leading tech companies, such as Mindstrong Health and Verily Life Sciences, the healthcare arm of Alphabet, the parent company of Google.

Acute and chronic stress disorders can affect both civilian and military populations. According to the National Center for PTSD, in the U.S. about 60% of men and 50% of women experience at least one trauma in their lives.[4] In the U.S. alone, one-third of ED visits (40-50 million patients per year) involve evaluation after trauma exposures, and in a 2014 study involving 3,157 US veterans, 87% reported exposure to at least one potentially traumatic event during their service.[5] Moreover, as many as 500,000 U.S. troops who served in wars between 2001 and 2015 were diagnosed with PTSD. [6]

The third poster, titled "*Integrating Automated High-Throughput Scratch Assay and Cell Painting for Comprehensive Analysis of Cell Migration and Wound Healing*", demonstrated optimization of a highly efficient scratch-wound assay development method. The scratch-wound assay, commonly used to study wound healing, has limitations that the study addresses by introducing an automated miniaturized high-throughput wound healing assay, enabling mass screening and identification of novel therapies for wound-healing. The screening technology was merged with cell-painting to allow discovery of morphological characteristics to identify mechanism of action of drugs for wound healing.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix recently announced the U.S. Department of Defense (DoD), Defense Threat Reduction Agency (DTRA) awarded it a contract for up to $34 million over five years in an Other Transaction Agreement (OTA) to develop TNX-4200 small molecule broad-spectrum antiviral agents targeting CD45 for the prevention or treatment of infections to improve the medical readiness of military personnel in biological threat environments. Tonix owns and operates a state-of-the art infectious disease research facility in Frederick, MD. The company's Good Manufacutring Practice (GMP)-capable advanced manufacturing facility in Dartmouth, MA was purpose-built to manufacture TNX-801 and the GMP suites are ready to be reactivated in case of a national or international emergency. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for TNX-102 SL, a product candidate for which two statistically significant Phase 3 studies have been completed for the management of fibromyalgia. The FDA has granted Fast Track designation to TNX-102 SL for the management of fibromyalgia. TNX-102 SL is also being

developed to treat acute stress reaction. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic designed to treat cocaine intoxication that has Breakthrough Therapy designation. Tonix's immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

*Tonix's product development candidates are investigational new drugs or biologics and have not been approved for any indication.

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. All other marks are property of their respective owners.

This press release and further information about Tonix can be found at www.tonixpharma.com.

1. *TNX-102 SL (cyclobenzaprine HCl sublingual tablets) has not been approved for any indication; (Tonmya™ is conditionally approved by FDA for the management of fibromyalgia)*
2. *Sullivan GM, et al. Randomized clinical trial of bedtime sublingual cyclobenzaprine (TNX-102 SL) in military-related PTSD and the role of sleep quality in treatment response. Psychiatry Res. 2021 Jul;301:113974.*
3. *Parmenter ME, et al. A phase 3, randomized, placebo-controlled, trial to evaluate the efficacy and safety of bedtime sublingual cyclobenzaprine (TNX-102 SL) in military-related posttraumatic stress disorder. Psychiatry Res. 2024 (In Press). https://doi.org/10.1016/j.psychres.2024.115764*
4. *Goldstein RB, et al. Soc Psychiatry Psychiatr Epidemiol. 2016. 51(8):1137-48*
5. *Wisco BE, et al. J Clin Psychiatry. 2014. 75(12):1338-46*
6. *Thompson M. Time. 2015;185(12):40-3*

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, 2023, as filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, 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.

Investor Contact

Jessica Morris
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(862) 904-8182

Peter Vozzo
ICR Westwicke
peter.vozzo@westwicke.com
(443) 213-0505

Media Contact

Ray Jordan
Putnam Insights
ray@putnaminsights.com
(949) 245-5432

Exhibit 99.02

Two Clinical Trials of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) in Military-Related Posttraumatic Stress Disorder (PTSD) Provide Rationale to Study TNX-102 SL in the Aftermath of Trauma to Reduce Acute Stress Disorder (ASD) and Prevent PTSD

Megan Parmenter[1], Seth Lederman[2], Jean Engels[2], Gregory M. Sullivan[2]

[1]Massachusetts General Hospital, Home Base Program, Charlestown, MA; [2]Tonix Pharmaceuticals, Inc., Chatham, NJ

Introduction

There is an urgent need for interventions to reduce rates of acute stress disorder (ASD) and posttraumatic stress disorder (PTSD) in the immediate aftermath of trauma (Astill Wright et al., 2019). Poor sleep is a symptom of ASD and PTSD, as well as a potential treatment target (Socci et al., 2020; RR739 2015). In two double-blind, randomized clinical trials of military-related PTSD, TNX-102 SL (TNX, cyclobenzaprine HCl sublingual tablets), a tricyclic with 5-HT2A, α1-adrenergic, H1, and M1 receptor activity, showed effects on sleep and PTSD symptoms after two and four weeks of therapy. Data from these trials support testing of a two-week course of TNX beginning within 24 hours of index trauma for effects on acute stress reaction (ASR) symptoms and incidence of PTSD. TNX is well-tolerated with no recognized liability for tolerance or abuse.

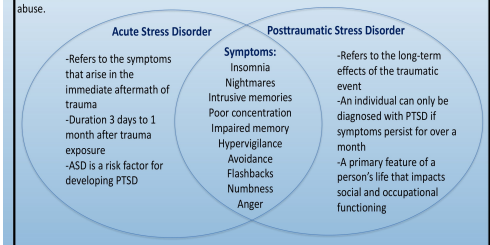


Figure 1. Intersection of ASD and PTSD Symptoms

Methods & Results

Phase 2 P201 ('AtEase') study and Phase 3 P301 ('HONOR') study were 12-week, multicenter, randomized, double-blind, placebo-controlled studies testing the efficacy and safety of TNX-102 SL in military-related PTSD. AtEase compared bedtime TNX at two doses (2.8 mg & 5.6 mg) and placebo. HONOR compared TNX 5.6 mg (2 x 2.8 mg tablets) and placebo.

Eligibility

- Age 18-65 (AtEase) and 18-75 (HONOR); service in the US military*; meeting PTSD diagnosis, assessed by the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5); screening and baseline CAPS-5 total ≥ 29 (AtEase) and ≥ 33 (HONOR); the incurred trauma(s) that resulted in PTSD during military service were 2001 or later. Other eligibility criteria included willingness to refrain from antidepressants and other excluded psychotropic medications.

Primary efficacy endpoint

- Mean change from baseline (MCFB) in total CAPS-5 score at Week 12. In AtEase, the CAPS-5 Past Week Version administered at baseline, and weeks 2, 4, 8, and 12. In HONOR, the CAPS-5 Past Week Version was administered at baseline, and weeks 4, 8, and 12.

Safety Assessments

- Safety monitoring includes following adverse events; changes from baseline in clinical labs, vital signs, weight; changes on the Columbia Suicide Severity Rating Scale (CSSRS); monitoring patient-rated morning sedation and changes in sexual function.

Statistical Methods

- Analyses of efficacy endpoints were performed on the modified Intention-To-Treat (mITT) population, defined as all randomized patients with at least one post-baseline CAPS-5 assessment.
- The primary analysis in both studies used mixed-model repeated-measures (MMRM) to estimate mean change from baseline in the total CAPS-5 score after 12 weeks of treatment in the TNX-102 SL 5.6 mg and placebo arms. HONOR employed multiple imputation (MI) for missing data, under a missing-not-at-random assumption that patients withdrawing for adverse events, lack of efficacy and lost to follow-up revert to values similar to the baseline distribution following discontinuation of study drug. AtEase employed MMRM without MI.

*N=2 military contractors in OEF/OIF deployment zones and N=6 law enforcement officers whose index traumas were incurred during work in 2010 or later were included in AtEase; N=2 military contractors in OEF/OIF deployment zones were included in HONOR.

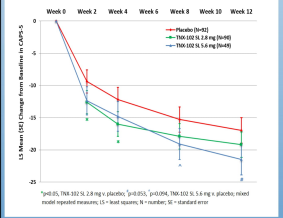
No clinically important differences in baseline demographic or clinical characteristics were identified between the TNX-102 SL and placebo groups within each of the two studies, AtEase and HONOR (Table 1).

Table 1. Participant Demographics and Baseline Characteristics (mITT Populations)

	AtEase		HONOR	
	Placebo N = 92	TNX-102 SL Total N = 139	Placebo N = 127	TNX-102 SL 5.6mg N = 125
Female, %	6.5%	7.2%	13.4%	8.0%
White, %	64.1%	66.9%	67.7%%	66.4%
Average age, years	32.0	34.6	35.5	35.9
Body Mass Index, kg/m2	28.9	29.0	29.3	29.9
Current Employment, %	58.7%	67.3%	63.0%	55.2%
Unable to work due to PTSD symptoms, %	9.8%	12.2%	12.6%	16.8%
Education, some college or higher, %	78.2%	87.1%	85.1%	82.4%
Active Duty/Veterans (at time of study), N	8/75	14/104	17/110	9/116
Time since trauma, mean years	7.04	6.9	9.2	9.1
Combat index trauma, %	80.4%	93.9%	77.2%	83.2%
Deployments, mean number	2.2	2.4	3.0	2.6
CAPS-5 total score, mean	39.5	39.4	42.4	40.0
PROMIS Sleep Disturbance T-score, mean*	63.1	62.2	67.0	67.4
SDS total score, mean*	17.7	17.2	18.4	19.9
Lifetime suicidal ideation with plan and intent,%**	7.4%	8.4%	13.6%	16.0%
Lifetime actual suicide attempt, %**	6.4%	4.9%	8.5%	10.9%

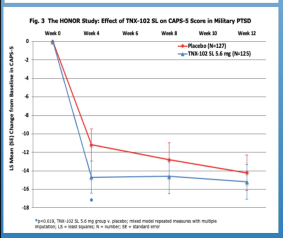
*TNX-102 SL 5.6mg; ** safety populations

Fig. 2 The AtEase Study: Effect of TNX-102 SL on CAPS-5 Score in Military PTSD



*p=0.05, TNX-102 SL 2.8 mg v. placebo; †p=0.053, ‡p=0.094, TNX-102 SL 5.6 mg v. placebo; mixed model repeated measures; LS = least squares; N = number; SE = standard error

Fig. 3 The HONOR Study: Effect of TNX-102 SL on CAPS-5 Score in Military PTSD



*p=0.019, TNX-102 SL 5.6 mg group v. placebo; mixed model repeated measures with multiple imputation; LS = least squares; N = number; SE = standard error

Despite a greater numerical decrease on the CAPS-5 at Week 12 by the TNX-102 SL 5.6 mg group, neither study reached statistical significance. Although TNX 2.8 mg showed nominal activity on CAPS-5 at Week 2 (p=0.040) and Week 4 (p=0.030) in AtEase (**Figure 2**), as did TNX 5.6 mg at Week 4 (p=0.019) in HONOR **(Figure 3).**

In both studies, TNX 5.6 mg improved sleep. The CAPS-5 "sleep disturbance" item showed nominal improvement at all time points in AtEase (Week 2, p<0.01; Week 4, p=0.032; Week 8, p<0.01; and Week 12, p=0.010) with similar results in HONOR (Week 4, p=0.002; Week 12, p=0.026). The PROMIS Sleep Disturbance total score also showed early nominal improvement with TNX 5.6 mg (e.g., Week 4 in AtEase, p<0.001; Week 4 in HONOR, p=0.015).

Safety

- No clinically meaningful changes from baseline to endpoint were observed in laboratory parameters or vital signs in either study. Nor was there any clinically meaningful pattern of changes in weight, sexual functioning, or suicidal ideation.
- Table 2 presents adverse events (AEs) at rates ≥ 5% in any TNX-102 SL group. In both studies, the most common was oral numbness (hypoaesthesia oral), an administration site reaction. The oral sensory AEs, oral numbness, oral tingling, and abnormal product taste were rated as mild and transient (last <60 min) in most cases, were never rated as severe, and only one subject discontinued due to one of these administration site reaction types (oral tingling in AtEase in TNX 2.8 mg group).
- Discontinuations due to AE in P301 were at a rate of 5.7% in the TNX-102 SL group versus 2.3% on placebo in P301; and 2.0% versus 3.2% in P201.

Table 2. Adverse Event Rates for Preferred Terms at ≥ 5% for Any TNX-102 SL Group*

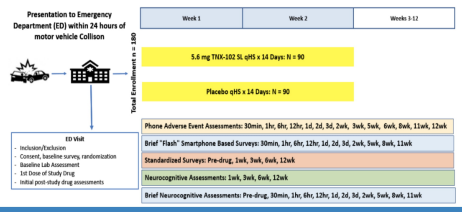
Category of Adverse Event	AtEase			HONOR	
Preferred Term	Placebo N = 94	TNX-2.8 mg N = 93	TNX-5.6 mg N = 50	Placebo N = 176	TNX-5.6 mg N = 175
Administration Site Reactions					
Hypoaesthesia oral	2.1%	38.7%	36.0%	1.1%	40.0%
Paraesthesia oral	3.2%	16.1%	4.0%	0.6%	9.1%
Product taste abnormal				2.3%	9.7%
Glossodynia	1.1%	3.2%	6.0%		
Systemic Adverse Events					
Somnolence	6.4%	11.8%	16.0%	8.5%	15.4%
Dry mouth	10.6%	4.3%	16.0%		
Headache	4.3%	5.4%	12.0%		
Insomnia	8.5%	7.5%	6.0%		
Sedation	1.1%	2.2%	12.0%		

*Safety populations; if rates of preferred terms are <5% for a TNX-102 SL groups in either study, the cells are gray for that study

Conclusions & Future Directions

- Supportive data on the effects of TNX-102 SL on reducing PTSD symptoms suggest early intervention immediately after trauma using TNX-102 SL has the potential to reduce ASR/ASD symptoms, which completely overlap those of PTSD (**Figure 1**).
- Since sleep disturbance plays a critical role in the development and maintenance of PTSD, improvement of sleep in the immediate aftermath of trauma may reorient the trajectory of posttraumatic pathology from acute trauma towards early recovery.
- In the DoD-funded OASIS trial (**O**ptimizing **A**cute **S**tress Reaction **I**nterventions with TNX-102 **SL**), to be conducted by the University of North Carolina under an Investigator-Initiated IND, 14 days of bedtime TNX-102 SL 5.6 mg will be tested in the immediate aftermath of motor vehicle collision (**Figure 4**).
- The study will test the potential for TNX-102 SL to target trauma-related sleep disturbance and its ability to facilitate recovery from ASR and to prevent development of PTSD.

Figure 4. OASIS trial Study Design



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- Astill Wright, L, Sijbrandij, M, Sinnerton, R, Lewis, C, Roberts, NP, & Bisson, JI (2019). Pharmacological prevention and early treatment of post-traumatic stress disorder and acute stress disorder: a systematic review and meta-analysis.
- Socci V, Rossi R, Talevi D, et al. Sleep, stress and trauma. Journal of Psychopathology 2020;26:92-8. https://doi.org/10.36148/2284-0249-375
- Troxel, WM, Shih, RA, Pedersen, ER, et al. Sleep in the Military: Promoting Healthy Sleep Among U.S. Servicemembers | RAND, 2015.

Disclosures

SL, JE, and GMS are employees of Tonix Pharmaceuticals, Inc., and own stock and/or have stock options in the company. MP consulted with Tonix on the preparation and presentation of these studies.
TNX-102 SL is an investigational new drug and has not been approved for any indication

Exhibit 99.03

Development of the AURORA Platform Trial Network to Test Interventions to Reduce Acute Stress Reaction Symptoms, and Illustration of Use Testing Sublingual Cyclobenzaprine TNX-102 SL

Samuel A McLean, MD[1], Christopher W. Jones, MD[2], Laura Germine, PhD[3], Seth Lederman, MD[4], Gregory M. Sullivan, MD[4], Christine Bizgu, MS[1], Council Mintz, BS, CCRP[1], Romina Soudavari, BS[1], Xinming An, PHD[1], Liana Matson, PhD[5], Emily Lowery-Gionta, PHD[5]

[1]University of North Carolina School of Medicine, Chapel Hill, NC, [2] Cooper University Health Care, Camden, NJ, [3] McLean Hospital & Harvard Medical School, Belmont, MA, [4] Tonix Pharmaceuticals, Inc., Chatham, NJ, [5]Walter Reed Army Institute of Research, Bethesda, MD

*TNX-102 SL is an investigational new drug and has not been approved for any indication

BACKGROUND

U.S. military personnel exposed to life-threatening traumatic events (e.g., intense firefights with multiple casualties, witnessing death) can experience **acute stress reactions (ASRs)** in the war theater, adversely affecting warfighter performance and safety and predisposing to chronic psychopathological outcomes. Symptoms of ASR include intrusions, dissociation, avoidance, arousal (including poor sleep), pain and other somatic symptoms, and negative mood. When symptoms persists >72 hours after the event, **acute stress disorder (ASD)** may be diagnosed, and when they persist for ≥ 1 month, **posttraumatic stress (PTS) and/or persistent pain, somatic symptoms, cognitive symptoms, and/or depressive symptoms, collectively termed adverse posttraumatic neuropsychiatric sequelae (APNS)** may be diagnosed. **To reduce ASR, PTS, and other acute and chronic APNS symptoms, it may be valuable to intervene in the immediate aftermath of trauma (Fig 1).** Many promising interventions exist to reduce such symptoms and improve warfighter function, but historically there has been no testing platform to rapidly assess candidate interventions for potential efficacy.

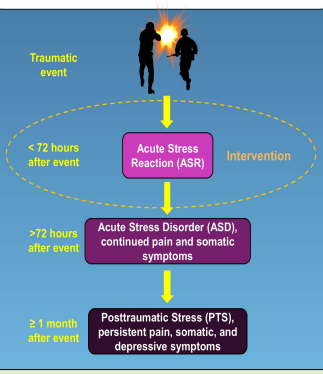


Fig. 1. Early intervention may reduce ASR symptoms and the subsequent development of posttraumatic stress (PTS) and/or persistent pain, somatic symptoms, cognitive symptoms, and/or depressive symptoms, collectively termed adverse posttraumatic neuropsychiatric sequelae (APNS)

The AURORA Research Network is a **US Emergency Department (ED)-based network** of trauma centers that performs prospective longitudinal studies of individuals experiencing traumatic stress. The AURORA Research Network has been in operation for more than 20 years. The Network has recruited more than 6,000 trauma survivors presenting to the ED for care after traumatic stress into observational and intervention studies evaluating the development of APNS and testing interventions to prevent APNS. We are dedicated to process improvement within and across studies, have a unique depth of experience with this work, and have developed screening tools to identify high risk individuals. These assets allow us to achieve high rates of recruitment and follow-up and complete studies successfully. The AURORA Research Network Coordinating Center is based at the University of North Carolina at Chapel Hill.

The AURORA APNS Platform is a standard platform randomized controlled trial (RCT) design. This standardized design and our experienced network sites allow us to rapidly onboard and complete studies testing medications and other early interventions for efficacy in reducing acute or persistent posttraumatic stress (**Fig 2**).

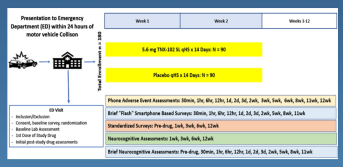


Fig. 2. General AURORA Platform Trial Design, using TNX-102 SL as example. This standard platform randomized controlled trial (RCT) design is being used to rapidly assess interventions, administered in the early aftermath of traumatic stress exposure (motor vehicle collision), for efficacy in reducing acute or chronic Adverse Posttraumatic Neuropsychiatric Sequelae (APNS). Such APNS include ASR/PTS symptoms, pain, somatic symptoms (e.g., dizziness, lightheadness), cognitive symptoms (concentration difficulty, taking longer to think), and depressive symptoms. The platform is currently contracted to test a number of different interventions.

One promising medication intervention to reduce acute and chronic APNS is TNX-102 SL. TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is in development by Tonix Pharmaceuticals Inc., for treating fibromyalgia and PTSD. Cyclobenzaprine **(Fig 3)** is the active ingredient in TNX-102 SL **(Fig. 4)**. This drug was previous evaluated in military PTSD in several randomized, double-blind, placebo-controlled Phase 2 and Phase 3 trials. In these studies, TNX-102 SL reduced PTSD symptom severity (3) and reduced sleep disturbance (a significant factor in stress recovery). TNX-102 SL has favorable tolerability with low rates and low severity of systemic side effects. Local effects, such as numbness/tingling under the tongue and/or awareness of bitter taste are common but generally mild.

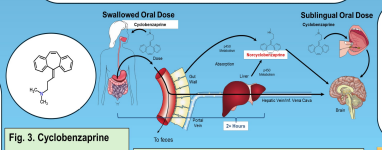


Fig. 3. Cyclobenzaprine

- Potent binding and antagonist activities at postsynaptic receptors:
  - serotonin-5-HT$_{2A}$
  - α_1-adrenergic
  - histaminergic-H$_1$
  - muscarinic-M$_1$
- Improves sleep quality but is not a traditional hypnotic or sedative

Fig. 4. TNX-102 SL (Sublingual Cyclobenzaprine HCl)

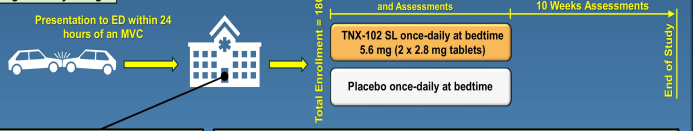
Advantages of the sublingual route:

- Faster absorption provides PK that is ideal for bedtime dosing, minimizing morning somnolence
- Bypasses "first-pass" hepatic metabolism.
  - Reduced metabolism of parent CBP to active metabolite norcyclobenzaprine (nCBP); increased CBP to nCBP ratio in blood

METHODS

The OASIS trial (**O**ptimizing **A**cute **S**tress Reaction **I**nterventions with TNX-102 **SL**), will evaluate the efficacy and safety of TNX-102 SL in civilians presenting to the Emergency Department (ED) after a motor vehicle collision (MVC) **(Fig 6)**. MVC is one of the most common traumatic events for which individuals seek ED care. The AURORA study (1) of more than 3,800 civilians showed that in the early aftermath of an MVC, the same ASR/ASD/PTSD symptoms occur as in servicemembers exposed to traumatic events in the war theater. Thus, civilians in a recent MVC are an optimal population to test interventions for evidence of efficacy, which could benefit both service members and civilians.

Fig. 6. Study Design



Emergency Department Visit

- Key inclusion criteria
  - ✓ ≥ 18 years and ≤ 55 years of age
  - ✓ Admitted to ED within 24 hours of MVC
  - ✓ Anticipated to be discharged home
  - ✓ PTSD prediction tool risk score ≥16; pain severity ≥4 (0-10 rating scale) (2)
- Key exclusion criteria
  - ✓ Substantial comorbid injury
  - ✓ Pregnant females
  - ✓ Chronic opioid use prior to MVC
  - ✓ Active psychosis, suicidal ideation, or homicidal ideation
- Consent, baseline surveys, and lab assessments
- Randomization to TNX-102 SL 5.6 mg (n = 90) or placebo (n = 90)
- 1st dose of study drug, and initial post-study drug assessments

Objective

Investigate the potential of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) to reduce the frequency and severity of the adverse effects of traumatic exposure, including ASR, ASD, and PTSD.

Primary Outcome Measure

- Acute Stress Disorder Scale (14-item self report inventory that indexes ASD and predicts PTSD) assessed at 7 and 21 days post MVC

Secondary Outcome Measures

- 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
- Detailed and brief neurocognitive assessments (e.g., generalized cognitive function, psychomotor vigilance, procedural reaction, response inhibition/control, visuospatial processing, and visuospatial attention tasks) performed from baseline to 12 weeks after MVC at specific timepoints throughout study participation period

Safety Assessments

In person or text/email adverse event assessments at 30 minutes, 1 hour, 6 hours, 12 hours, 1 day, 2 days, 3 days, 1 week, 2 weeks, 3 weeks, 5 weeks, 6 weeks, 8 weeks, 11 weeks, and 12 weeks after drug administration. The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) will be used to assess AE severity.

CONCLUSIONS

- According to the National Center for PTSD, about 60% of men and 50% of women in the US are exposed to at least one traumatic experience in their lives (4). In the US alone, one-third of ED visits (40-50 million patients per year) are for evaluation after trauma exposure (5). No medications are currently available at or near the point of care to treat patients suffering from acute trauma and support long-term health.
- Previous trials showed that TNX-102 SL reduced military PTS symptoms, in as early as 2 weeks, with favorable tolerability.
- TNX-102 SL is hypothesized to reduce ASR symptoms in the immediate aftermath of an MVC.
- The first participant for the OASIS trial is expected to enroll in Q3 2024.
- The results may ultimately provide military personnel with a new treatment option that, when administered in the early aftermath of a traumatic event to individuals with ASR symptoms, improves warfighter function

ACKNOWLEDGEMENTS

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DISCLOSURES

SL, and GS are employees of Tonix Pharmaceuticals, Inc., and own stock and/or have stock options in the company. CWJ, LG, XA, CM, CB, RS, and SAM declare no conflicts of interest related to this work.

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For information regarding testing medications or device interventions using the AURORA research network/platform, contact Meredith_Bucher@med.unc.edu or Megan_Henderson@med.unc.edu

Exhibit 99.04

Integrating Automated High-Throughput Scratch Assay and Cell Painting for Comprehensive Analysis of Cell Migration and Wound Healing

Krishna P. Kota, Jiayi Wei, Jennifer Y. Cho, Junzhong Peng, David Ordonez, Bruce Daugherty, Sina Bavari
Research and Development Center, Tonix Pharmaceuticals, Frederick MD

Abstract

Cell migration is a complex process influenced by various factors. The scratch assay is commonly used to study cell motility, but it has limitations like scratch size variability and difficulty in quantification. To address these issues, we introduce an automated High Content Imaging-based scratch assay for 96/384-well plates. It enables reproducible quantification of cell migration, high-throughput screening, and evaluation of compound libraries' effects on migration. We also incorporate cell painting, using fluorescent dyes to visualize morphological changes during migration and wound healing. This research identifies key morphological characteristics and their importance in migration, highlighting a correlation between actin polymerization, mitochondrial distribution, and cell migration.

Introduction

Cell migration is a complex cellular process influenced by various signaling pathways and microenvironments, crucial for physiological functions and implicated in diseases like cancer metastasis and autoimmune disorders[1]. High throughput screening (HTS) assays, including scratch assays, are used to assess compounds' effects on cell migration for drug discovery. Scratch assays, involving the creation of a gap in a cell monolayer, are commonly employed in cell biology and drug research to study cell motility and evaluate drug impacts on migration and proliferation. Despite some limitations, such as variability and difficulty in quantification, they are often combined with other assays for a comprehensive understanding. Automated 384 well-based scratch assays provide enhanced speed, accuracy, and reproducibility in studying cell migration, making them valuable tools for identifying potential therapies targeting abnormal migration in diseases like cancer and autoimmune disorders[2].
Automated scratch assays involve specialized instruments and robotic systems to create scratches, followed by automated imaging and quantitative analysis of cell migration over time. These automated assays offer advantages over manual methods, including high-throughput capabilities and flexibility for complex experimental designs, such as compound concentration testing or multiple cell type assessments. Overall, automated scratch assays are powerful tools for investigating cell migration dynamics and discovering compounds with therapeutic potential for diseases associated with abnormal cell migration. Additionally, the incorporation of cell painting, a technique employing fluorescent dyes to label cellular components, enhances our ability to visualize and understand the morphological changes underlying cell migration and wound healing processes in scratch assays[3].

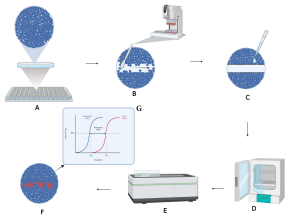

Fig 1. High-Throughput Screening Utilizing a Scratch Wound Healing Assay
A Screening Procedure in a 96 / 384-well Plate Configuration.BDiagram illustrating the wound generation process. C. Diagram illustrating the compound addition at a scratch boundary D.Plate Incubation E. Live cell image acquisition using Opera Phenix. F. Diagram illustrating the wound healing process at a scratch boundary G. Data analysis

Methods

Fig 2 Illustration of the Wound Healing Process and Quantification of Cell Migration
Throughout the experiment, the remaining percentage of scratch area, A(t), is continually monitored and calculated as: A(t) = (A(t) / A(0)) x 100%, where A(t) is the scratch area at a specific time (t), and A(0) is the initial scratch area at time zero (0).

Results

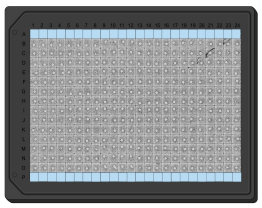

Fig 3 Automated Scratch: In the automated scratch assay: MCF10A cells are seeded onto collagen I-coated 96-well and 384-well plates. After 18 hours, a custom script automates the creation of a clear scratch in the center of the well using an Integra Viaflo pipetting robot. Following the scratch, cells are exposed to a test compound for 24 to 48 hours. During this period, cell migration into a detection zone at the scratch site is monitored using fluorescent / non-fluorescent cells .

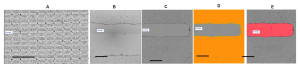

Fig 4 Automated Scratch Wounding Assay and Image Analysis in MCF10A Cells
MCF10A cells are seeded on collagen I-coated 96-well plates, then subjected to automated scratch wounding using an Integra Viaflo robot (Figure a). These cells migrate towards a detection zone while exposed to fluorescently monitored test compounds. Image analysis scripts, employing supervised machine learning in Harmony Image Analysis Software (Revvity, MA), are used to measure total cell areas in both scratched and non-scratched regions at different time points (Figures b-e).

Results

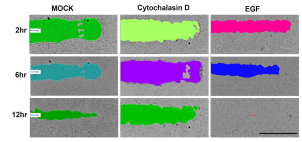

Fig 5 Effect of Cytochalasin D and Epidermal Growth Factor on MCF10A Cell Migration:MCF10A cells are seeded on collagen I-coated 96-well plates, then subjected to automated scratch wounding using an Integra Viaflo robot (Figure 1). These cells migrate towards a detection zone while exposed to test compounds (Cytochalasin D and Epidermal Growth Factor (EGF). Cytochalasin D is actin depolymerisering which revelry effect the migration of the cells. EGF enhances the migration of the cells into the scratch area compared to mock cells

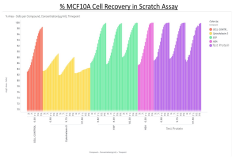

Fig 6 Quantification of Cell Migration in MCF10A Cells exposed to Cytochalasin D, Epidermal Growth Factor (EGF), and Protein X at Various Concentrations and Time Points. Cytochalasin D treatment leads to reduced cell migration, while EGF significantly enhances migration. Cell migration remains unaffected by the test protein across different concentrations and time points. The study monitored cell migration for 24 hours with images captured every 2 hours

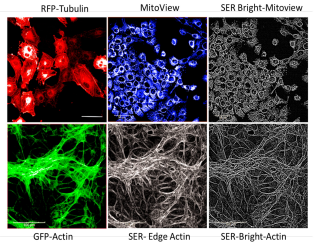

Fig 7 Visual Examples of Cell Painting Staining Patterns: Images are captured using the Opera Phenix Plus high-content screening system. Phenotypic characteristics are extracted from these images utilizing a dedicated cell painting building block within the Harmony imaging and analysis software.

Results

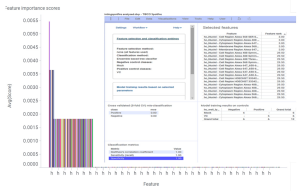

Fig 8 **Cell Painting and Exploring Cellular Phenotypic Clusters through Computational Analysis with Principal Component Analysis:** Cell features are analyzed using computational models, e.g. principal component analysis in Revvity Signals VitroVivo analysis platform, to differentiate clusters of cellular phenotypes.

Conclusion

In conclusion, this study successfully optimized a highly efficient scratch assay development method for both 96 and 384-well plates, serving as a proof of principle. We also designed and implemented high-content imaging scripts to monitor wound closure in real-time. Additionally, the application of cell painting techniques allowed us to fluorescently label cell organelles and the cytoskeleton, enabling us to measure phenotypic changes during cell migration. Our findings revealed a pivotal role played by mitochondrial number and activity in the process of cell migration towards wound healing.

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3. The figure1 was constructed using the Biorender platform's tools and features

4. Figure 2 was sourced from the Biorender repository of illustrations

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