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): November 15, 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 November 15, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced the completion of the clinical phase of the Phase 3 registration-quality, double-blind, placebo-controlled RESILIENT study of its TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg product candidate for the management of fibromyalgia. A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference.

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. A copy of the presentation is filed as Exhibit 99.02 hereto and incorporated herein by reference. The Company also updated its TNX-1900 and TNX-102 SL product candidate presentations, which it intends to place on its website and which may contain nonpublic information. Copies of the presentations are filed as Exhibits 99.03 and 99.04 hereto 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 November 15, 2023, the Company announced the completion of the clinical phase of the Phase 3 RESILIENT study of TNX-102 SL for the management of fibromyalgia. A total of 457 patients were enrolled in this multi-site study in the U.S. Topline results are expected in late December 2023. If successful, the Company believes that the RESILIENT study may be the final, well-controlled efficacy trial required for submission of a New Drug Application for approval by the U.S. Food and Drug Administration. The preliminary unaudited rate of adverse-event ("AE") related discontinuations in the RESILIENT study was 4.8%, which compares favorably to the blinded AE-related discontinuation rates in the two previous Phase 3 trials of TNX-102 SL: 6.0% in the RELIEF trial, which achieved statistical significance on the primary endpoint (p=0.010), and 10.7% in the RALLY trial, which was stopped at the interim analysis. The Company believes that an unexpectedly high rate of AE-related discontinuations in

the RALLY trial contributed to missing its primary endpoint, as the study was conducted during the Delta wave of the COVID pandemic, which we may have contributed to patient discontinuations. AE-related discontinuations are treated as negative outcomes in the 'missing data' multiple imputation approach that is part of the analysis of the primary endpoint.

The Company is actively exploring strategic partnerships and out-licensing opportunities for certain of its product candidates, including TNX-1500.

Forward- Looking Statements

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

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

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press release of the Company, dated November 15, 2023
99.02	Corporate Presentation by the Company for November 2023
99.03	TNX-1900 Product Presentation
99.04	TNX-102 SL Product Presentation
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: November 15, 2023

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

Exhibit 99.01

Tonix Pharmaceuticals Completes Clinical Stage of Phase 3 RESILIENT Study of TNX-102 SL for the Management of Fibromyalgia

Topline results expected late December 2023

RESILIENT is expected to be the final efficacy trial required for submission of a New Drug Application to FDA; first successful Phase 3 trial, RELIEF, achieved statistical significance (p=0.010),

Preliminary unaudited rate of adverse-event (AE) related discontinuations in the RESILIENT study was 4.8% which compares favorably with prior studies: RELIEF 6.0% and RALLY 10.7%

TNX-102 SL is a centrally acting, non-opioid analgesic

CHATHAM, N.J., November 15, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced the completion of the clinical phase of the Phase 3 registration-quality, double-blind, placebo-controlled RESILIENT[1] study of TNX-102 SL[2] (cyclobenzaprine HCl sublingual tablets) 5.6 mg for the management of fibromyalgia. A total of 457 patients were enrolled in this multi-site study in the U.S. Topline results are expected in late December 2023. If successful, it is expected to be the final, well-controlled efficacy trial required for submission of a New Drug Application (NDA) for approval by the U.S. Food and Drug Administration (FDA).

“There are an estimated 6-12 million individuals in the U.S. suffering from this debilitating condition, most of whom are women,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “TNX-102 SL is a centrally-acting, non-opioid analgesic bedtime medication designed to be used on a chronic basis for the management of fibromyalgia. We believe TNX-102 SL works by improving sleep quality, which leads to improvement of other symptoms. In previous studies, TNX-102 SL showed broad coverage across the symptoms of fibromyalgia, including chronic widespread pain, fatigue and sleep disturbance.”

“ The preliminary unaudited rate of adverse-event (AE) related discontinuations in the RESILIENT study was 4.8%,” said Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. “This compares favorably to the blinded AE-related discontinuation rates in our two previous Phase 3 trials: 6.0% in RELIEF which achieved statistical significance on the primary endpoint (p=0.010), and 10.7% in RALLY which was stopped at the interim analysis. We later learned that an unexpectedly high rate of AE-related discontinuations in RALLY contributed to missing the primary endpoint. The study was conducted during the Delta wave of the COVID pandemic, which we believe may have contributed to patient discontinuations. AE-related discontinuations are treated as negative outcomes in the ‘missing data’ multiple imputation approach that is part of the analysis of the primary endpoint.”

In December 2020, Tonix reported positive results from the first Phase 3 RELIEF study of TNX-102 SL 5.6 mg for the management of fibromyalgia[3]. TNX-102 SL met its pre-specified primary endpoint in the Phase 3 RELIEF trial, significantly reducing daily pain compared to placebo (p=0.010) in participants with fibromyalgia. Also, when the primary endpoint was analyzed as a ≥30% pain responder analysis, there was a higher rate of responders to TNX-102 SL (47%) than to placebo (35%; p=0.006). TNX-102 SL at 5.6 mg also showed activity in key secondary endpoints, demonstrating improvements in sleep quality, mitigation of fatigue, and fibromyalgia-specific global symptomatic and functional recovery. TNX-102 SL was generally safe and well tolerated in patients with fibromyalgia, with overall adverse event profile comparable to prior fibromyalgia studies. The most common treatment-emergent adverse events were oral hypoesthesia, oral paresthesia, and product taste abnormal.

[1]Clinical Trials.gov I.D. NCT05273749

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

[3]Lederman S, et al. *Arthritis Care Res*. 2023. 75(11):2359-2368.

About the Phase 3 RESILIENT Study

The RESILIENT study is a double-blind, randomized, placebo-controlled trial designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) in the management of fibromyalgia. The two-arm trial randomized 457 participants across 33 sites in the U.S. The first two weeks of treatment consist of a run-in period in which participants start on TNX-102 SL 2.8 mg (1 tablet) or placebo. Thereafter, all participants increase their dose to TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) or two placebo tablets for the remaining 12 weeks. The primary endpoint is the daily diary pain severity score change from baseline to Week 14 (using the weekly averages of the daily numerical rating scale scores) for TNX-102 SL 5.6 mg vs. placebo, analyzed by mixed model repeated measures with multiple imputation.

For more information, see ClinicalTrials.gov Identifier: NCT05273749.

About Fibromyalgia

Fibromyalgia is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system. Fibromyalgia afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women. Symptoms of fibromyalgia include chronic widespread pain, nonrestorative sleep, fatigue, and morning stiffness. Other associated symptoms include cognitive dysfunction and mood disturbances, including anxiety and depression. Individuals suffering from fibromyalgia struggle with their daily activities, have impaired quality of life, and frequently are disabled. Physicians and patients report common dissatisfaction with currently marketed products.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which provides rapid transmucosal absorption and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. As a multifunctional agent with potent binding and antagonist activities at the 5-HT2A-serotonergic, α1-adrenergic, H1-histaminergic, and M1-muscarinic receptors, TNX-102 SL is in development as a daily bedtime treatment for fibromyalgia, Long COVID (formally known as post-acute sequelae of COVID-19 [PASC]), alcohol use disorder and agitation in Alzheimer’s disease. The United States Patent and Trademark Office (USPTO) issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in the patent are important elements of Tonix’s proprietary TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults. Tonix’s development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix’s CNS development portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix’s lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment of a potentially confirmatory Phase 3 study in the third quarter of 2023, with topline data expected in late December 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 proof-of-concept study has been completed, and topline results were reported in the third quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), is in development as a preventive treatment for chronic

migraine, and enrollment has been 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, bone health in autism, 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. 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

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 world-class academic & research organizations to bring innovative therapeutics to market faster

Late-Stage Clinical Portfolio

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)*			
	FM-Type Long COVID	*Phase 2 Topline Results Reported 3Q'23*			
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*			

*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]

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

- 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)

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

Retail Product Sales for the 12 months ended December 31st 2022
- Retail sales: ~$23 M (Zembrace ~$19.6 M and Tosymra ~$3.5 M)[4]

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. 2006;28(4):517-526.

Tonix has contracted to acquire the Zembrace, SymTouch and Tosymra trademarks. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc.

TONIX PHARMACEUTICALS

CNS PORTFOLIO

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-zavzpretm-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/

TONIX PHARMACEUTICALS

CNS PORTFOLIO

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

TNX-102 SL

Cyclobenzaprine (Protectic®)

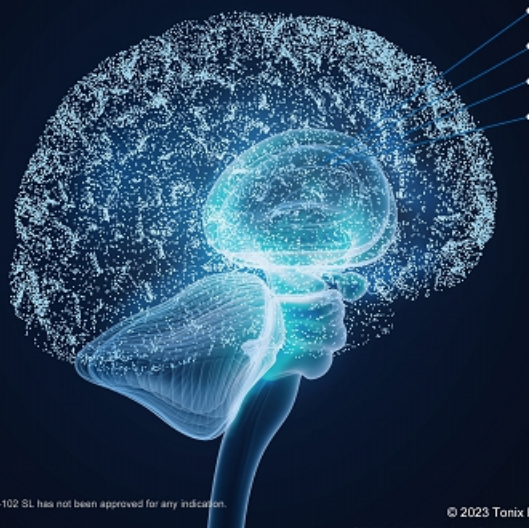
A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

TONIX PHARMACEUTICALS

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.

TONIX PHARMACEUTICALS

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, 2018)
[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

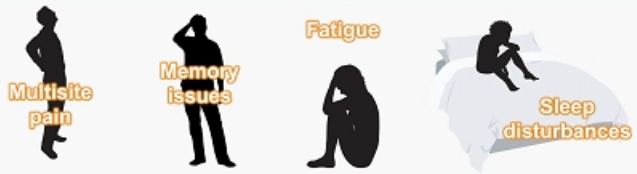
ClinicalTrials.gov Identifier: NCT05273749
A Phase 3 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With Fibromyalgia (RESILIENT)

TONIX PHARMACEUTICALS

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 <u>overlap with core symptoms of fibromyalgia</u>

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

TONIX PHARMACEUTICALS

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)*

Placebo once-daily at bedtime

14 weeks

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

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)"

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

TONIX PHARMACEUTICALS

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/3Z6FQHQ
[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.

TONIX PHARMACEUTICALS

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)

*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

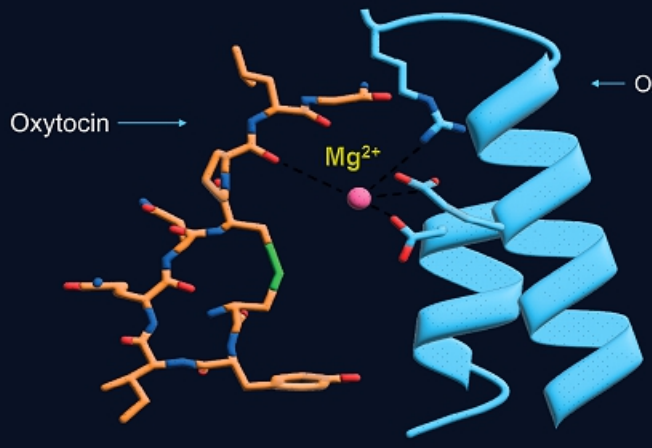
Intranasal Potentiated Oxytocin with Magnesium

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

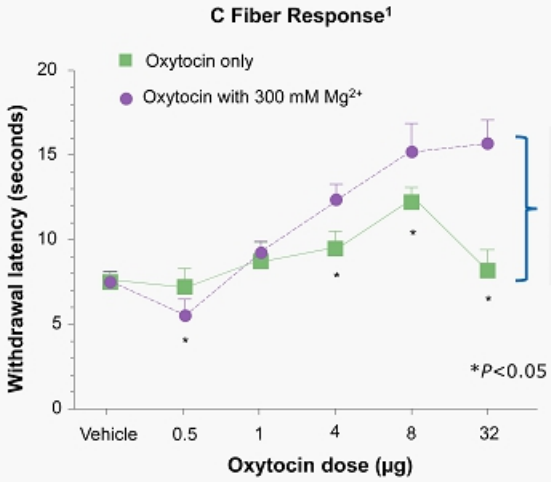
[1]Antoni et al., 1989. *Biochem J.* 257(2):611-4
[2]Meyerowitz et al., 2022. *Nat Struct Mol Biol.* (5):274-281
*TNX-1900 and TNX-2900 have not been approved for any indication.

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.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

TNX-1900: Phase 2 PREVENTION Study Design

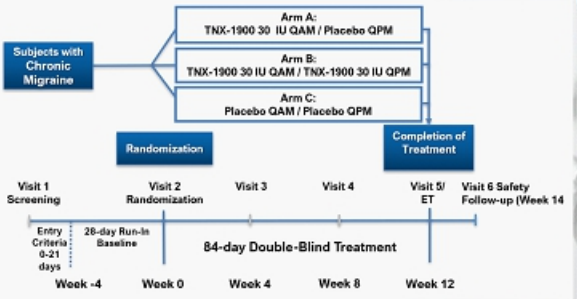
PREVENTION Study

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



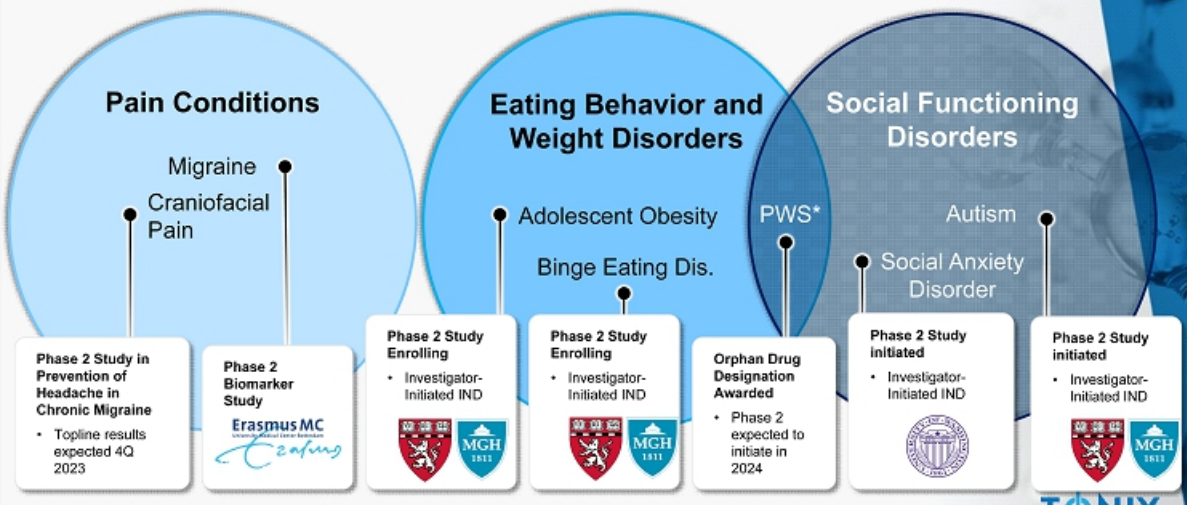
ClinicalTrials.gov Identifier: NCT05679908
A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)

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

CNS PORTFOLIO

TONIX PHARMACEUTICALS

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



*Prader-Willi Syndrome

TONIX PHARMACEUTICALS

TNX-1900 – Other Studies in Collaboration with Academic Investigators

CNS PORTFOLIO

Pharmacodynamic biomarker study related to headache[1]

- Testing TNX-1900 effects on capsaicin- or electrical stimulation-induced forehead dermal blood flow in healthy female human volunteers
- Forehead dermal blood flow is considered a trigeminovascular biomarker for antimigraine drugs.
  - Both a CGRP inhibitor and a triptan have been successfully tested in the model and have been found to inhibit the forehead dermal blood flow response to capsaicin in migraineurs and healthy volunteers, respectively.[2,3]
- Erasmus University Medical Center, Dr. Antoinette Maassen van den Brink, Principal Investigator (P.I.)

Pediatric Obesity[4]

- 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[5]

- 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[6]

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

[1]Tonix Press Release May 22, 2023: https://ir.tonixpharma.com/news-events/press-releases/detail/1391/tonix-pharmaceuticals-announces-clinical-proof-of-concept
[2]de Vries Lentsch S, et al. 2022 "CGRP-mediated trigeminovascular reactivity in migraine patients treated with erenumab." *J Neurol Neurosurg Psychiatry.* Aug;93(8):911-912.
[3]Ibrahimi K, et al. 2017 "A human trigeminovascular biomarker for antimigraine drugs: A randomized double-blind, placebo-controlled, crossover trial with sumatriptan." *Cephalalgia.* Jan;37(1):94-98.
[4]Tonix Press Release July 10 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1404/tonix-pharmaceuticals-announces-initiation-of-enrollment-in
[5]Tonix Press Release July 17, 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1405/tonix-pharmaceuticals-announces-agreement-and-initiation-o
[6]Tonix Press Release July 31, 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1419/tonix-pharmaceuticals-announces-enrollment-initiated-in-the

TONIX PHARMACEUTICALS

TNX-1900 for Pediatric Autism

- Children with Autism Spectrum Disorder (ASD) are at risk for low bone density
- Preliminary data suggest that administration of oxytocin may favorably impact bone formation and strength
- Recent meta-analysis reported that plasma oxytocin levels tend to be lower in children with Autism Spectrum Disorder than controls[1]

"BOX" Investigator-Initiated Study in Pediatric Autism at MGH

- Randomized, placebo-controlled study to evaluate the effects of twice daily administration of TNX-1900 on bone measures in children with ASD
- Study subjects, ages six to 18 years old, will be randomized 1:1 to receive TNX-1900 twice per day or placebo for 12 months in the double-blind phase, followed by a six-month open label phase during which all study subjects will receive TNX-1900 twice daily
- Primary endpoint: difference between TNX-1900 compared to placebo groups in 12-month change in whole body less head bone mineral density Z-scores
  - Z-score compares one's bone density to the average bone density of age and gender matched controls

CNS PORTFOLIO

TONIX PHARMACEUTICALS

[1]John S and Jaeggi, AV. *Autism*. 2021. 25:2152-2161

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

RARE DISEASE & IMMUNOLOGY PORTFOLIOS

TONIX PHARMACEUTICALS

[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

TONIX PHARMACEUTICALS

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

[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.

TNX-1500

Anti-CD40L Monoclonal Antibody

Next Generation mAb preserves efficacy without risk of thrombosis

TNX-1500: Next Generation anti-CD40L mAb

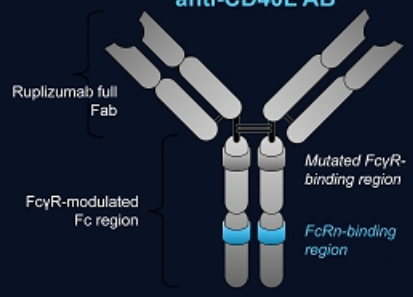
Re-engineered to better modulate the binding of FcγR and mitigate risk of thrombosis

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.

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

Actively 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

IMMUNOLOGY PORTFOLIO

TONIX PHARMACEUTICALS

TNX-1700

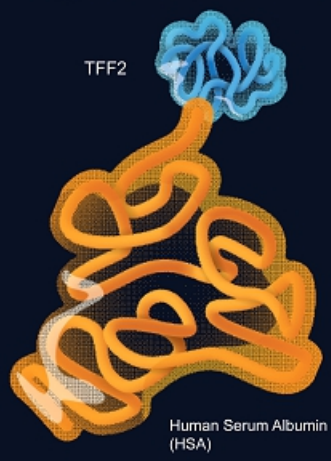
Recombinant Trefoil Factor Family Member 2 (rTFF2-HSA) Fusion Protein

Targeting the toxic tumor micro-environment

TONIX PHARMACEUTICALS

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/48nlRHM

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

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

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

TNX-801

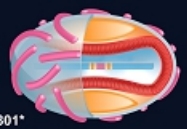
Live Virus Vaccine

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

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

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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TEAM, NETWORK, & UPCOMING MILESTONES

Key Development Partners

TNX-1500: ALLOGRAFT REJECTION

Massachusetts General Hospital · Harvard Medical School

TNX-1300: COCAINE INTOXICATION
TNX-1700: GASTRIC AND COLORECTAL CANCERS

Columbia University

TNX-1900: MIGRAINE & OTHER INDICATIONS

Stanford University · Université de Genève · Massachusetts General Hospital · Harvard Medical School

TNX-801: SMALLPOX AND MONKEYPOX VACCINE

University of Alberta · SR Southern Research

TNX-2900: PRADER-WILLI SYNDROME

InsermTransfert · CHU de Toulouse · Aix-Marseille université

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 Silicon Valley 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

THANK YOU

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.

TONIX PHARMACEUTICALS

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.

TONIX PHARMACEUTICALS

Exhibit 99.03

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; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. 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

TNX-1900 for the Treatment of Migraine: Prevalence

One billion individuals worldwide suffer from migraines (~14% of population)[1]

Migraine is the second leading cause of years lived with disability[1]

In U.S., the estimated cost of all migraine headaches was $78 billion in 2014[2]

- Approximately 30% of those costs ($23 billion) were direct medical costs

Chronic migraine (≥ 15 headaches / month) effects about 1-2% of individuals[3]

- 75-150 million individuals worldwide
- 3-7 million in the U.S.

CGRP antibodies are the only migraine specific prophylaxis drugs approved in decades

- Requires parenteral administration (systemic effects on peripheral CGRP pathways)
- Long term safety concerns with prolonged systemic blockade of CGRP receptor[4]

[1] GBD 2016 Headache Collaborators, Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Neurol 2018; 17: 954–76
[2] Gooch, C. L., et al., The Burden of Neurological Disease in the United States: A Summary Report and Call to Action. Ann Neurol. 2017; 81:479–484
[3] Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[4] 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 for the Treatment of Migraine and Craniofacial Pain: Overview

Novel intranasal oxytocin formulation being developed as a prophylactic treatment for chronic migraine

- Based on a propriety formulation of oxytocin*, a naturally occurring human hormone that acts as a neurotransmitter in the brain

Clinical and preliminary research has shown that low oxytocin levels in the body can lead to increase in headache frequency, and that increased oxytocin levels can relieve headaches

- Certain other chronic pain conditions are also associated with decreased oxytocin levels

Oxytocin when delivered via the nasal route, results in enhanced binding of oxytocin to receptors on neurons in the trigeminal system, inhibiting transmission of pain signals

Intranasal oxytocin has been shown in animals that it can also block CGRP release, a pathway known to be critical to the pathogenesis of migraine attacks.

*Oxytocin is approved by the U.S. Food and Drug Administration (FDA) as Pitocin®, an intravenous infusion or intramuscular injection drug, for use in pregnant women to induce labor. An intranasal form of oxytocin was marketed by Novartis to assist in nursing as Syntocinon®, but the product was withdrawn and the New Drug Application (NDA) has been discontinued.

TNX-1900 for the Treatment of Migraine: Mechanism of Action

Preclinical research showed that nasally applied TNX-1900 selectively inhibits the activity of trigeminal pain-sensing nerve cells and blocks the release of CGRP

- TNX-1900 is believed to interrupt pain signals at the trigeminal ganglia by suppressing electrical impulses, a potentially different activity than drugs that just block CGRP

Migraine attacks are caused, in part, by the release of CGRP from pain-sensing nerve cells that are part of the trigeminal system

- The CGRP binds to receptors on other nerve cells and starts a cascade of events that eventually results in a severe headache. This, in turn, reduces various kinds of trigeminal nerve associated pain and prevents CGRP from acting at receptors in the central nervous system that are involved in migraine.

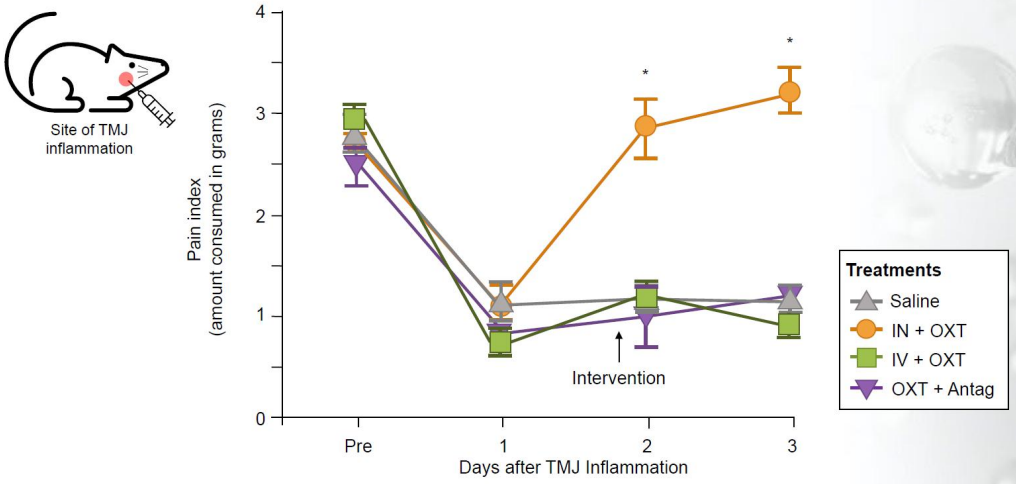
We believe targeted delivery of oxytocin could translate into selective blockade of CGRP release in the trigeminal ganglion and not throughout the body, which could be a potential safety advantage over systemic CGRP inhibition

- In addition, daily dosing is more quickly reversible, in contrast to monthly or quarterly dosing, giving physicians and their patients greater control

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Efficacy of Intranasal Oxytocin After Inflammation of the Temporomandibular Joint (TMJ)



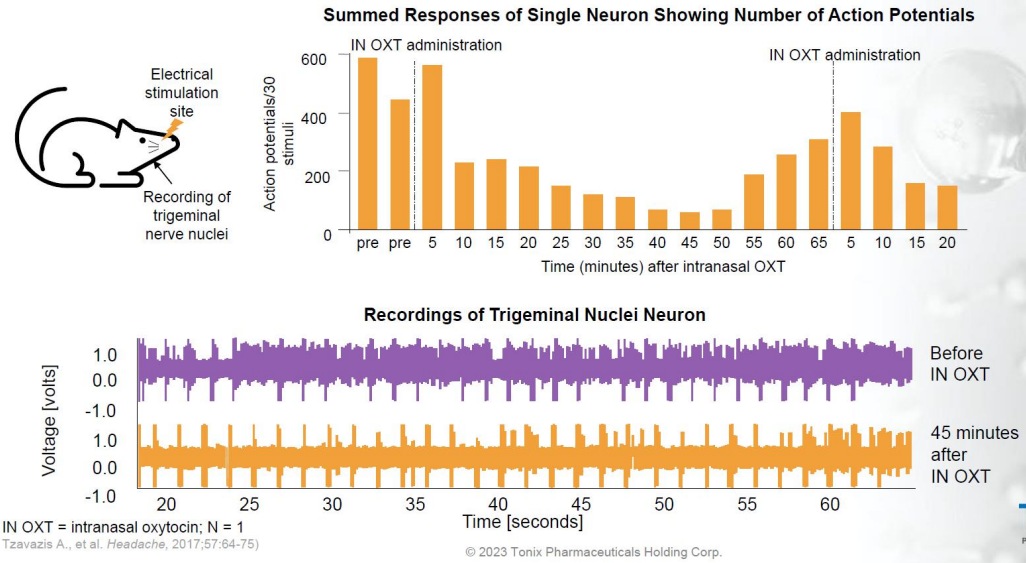
IN = intranasal; IV = interveinal; OXT = oxytocin; *P <0.05; N = 8 per group

Yeomans D. 2022. *unpublished*

CNS PORTFOLIO

TONIX PHARMACEUTICALS

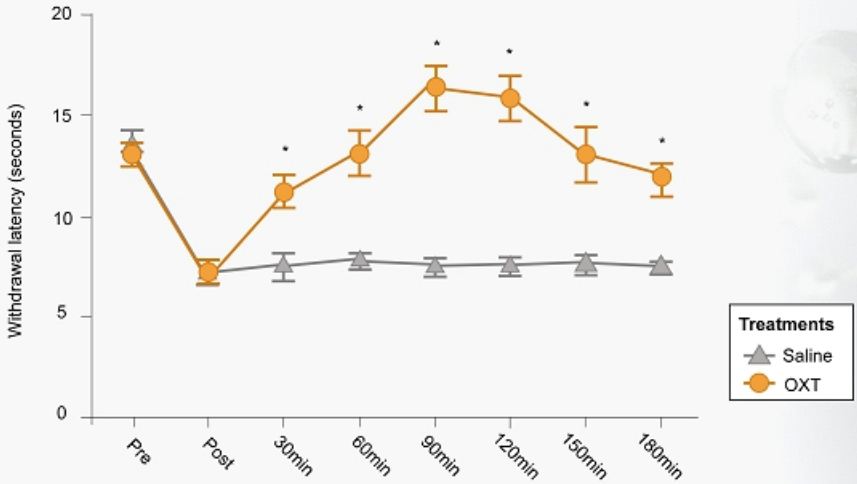
Effects of IN OXT on Trigeminal Nerve Nuclei Neuron Activity Induced by Noxious Electrical Stimulation to the Face.



IN OXT = intranasal oxytocin; N = 1

Tzavazis A., et al. *Headache*, 2017;57:64-75)

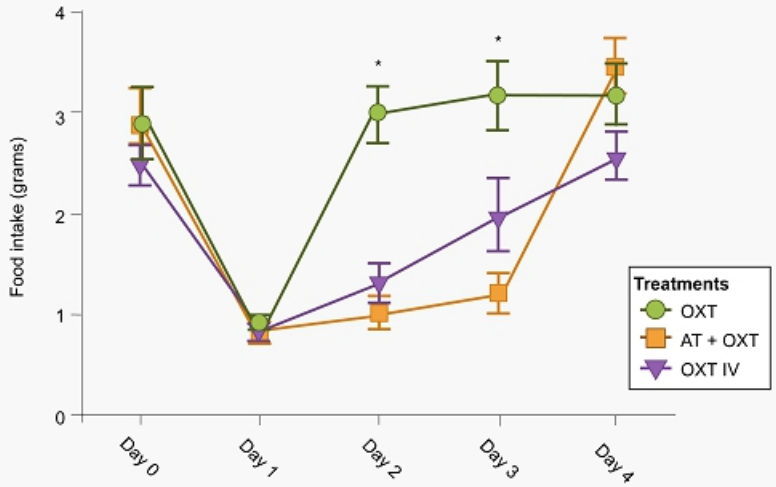
Thermal Hyperalgesia in Inflamed Facial Skin



OXT = oxytocin; *P <0.05; N = 6 per group

Tzavazis A., et al. *Headache*, 2017;57:64-75)

Reduced Food Intake with TMJ Pain



OXT = oxytocin; AT = Atosiban® ; IV = interveinal; *P <0.05; N = 8 per group

Tzavazis A., et al. *Headache*, 2017;57:64-75)

CNS PORTFOLIO

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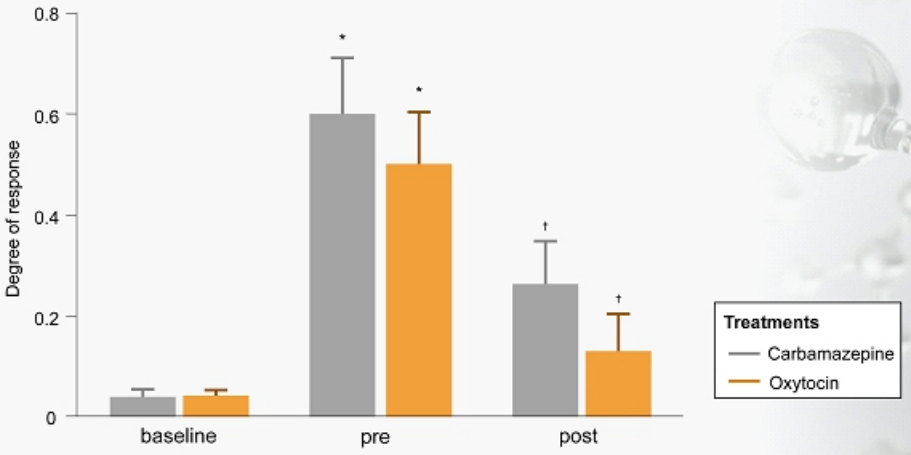
Mechanical Allodynia in Trigeminal Neuralgia



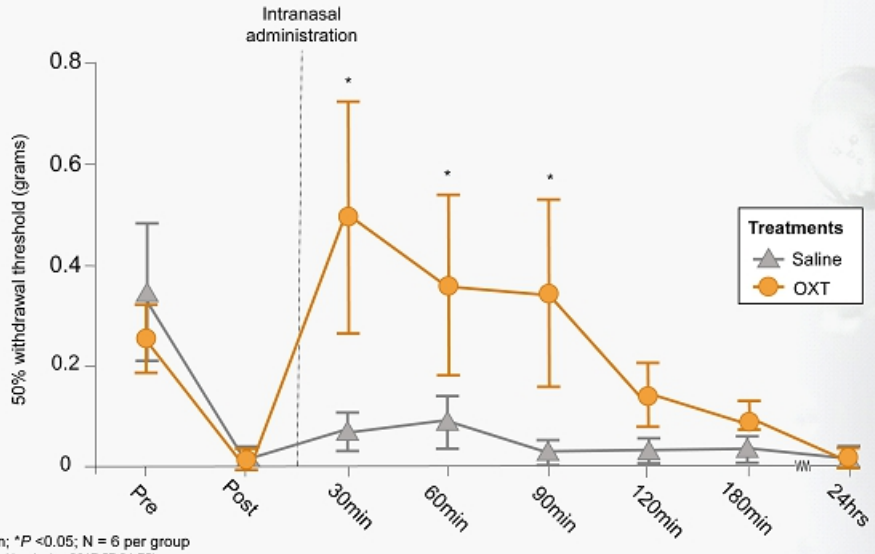
*P <0.05 pre vs baseline; †P<0.5 pre vs post; N = 4 per group

Tzavazis A., et al. *Headache*, 2017;57:64-75)

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Mechanical Allodynia After Facial Incision



OXT = oxytocin; *P <0.05; N = 6 per group

Tzavazis A., et al. *Headache*, 2017;57:64-75)

CNS PORTFOLIO

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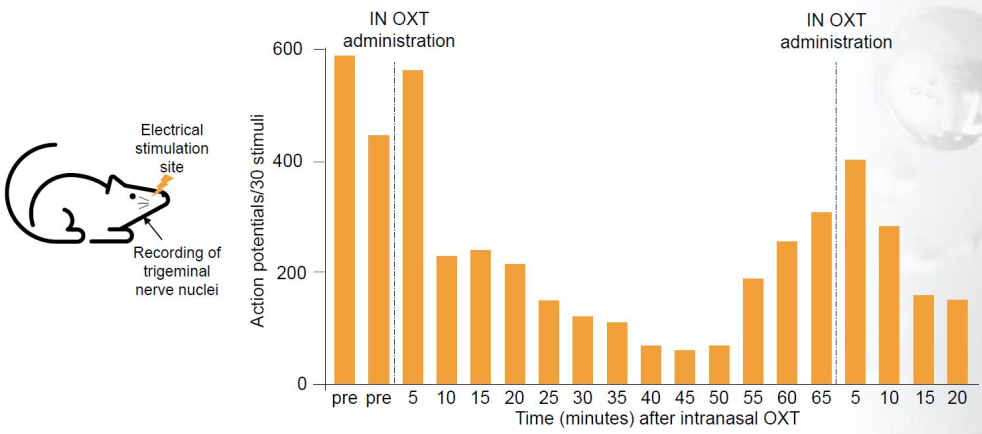
Totaled Responses of Representative Neuron Showing Overall Number of Action Potentials Before and After IN OXT Administration



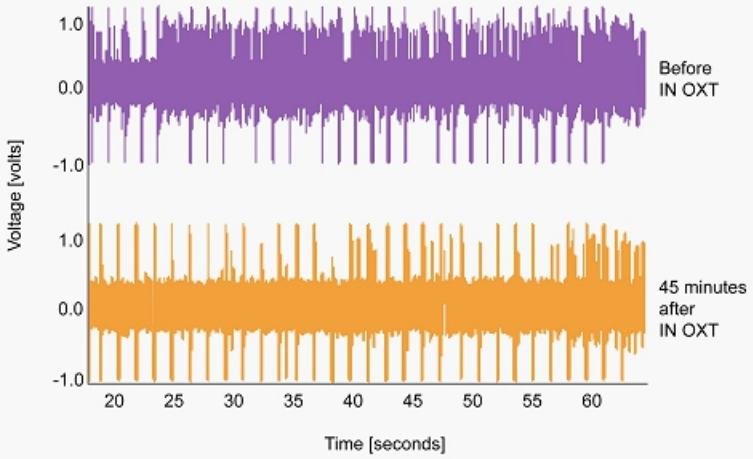
IN OXT = intranasal oxytocin; N = 1

Tzavazis A., et al. *Headache*, 2017;57:64-75)

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Recordings of Trigeminal Nuclei Neuron Before IN OXT Administration And After IN OXT Administration

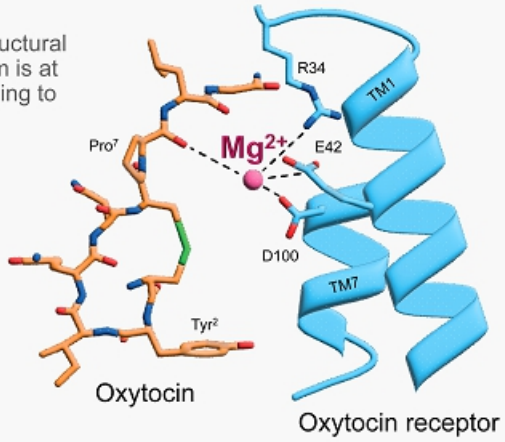


IN OXT = intranasal oxytocin

Tzavazis A., et al. *Headache*, 2017;57:64-75)

TNX-1900 for Migraine
Magnesium (Mg^{2+}) is at the Core of Oxytocin Binding[1]

TNX-1900 contains magnesium: Recent structural studies show magnesium is at the core of oxytocin binding to oxytocin receptor[1]

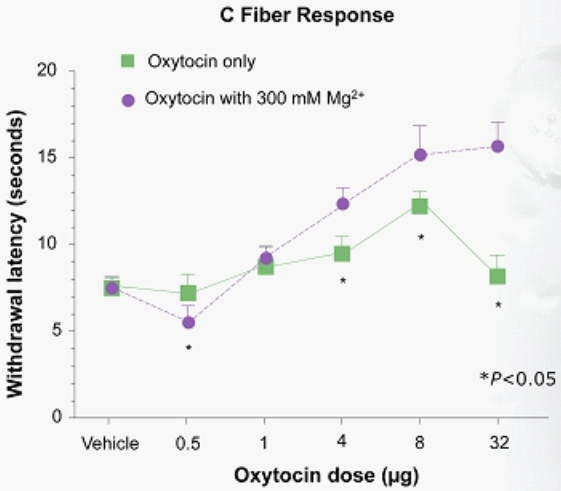


[1]Adapted from Meyerowitz, J.G., Robertson, M.J., Barros-Álvarez, X. *et al.* The oxytocin signaling complex reveals a molecular switch for cation dependence. *Nat Struct Mol Biol* 29, 274–281 (2022). https://doi.org/10.1038/s41594-022-00728-4

TNX-1900 for Migraine

Addition of Mg2+ Augments Oxytocin-Induced Analgesia in Animal Model

***in vivo* effect of Mg^{2+} ion addition with intranasal oxytocin-induced craniofacial analgesia on the withdrawal response time to noxious heat stimulation of the cheek of pre-inflamed rat**



Bharadwaj VN, et al. *Pharmaceutics*. 2022;14(5):1105.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

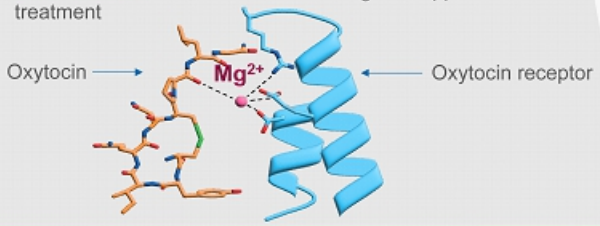
TNX-1900*: Prevention of Headache in Chronic Migraine

Intranasal Potentiated Oxytocin (OT) with Magnesium

PROFILE

- Intranasal OT has potential utility in treating migraine[1]
- Magnesium is known to potentiate the binding of OT to its receptor[2,3]
- One billion individuals worldwide suffer from migraines

Differentiator: Novel non-CGRP antagonist approach to treatment



Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Chronic Migraine

Additional Indications: Acute Migraine, Craniofacial Pain, Insulin Resistance, Binge Eating Disorder

Status: Phase 2 study PREVENTION enrollment complete[4]

Next Steps: Topline results from PREVENTION expected 4Q 2023

Investigator initiated Phase 2 trials in adolescent obesity, social anxiety disorder, and binge eating disorder are enrolling 3Q 2023

*TNX-1900 has not been approved for any indication. CGRP = calcitonin gene-related peptide.

[1]Tzabazis et al., 2017. *Headache*. 57 Suppl 2:64-75
[2]Antoni et al., 1989. *Biochem J*. 257(2):611-4
[3]Meyerowitz et al., 2022. *Nat Struct Mol Biol*. (3):274-281
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

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TNX-1900: Phase 2 PREVENTION Study Design

PREVENTION Study

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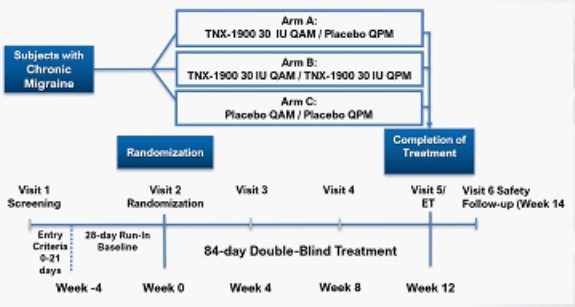
General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms– two treatment regimens and one placebo) in chronic migraine
- U.S. sites only
- Fully enrolled with 88 patients
- Topline results expected 4Q'23

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)



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

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17

TNX-1900 for the Treatment of Migraine: Mechanism of Action (continued)

CNS PORTFOLIO

CGRP: NEUROTRANSMITTER THAT HAS BEEN VALIDATED AS KEY MIGRAINE TARGET

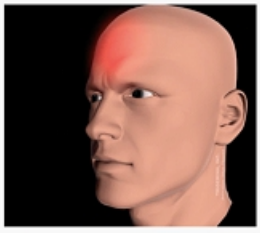
TNX-1900 believed to partially block release of CGRP in the trigeminal nerve

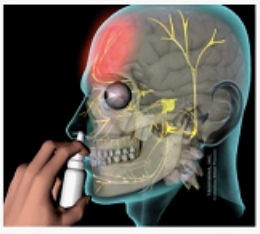
Proprietary Nasal to Brain Delivery

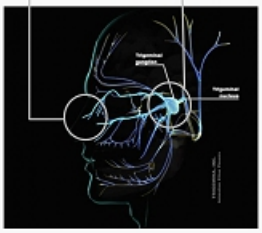
Permeates nasal mucosa

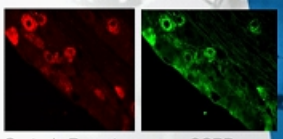
Transported to trigeminal system and brain

Oxytocin Receptors Co-Localize with CGRP in most Trigeminal Ganglia Neurons



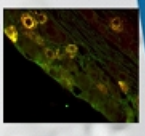






Oxytocin Receptors CGRP

Overlay of Oxytocin Receptors and CGRP Staining



HEAD PAIN

PATIENT USES TNX-1900

TARGETED DELIVERY

CGRP = calcitonin gene-related peptide

TONIX PHARMACEUTICALS

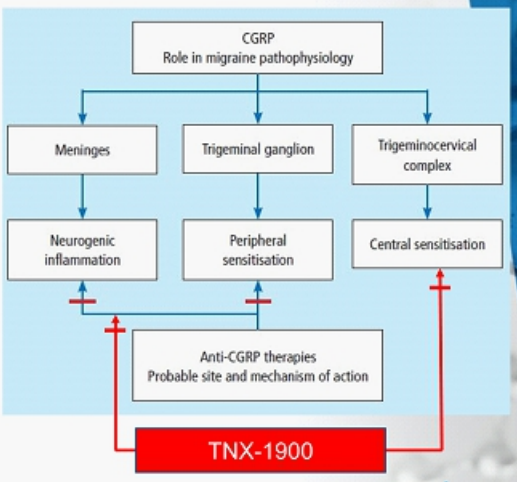
18

TNX-1900 for the Treatment of Migraine: Mechanism of Action (continued)

In animal models, intranasal oxytocin concentrates in the trigeminal system

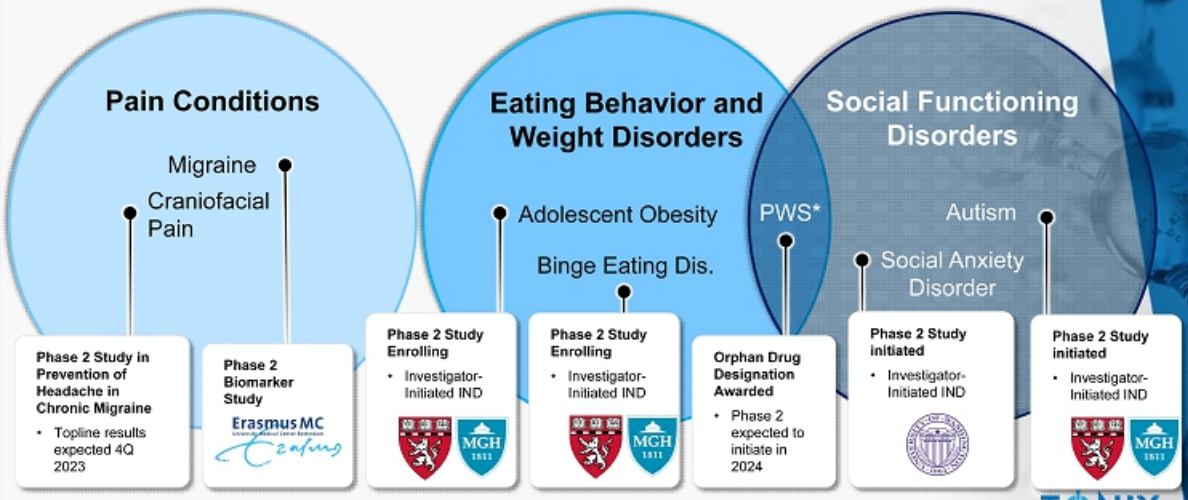
Inhibits trigeminal neuronal firing, and decreases CGRP (and PACP) release onto meningeal vasculature and within the brainstem

- **Believed to have effects on:**
  - Neurogenic inflammation
  - Peripheral sensitization, where CGRP otherwise promotes neuronal-glial signaling of pain to trigeminal ganglion
  - Central sensitization, in which CGRP otherwise causes sensitization of NMDA receptor, reducing threshold for glutamate – creating allodynia
- **Anti-CGRP antibodies may only work on inflammation and peripheral sensitization**
  - Due to poor blood brain barrier penetration



CGRP= calcitonin gene-related peptide; PACP = pituitary adenylate cyclase-activating peptide
Figure adapted from Krishnaswamy R et al. Anti-CGRP monoclonal antibodies: breakthrough in migraine therapeutics. Progress in Neurology and Psychiatry. Vol 23.03, July-Sept, 2019.

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



*Prader-Willi Syndrome

TNX-1900 – Other Studies in Collaboration with Academic Investigators

Pharmacodynamic biomarker study related to headache[1]

- Testing TNX-1900 effects on capsaicin- or electrical stimulation-induced forehead dermal blood flow in healthy female human volunteers
- Forehead dermal blood flow is considered a trigeminovascular biomarker for antimigraine drugs.
  - Both a CGRP inhibitor and a triptan have been successfully tested in the model and have been found to inhibit the forehead dermal blood flow response to capsaicin in migraineurs and healthy volunteers, respectively.[2,3]
- Erasmus University Medical Center, Dr. Antoinette Maassen van den Brink, Principal Investigator (P.I.)

Pediatric Obesity[4]

- 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[5]

- 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[6]

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

[1]Tonix Press Release May 22, 2023: https://ir.tonixpharma.com/news-events/press-releases/detail/1391/tonix-pharmaceuticals-announces-clinical-proof-of-concept
[2]de Vries Lentsch S, et al. 2022 "CGRP-mediated trigeminovascular reactivity in migraine patients treated with erenumab." *J Neurol Neurosurg Psychiatry*. Aug;93(8):911-912.
[3]Ibrahimi K, et al. 2017 "A human trigeminovascular biomarker for antimigraine drugs: A randomized double-blind, placebo-controlled, crossover trial with sumatriptan." *Cephalalgia*. Jan;37(1):94-98.
[4]Tonix Press Release July 10 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1404/tonix-pharmaceuticals-announces-initiation-of-enrollment-in
[5]Tonix Press Release July 17, 2023 – https://ir.tonixpharma.com/news-events/press-releases/detail/1405/tonix-pharmaceuticals-announces-agreement-and-initiation-o
[6]Tonix Press Release July 31, 2023 – https://ir.tonixpharma.com/news-events/press-releases/2023/07-31-Tonix-Pharmaceuticals-Announces-Enrollment-Initiated-in-the

CNS PORTFOLIO

TNX-1900 for Pediatric Autism

- Children with Autism Spectrum Disorder (ASD) are at risk for low bone density
- Preliminary data suggest that administration of oxytocin may favorably impact bone formation and strength
- Recent meta-analysis reported that plasma oxytocin levels tend to be lower in children with Autism Spectrum Disorder than controls[1]

"BOX" Investigator-Initiated Study in Pediatric Autism at MGH

- Randomized, placebo-controlled study to evaluate the effects of twice daily administration of TNX-1900 on bone measures in children with ASD
- Study subjects, ages six to 18 years old, will be randomized 1:1 to receive TNX-1900 twice per day or placebo for 12 months in the double-blind phase, followed by a six-month open label phase during which all study subjects will receive TNX-1900 twice daily
- Primary endpoint: difference between TNX-1900 compared to placebo groups in 12-month change in whole body less head bone mineral density Z-scores
  - Z-score compares one's bone density to the average bone density of age and gender matched controls

[1]John S and Jaeggi, AV. *Autism*. 2021. 25:2152-2161

CNS PORTFOLIO

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

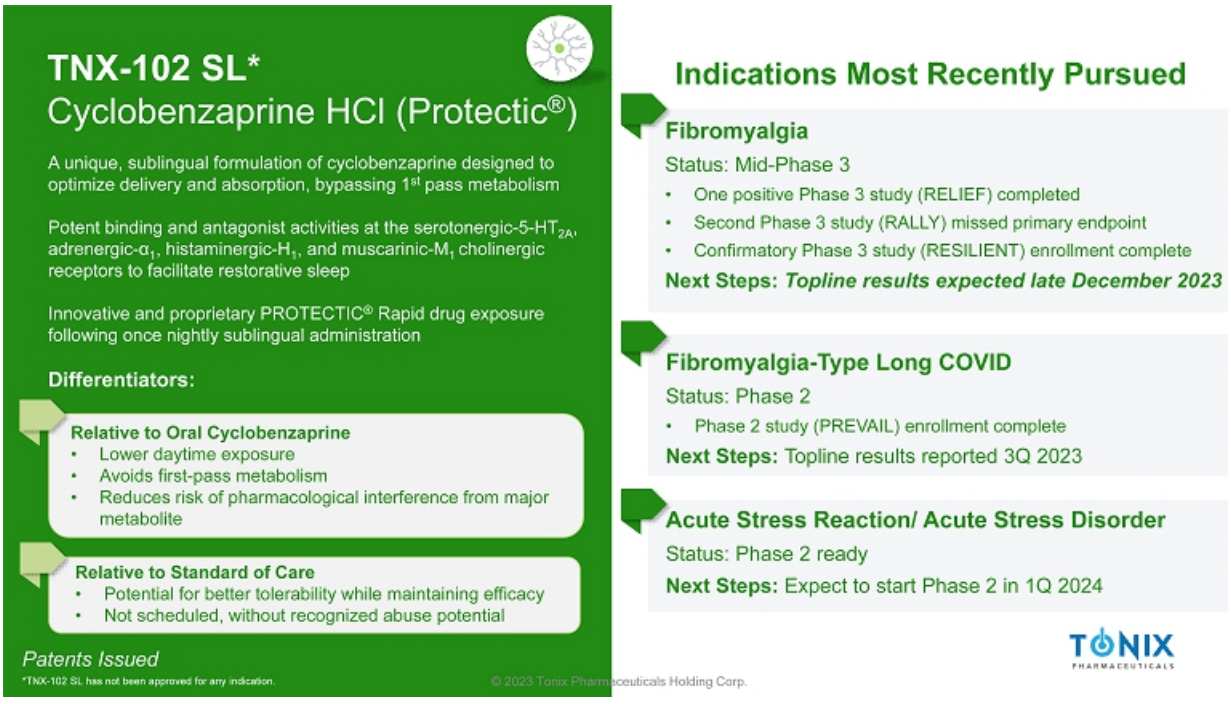
[1]Miller et al., 2011. *Am J Med Genet A.* 155A(5):1040-1049
[2]Butler et al., 2017. *Genet Med.* 19(6):635-642
[3]Butler MG. NORD. Updated 2018. Accessed May 25, 2022. https://rarediseases.org/rare-diseases/prader-willi-syndrome/
[4]Prader-Willi Syndrome Association USA. Accessed May 25, 2022. https://www.pwsausa.org/what-is-prader-willi-syndrome/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

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

THANK YOU

Exhibit 99.04



TNX-102 SL*: Fibromyalgia
Cyclobenzaprine Protectic® Sublingual Tablets

CNS PORTFOLIO

PROFILE

Fibromyalgia (FM) is a chronic pain disorder resulting from amplified sensory and pain signaling within the CNS

- Afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women[1]
- Symptoms include chronic widespread pain, nonrestorative sleep, fatigue, and cognitive dysfunction
- Patients struggle with daily activities, have impaired quality of life, and frequently are disabled
- Physicians and patients report common dissatisfaction with currently marketed products

When the check engine light malfunctions, the light is on even though the car is not malfunctioning

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia

Additional Indications: Long COVID, PTSD, Agitation in Alzheimer's, Alcohol Use Disorder

Status: One Positive Phase 3 study RELIEF completed[2]

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT enrollment complete

Next Steps: Topline results expected late December 2023

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

[1]American Chronic Pain Association (www.theacpa.org, 2019)
[2]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.

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TNX-102 SL: Fibromyalgia
Program Update

CNS PORTFOLIO

Phase 3 Study, RESILIENT, will compare TNX-102 SL 5.6 mg and placebo

- First patient enrolled in April 2022
- Parallel design, double-blind, randomized placebo-controlled study, all US sites
- Primary endpoint is pain at Week 14 analyzed by MMRM with MI
- Projecting adverse event-related discontinuations to decrease towards rates in RELIEF and PTSD Studies

Phase 3 Study, RALLY, comparison of TNX-102 SL 5.6 mg and placebo

- As expected from interim analysis results published in July 2021, RALLY Study missed primary endpoint
- Unexpected ~80% increase in adverse event-related discontinuations in both drug and placebo arms
- Multiple imputation approach on 'Missing Data' attenuated statistical significance of efficacy endpoints'
- TNX-102 SL was generally well tolerated with overall adverse event profile comparable to prior studies; no new safety signals observed

TONIX PHARMACEUTICALS

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)

TONIX PHARMACEUTICALS

TNX-102 SL: RALLY Study
Increased Adverse Event-Related Discontinuations

CNS PORTFOLIO

Increases in AE-Related discontinuations in RALLY study compared with RELIEF study in both placebo and TNX-102 SL groups

	RALLY (F306)	RELIEF (F304)	RALLY (F306)	RELIEF (F304)
	Placebo		TNX-102 SL	
Patients with at least one TEAE leading to early discontinuation	6.2%	3.5%	15.2%	8.5%
Ratio of patients with at least one TEAE leading to early discontinuation in F306 to F304 (F306/F304)	1.77		1.79	

TEAE = treatment-emergent adverse event

Adverse events in RALLY

- TNX-102 SL 5.6 mg was well tolerated.
- Among participants randomized to drug and placebo groups, 73.8% and 81.4%, respectively, completed the 14-week dosing period.
- As expected, based on prior TNX-102 SL studies, oral administration site reactions were higher in the drug treatment group, including rates of tongue/mouth numbness, pain/discomfort of tongue/mouth, and product taste abnormal (typically a transient bitter aftertaste)
- Tongue/mouth numbness or tingling and product aftertaste were local effects nearly always temporally related to dose administration and transiently expressed (<60 minutes) in most occurrences.
- Adverse events resulted in premature study discontinuation in TNX-102 SL and placebo groups at rates of 15.2% and 6.2%, respectively
- Approximately 95% of adverse events in both the drug treatment and placebo groups were rated as mild or moderate.

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TNX-102 SL: RALLY Study
Impact of Missing Data on *p*-Values in RALLY

Since 2010, FDA has generally required that "missing data" be accounted for by using a statistical method called "multiple imputation" or MI

- MI data approach can attenuate *p*-values in the setting of missing data

RALLY (F306) results without MI treatment for missing data are comparable to prior positive RELIEF (F304) study

- Efficacy results in the table without MI are labelled "MMRM"

MI missing data treatment attenuated *p*-values in RALLY

- At the current time, we expect MI will be part of the statistical analysis for the RESILIENT trial

	RALLY (F306)			
	MMRM+MI*		MMRM**	
Endpoints	LSMD (SE)	*p*-value	LSMD (SE)	*p*-value
Pain by Diary[#]	-0.2 (0.16)	**0.115**	-0.4 (0.16)	0.014
FIQR Symptom domain	-1.9 (1.52)	0.216	-3.4 (1.55)	0.030
FIQR Function domain	-0.4 (1.46)	0.797	-1.6 (1.48)	0.266
PROMIS Sleep Disturbance	-2.3 (0.80)	0.004	-3.3 (0.73)	<0.001
PROMIS Fatigue	-1.2 (0.74)	0.101	-2.0 (0.73)	0.007
Sleep Quality by Diary	-0.3 (0.16)	0.094	-0.4 (0.16)	0.008
	RELIEF (F304)			
	MMRM+MI*		MMRM**	
Endpoints	LSMD (SE)	*p*-value	LSMD (SE)	*p*-value
Pain by Diary[#]	-0.4 (0.16)	**0.010**	-0.5 (0.16)	0.004
FIQR Symptom domain	-4.3 (1.60)	0.007	-5.6 (1.60)	<0.001
FIQR Function domain	-4.4 (1.69)	0.009	-5.2 (1.63)	0.001
PROMIS Sleep Disturbance	-2.9 (0.82)	<0.001	-3.3 (0.82)	<0.001
PROMIS Fatigue	-1.8 (0.76)	0.018	-2.1 (0.79)	0.007
Sleep Quality by Diary	-0.6 (0.17)	<0.001	-0.7 (0.17)	<0.001

FIQR = Fibromyalgia Impact Questionnaire-Revised; LSMD = least squares mean difference (between TNX-102 SL and placebo); MMRM = mixed model repeated measures; MI = multiple imputation; PROMIS = Patient-Reported Outcomes Measurement Information System; SE = standard error

* MMRM with MI was the pre-specified primary analysis

**MMRM without MI was a pre-specified analysis

[#] Primary efficacy endpoint: change from baseline in the weekly average of daily diary pain severity numerical rating scale scores

CNS PORTFOLIO

TONIX PHARMACEUTICALS

TNX-102 SL*: Fibromyalgia-Type Long COVID (PASC)
Cyclobenzaprine Protectic® Sublingual Tablets

PROFILE

- Occurs in approximately 19% of recovered COVID-19 patients[1]
- As many as 40% of Long COVID patients experience multi-site pain, a hallmark of fibromyalgia[2,3]
- Symptoms of Long COVID, like multi-site pain, fatigue and insomnia, are the hallmarks of chronic pain syndromes like fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)
- In August 2022, the HHS released the National Research Action Plan on Long COVID[4] which endorses the connection between Long COVID and ME/CFS

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia-Type Long COVID (PASC)

Additional Indications: Fibromyalgia, PTSD, Agitation in Alzheimer's, Alcohol Use Disorder

Status: Phase 2 study PREVAIL topline reported

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

Patents Issued

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

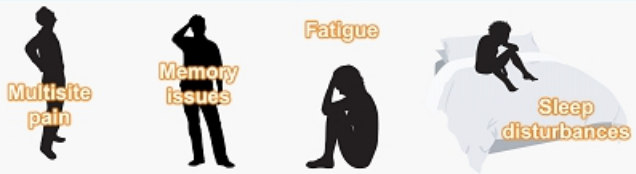
[1]June 22, 2022- CDC - https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm
[2]Harris, H, et al. Tonix data on file. 2022
[3]TriNetX Analytics
[4]Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

About Fibromyalgia-Type Long COVID

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

TONIX PHARMACEUTICALS

TNX-102 SL: Phase 2 PREVAIL Study Design

PREVAIL Study

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***

TONIX PHARMACEUTICALS

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

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/3Z6FQHQ
[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.

Next Steps

Tonix plans to meet with FDA to discuss a path to registration

- Expected date of End of Phase 2 meeting is 1st Quarter 2024

Fatigue is the principal symptom overlapping with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and fibromyalgia syndromes

- Expected date of fibromyalgia topline is late December 2023

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

THANK YOU

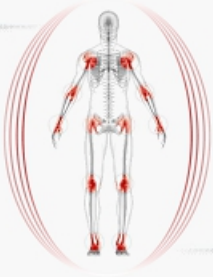
APPENDIX

TONIX PHARMACEUTICALS

Chronic Overlapping Pain Conditions (COPC) Believed to Result from Shared Brain Processes

- COPC is a set of disorders that coaggregate; these disorders can include but are not limited to[1,2]:

- Temporomandibular disorder
- Fibromyalgia
- Irritable bowel syndrome
- Vulvodynia
- CFS/ME[3]
- Interstitial cystitis/painful bladder syndrome



- Endometriosis
- Chronic tension-type headache
- Migraine headache
- Chronic lower back pain

- Similar central mechanisms play significant roles in all pain conditions, even those with known peripheral contributions[1,2]

CNS PORTFOLIO

[1]Maixner W, et al. *J Pain*. 2016;17(9 Suppl):T93-T107.
[2]Veasley C, et al. http://www.chronicpainresearch. org/public/CPRA_WhitePaper_2015-FINAL-Digital.pdf. Published May 2015. Accessed July 26, 2021.
[3]CFS/ME – chronic fatigue syndrome/myalgic encephalomyelitis

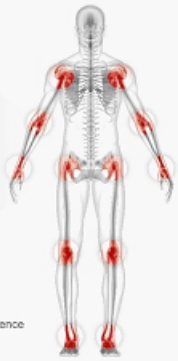
TONIX PHARMACEUTICALS

Role of Infections in Triggering Fibromyalgia or Chronic fatigue (CFS)-Like Illnesses

- Symptoms of Long COVID, like multi-site pain, fatigue and insomnia, are the hallmarks of chronic pain syndromes like fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).
- In August 2022, the HHS released the *National Research Action Plan on Long COVID*[1] which endorses the connection between Long COVID and chronic fatigue syndrome.

Infection initiates an autoreactive process, which affects several functions, including brain and energy metabolism[2-7]

- Infections can trigger any of these conditions in approximately 10% of exposed individuals
- The initial location of the infection determines the subsequent pain syndrome
- Any type of infectious diarrhea will trigger irritable bowel syndrome (IBS) in 10% to 20% of those exposed



[1]Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID, 200 Independence Ave SW, Washington, DC 20201.
[2]Blomberg J, et al. Front Immunol. 2018;9:229. Published 2018 Feb 15.
[3]Warren JW, et al. Urology. 2008;71(6):1085-1090.
[4]Buskila D, et al. Autoimmun Rev. 2008;8(1):41-43.
[5]Hickie I, et al. BMJ. 2006;333(7568):575.
[6]Parry SD, et al. Am J Gastroenterol. 2003;98(9):1970-1975.
[7]Halvorson HA, et al. Am J Gastroenterol. 2006;101(8):1894-1942.

New Classification for Central Pain: Nociplastic Pain[1]

Pain due to the activation of nociceptors that arises from actual or threatened damage to non-neural tissue

Nociceptive pain

Neuropathic pain

Pain caused by a lesion or disease of the somatosensory nervous system

Pain that arises from altered nociception despite no clear evidence of tissue damage, or for disease or lesion of the somatosensory system causing the pain

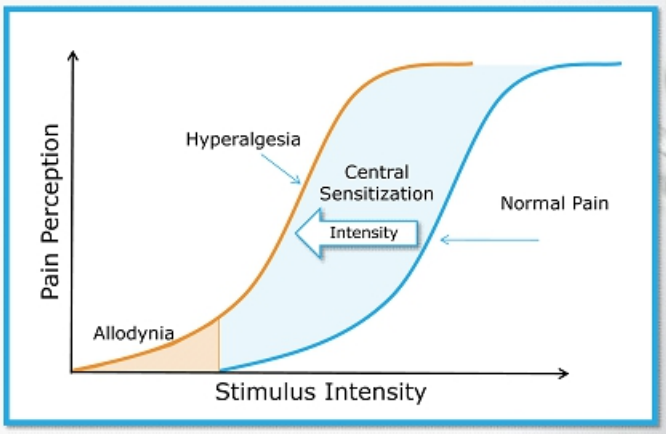
Nociplastic pain

Central and Peripheral Sensitization

[1]Trouvin AP, et al. *Best Pract Res Clin Rheumatol*. 2019;33(3):101415.

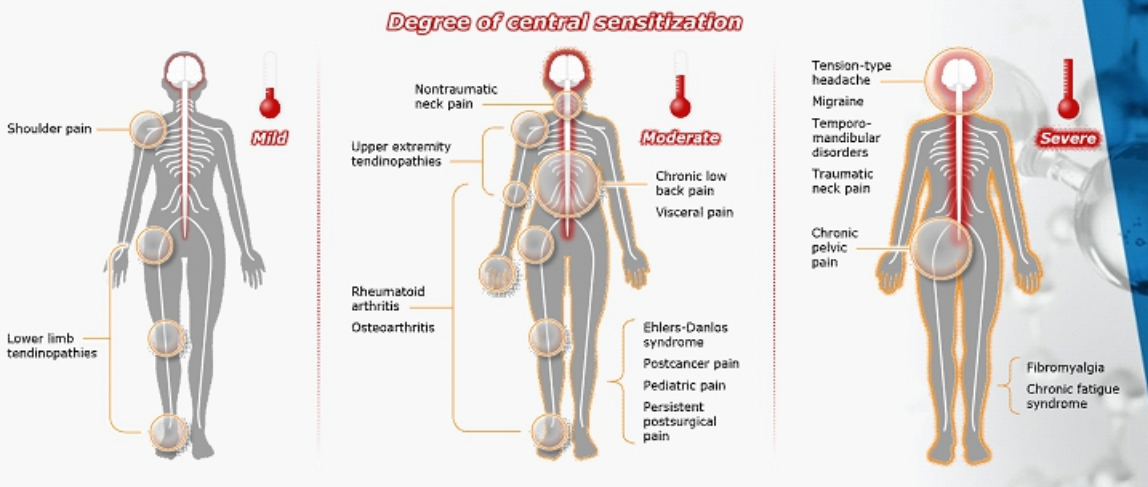
Central Sensitization (CS)
A Feature of Many Nociplastic Pain Syndromes

- CS is caused by amplified neural signaling in CNS pain circuits[1-3]
- Patients with CS perceive higher pain to a slightly noxious stimuli than in non-CS individuals (hyperalgesia)[1]
- Severe CS can lead to hypersensitivity to stimuli that are not typically painful (allodynia)[2]
- CS varies in severity and is observed in syndromes including FM and ME/CFS[1,3]



[1]CFS/ME – chronic fatigue syndrome/myalgic encephalomyelitis
[2]FM - fibromyalgia
[3]Nijs J, et al. *Lancet*. 2021;3(5):e383-e392.

Central Sensitization (CS)
Can Occur in a Range of Diseases and Conditions



Nijs J, et al. *Lancet*. 2021;3(5):e383-e392.