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

FORM 8-K

CURRENT REPORT

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

Date of report (date of earliest event reported): August 12, 2024

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

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

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

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

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

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

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

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

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

Emerging growth company ☐

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

Item 7.01 Regulation FD Disclosure.

On August 12, 2024, the Company announced data from a Phase 3 RESILIENT trial of its Tonmya™ (TNX-102 SL, cyclobenzaprine HCl sublingual tablets) product candidate for the management of fibromyalgia in a poster presentation (the "Presentation") at the International Association for the Study of Pain 2024 World Congress on Pain ("IASP"). A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference. A Copy of the Presentation is furnished hereto as Exhibit 99.02 and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.01 and 99.02 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

On August 12, 2024, the Company presented data from the Presentation at the IASP. The Presentation, entitled, "*Targeting Fibromyalgia Non-Restorative Sleep with Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl): Results of the Positive Phase 3 RESILIENT Trial Consistent with Syndromal Improvement,*" presented a new *post hoc* analysis showing correlations between improvements in pain and sleep quality at Week 14 in both treatment groups of the Resilient trial. The Company believes that these findings are consistent with the hypothesis that improving sleep quality may lead to a corresponding improvement in pain, supporting the targeting of sleep to achieve syndromal improvement in fibromyalgia.

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities

and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

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

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description
99.01	Press Release of the Company, August 12, 2024
99.02	Targeting Fibromyalgia Non-Restorative Sleep with Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl): Results of the Positive Phase 3 RESILIENT Trial Consistent with Syndromal Improvement
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

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

TONIX PHARMACEUTICALS HOLDING CORP.

Date: August 12, 2024

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

Exhibit 99.01

Tonix Pharmaceuticals Presented Data and Analyses of TNX-102 SL Treatment Effects on Fibromyalgia, the Prototypic Nociplastic Pain Syndrome, at the IASP 2024 World Congress on Pain

Bedtime TNX-102 SL (sublingual cyclobenzaprine HCl) treatment in the Phase 3 RESILIENT study resulted in statistically significant improvement in the primary endpoint of fibromyalgia nociplastic pain and in all six key secondary endpoints, including sleep quality

Post hoc analyses highlight the strong correlations between improvements in nociplastic pain and sleep quality

Nociplastic pain originates from altered pain perception in the brain and is the type of pain that manifests in fibromyalgia and other chronic overlapping pain conditions (COPCs)

FDA granted TNX-102 SL Fast Track designation for the management of fibromyalgia; NDA submission on track for second half 2024

CHATHAM, N.J., August 12, 2024 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, presented data in a poster presentation at the International Association for the Study of Pain (IASP) 2024 World Congress on Pain, held August 5-9, 2024 in Amsterdam, the Netherlands. A copy of the Company's poster presentation titled, " *Targeting Fibromyalgia Non-Restorative Sleep with Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl): Results of the Positive Phase 3 RESILIENT Trial Consistent with Syndromal Improvement*", is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

TNX-102 SL met the pre-specified primary endpoint in the Phase 3 RESILIENT study, significantly reducing daily pain compared to placebo (p-value=0.00005) in participants with fibromyalgia. TNX-102 SL also demonstrated broad syndromal benefits with statistically significant improvement in all six pre-specified key secondary endpoints including those related to improving sleep quality, reducing fatigue, and improving patient global ratings and overall fibromyalgia symptoms and function. A new *post hoc* analysis showed correlations between improvements in pain and sleep quality at Week 14, supporting the concept that targeting sleep quality has the potential to achieve syndromal improvement in fibromyalgia. TNX-102 SL was well tolerated with an adverse event profile comparable to prior studies and no new safety signals observed.

"Approximately 50 years ago, the central role of nonrestorative sleep in the pathogenesis and persistence of fibromyalgia was recognized by Dr. Harvey Moldofsky[1,2]", said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "TNX-102 SL was designed as a bedtime treatment to target non-restorative sleep and improve sleep quality. The statistically significant results of TNX-102 SL in two positive Phase 3 studies provide evidence of the activity and tolerability of TNX-102 SL in fibromyalgia and also support the critical role of sleep quality in the pathogenesis, persistence and exacerbations of fibromyalgia originally proposed by Dr. Moldofsky."

Greg Sullivan, M.D., Chief Medical Officer, added, "Today, fibromyalgia is recognized as the prototypic 'nociplastic syndrome'. Understanding nociplastic syndromes is crucial for developing effective treatment strategies for chronic overlapping pain conditions (COPCs)[3,4,5]. Traditional analgesics like NSAIDs or opioids often prove ineffective if not deleterious in these conditions. In contrast, TNX-102 SL provided broad-spectrum symptom relief in the RESILIENT study. We believe TNX-102 SL has the potential to be the first new treatment option for fibromyalgia patients in 15 years."

TNX-102 SL was recently granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for the management of fibromyalgia. Tonix remains on track to submit an NDA to the FDA in the second half of 2024 for TNX-102 SL for the management of fibromyalgia.

1 Moldofsky H, et al. *Psychosom Med.* 1975;37:341-51

2 Moldofsky H, Scarisbrick P. *Psychosom Med.* 1976;38:35-44

3 Fitzcharles MA, et al. *Lancet.* 2021;397:2098-110

4 Clauw DJ. *Ann Rheum Dis.* Published Online First: 2024

5 Kaplan CM, et al. *Nat Rev Neurol.* 2024;20, 347–363

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 more than 10 million adults in the U.S., the majority of whom are women. Symptoms of fibromyalgia include chronic widespread pain, non-restorative sleep, fatigue, and brain fog (or cognitive dysfunction). Other associated symptoms include mood disturbances, including anxiety and depression, headaches, and abdominal pain or cramps. 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. According to the recent report from the U.S. National Academies of Sciences, fibromyalgia is a diagnosable condition that may also occur in the context of Long COVID.

About TNX-102 SL

TNX-102 SL is a centrally acting, non-opioid, non-addictive, bedtime investigational drug. The tablet is a patented sublingual formulation of cyclobenzaprine hydrochloride developed for the management of fibromyalgia. In December 2023, the company announced highly statistically significant and clinically meaningful topline results in RESILIENT, the second pivotal Phase 3 clinical trial of TNX-102 SL for the management of fibromyalgia. In the study, TNX-102 SL met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.00005) in participants with fibromyalgia. Statistically significant and clinically meaningful results were also seen in all six key secondary endpoints related to improving sleep quality, reducing fatigue and improving overall fibromyalgia symptoms and function. RELIEF, the first statistically significant Phase 3 trial of TNX-102 SL in fibromyalgia, was completed in December 2020. It met its pre-specified primary endpoint of daily pain reduction compared to placebo (p=0.010) and showed activity in key secondary endpoints. In both pivotal studies, the most common treatment-emergent adverse event was tongue or mouth numbness at the administration site, which was temporally related to dosing, self-limited, never rated as severe, and rarely led to study discontinuation (one participant in each study). TNX-102 SL was recently granted Fast Track Designation by the FDA for the management of fibromyalgia and remains on track to submit an NDA to the U.S. Food and Drug Administration in the second half of 2024.

About Nociplastic Pain

Nociplastic pain is the third category of pain distinct from nociceptive pain and neuropathic pain. Nociplastic pain is characterized by pain arising from altered nociception despite no evidence of actual or threatened tissue damage causing activation of peripheral nociceptors or somatosensory system disease or lesion. Its underlying pathophysiology involves altered pain processing by the central nervous system (CNS). Nociplastic syndromes, officially recognized by the International Association for the Study of Pain (IASP) in 2017, also include several other chronic overlapping pain conditions: myalgic encephalomyelitis/chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorders, forms of chronic back pain and chronic headache. The pathophysiology of nociplastic pain involves central sensitization (CS), where neurons of the CNS become hyperexcitable, amplifying pain signals. CS can be triggered by peripheral pain stimuli, emotional stress, or other factors, leading to persistent pain despite no peripheral nociceptive input.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for TNX-102 SL, a product candidate for which two statistically significant Phase 3 studies have been completed for the management of fibromyalgia. The FDA has granted Fast Track designation to TNX-102 SL for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic designed to treat cocaine intoxication that has Breakthrough Therapy designation. Tonix's immunology development portfolio consists of biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. Tonix also has product candidates in development in the areas of rare disease and infectious disease. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

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

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, 2023, as filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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

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

Media Contact
Katie Dodge
LaVoieHealthScience
kdodge@lavoiehealthscience.com
(978) 360-3151

Exhibit 99.02

Targeting Fibromyalgia Non-Restorative Sleep with Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl): Results of the Positive Phase 3 RESILIENT Trial Consistent with Syndromal Improvement

TNX-102 SL (Tonmya®) is an investigational drug and has not been approved for any indication
*Tonmya is conditionally accepted by the US FDA as the tradename for TNX-102 SL

Seth Lederman, MD[1], Mary Kelley, MPH[1], Ben Vaughn, MS,[2] Jean Engels, MS,[1] Gregory M. Sullivan, MD[1]
[1]Tonix Pharmaceuticals, Inc., Chatham, NJ, USA; [2]Rho Inc, Chapel Hill, NC, USA

INTRODUCTION

Fibromyalgia (FM) is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system (CNS). FM afflicts an estimated 6 to 12 million adults in the U.S., the majority of whom are women. Symptoms of FM include chronic widespread pain, nonrestorative sleep, fatigue, and cognitive dysfunction. Physicians and patients report common dissatisfaction with currently marketed products. TNX-102 SL (Tonmya™)* is an innovative sublingual tablet formulation of cyclobenzaprine HCl (CBP) which is distinct from oral immediate-release CBP in providing rapid sublingual transmucosal absorption, greater bioavailability, and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. CBP potently binds and antagonizes 5-HT_{2A}-serotonergic, α_1-adrenergic, M_1-muscarinic acetylcholine, and H_1-histaminergic receptors, each of which impacts aspects of sleep architecture. TNX-102 SL is believed to work in FM by targeting improvement in sleep quality.

About 50 years ago, the central role of nonrestorative sleep in the pathogenesis and persistence of FM was recognized by Dr. Harvey Moldofsky.[1,2] More recently, FM has been understood as the prototypic 'nociplastic syndrome'. Nociplastic pain, a third category of pain distinct from nociceptive pain and neuropathic pain, is characterized by pain arising from altered nociception despite no evidence of actual or threatened tissue damage causing activation of peripheral nociceptors or somatosensory system disease or lesion. Its underlying pathophysiology involves altered pain processing by the central nervous system (CNS). Nociplastic syndrome, officially recognized by the International Association for the Study of Pain (IASP) in 2017, also includes several other chronic overlapping pain conditions (COPCs): myalgic encephalomyelitis/chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorders, forms of chronic back pain and chronic headache. The pathophysiology of nociplastic pain involves central sensitization (CS), where neurons of the CNS become hyperexcitable, amplifying pain signals. CS can be triggered by peripheral pain stimuli, emotional stress, or other factors, leading to persistent pain despite no peripheral nociceptive input.

Understanding nociplastic syndrome is crucial for developing effective treatment strategies. Traditional analgesics like NSAIDs or opioids often prove ineffective if not deleterious.

The current study of TNX-102 SL assesses its efficacy and safety in fibromyalgia and a test of the role of sleep quality in the pathogenesis, persistence and exacerbations of fibromyalgia.

METHODS

Across 33 U.S. sites, RESILIENT enrolled 457 FM patients; the intent-to-treat (ITT) population received TNX-102 SL 2.8 mg for 2 weeks followed by 5.6 mg for 12 weeks (N=231), or matching placebo (N=225) for 14 weeks. The primary endpoint was change from baseline at Week 14 in weekly average of daily diary pain numeric rating scale (NRS) scores analyzed by mixed model repeated measures (MMRM) with multiple imputation (MI) for missing data. Key secondary endpoints included Patient Global Impression of Change (PGIC), Fibromyalgia Impact Questionnaire - Revised (FIQR) Symptoms and Function domains, PROMIS Sleep Disturbance and Fatigue instruments, and daily diary sleep quality NRS scores. Other endpoints included the Beck Depression Inventory-II (BDI-II). Safety was assessed by adverse events, vital signs/weight, physical exams, and Changes in Sexual Functioning Questionnaire short form (CSFQ-14). Continuous key secondary endpoints were analyzed in same manner as primary, MMRM with MI. The responder analysis of PGIC was by Pearson Chi-Squared with differences in proportions from Z-test. Exploratory endpoints, BDI-II total score and individual FIQR item scores, by MMRM, and the CSFQ-14 analyses, by ANCOVA, were not corrected for multiple comparisons.

RESULTS

A total of 813 subjects were assessed for eligibility, 457 were randomized, and 456 were in the Intent-to-Treat population. Of those randomized, 231 received TNX-102 SL and 225 received placebo. Completion rates were 81.0% for TNX-102 SL and 79.2% for placebo. Discontinuation reasons included: adverse event (14 TNX-102 SL; 8 placebo); insufficient therapeutic response (2 TNX-102 SL; 8 placebo). Demographics and baseline characteristics are shown in **Table 1.**

Table 1: Demographics and Baseline Characteristics in Safety Population

	TNX-102 SL (N=231)	Placebo (N=226)	Total (N=457)
Females, n (%)	224 (97.0%)	212 (93.8%)	436 (95.4%)
Age in years, mean (SD)	49.3 (10.45)	49.5 (11.32)	49.4 (10.88)
Race, n (%)			
White/Caucasian	194 (84.0%)	192 (85.0%)	386 (84.5%)
Black/African American	32 (13.9%)	27 (11.9%)	59 (12.9%)
Asian	1 (0.4%)	5 (2.2%)	6 (1.3%)
Ethnicity, n (%)			
Hispanic or Latino	36 (15.6%)	35 (15.5%)	71 (15.5%)
BMI, kg/m², mean (SD)	31.1 (6.34)	31.1 (6.32)	31.1 (6.33)
Employed currently, n (%)	147 (63.6%)	150 (66.4%)	297 (65.0%)
Unable to work due to FM symptoms, n (%)	13 (5.6%)	12 (5.3%)	25 (5.5%)
Education, some college or beyond, n (%)	187 (81.0%)	193 (85.4%)	380 (83.2%)
Duration of FM disease in years, mean (SD)	8.6 (8.44)	9.9 (9.52)	9.2 (9.00)
Pain at baseline, NRS, mean (SD)	5.9 (1.05)	5.9 (1.08)	NC

NC = not calculated

As seen in **Table 2**, TNX-102 SL demonstrated highly statistically significant improvement in primary endpoint of mean weekly pain scores over placebo at Week 14 ($p = 0.00005$) (**Figure 1**). Furthermore, all six key secondary endpoints were statistically significant (all p-values ≤ 0.001). Effect size for primary endpoint was 0.38 and all five continuous key secondaries in range of 0.30 – 0.50. All items, including affective and cognitive items on FIQR in **Table 3** show similar improvement by MMRM. Correlation between sleep and pain improvement was similar in drug and placebo groups in **Figure 2**. Safety and tolerability is presented in **Table 4**.

Table 2: Summary of Results of the Primary and 6 Key Secondary* Endpoints at Week 14

	PBO LS Mean (SE)	TNX-102 SL LS Mean (SE)	LS Mean (SE) Difference	*P*-value	Effect Size
Primary Endpoint					
Daily Diary Pain ratings	-1.16 (0.118)	-1.82 (0.116)	-0.65 (0.161)	**0.00005**	0.38
Key Secondary Endpoints					
PGIC, responders†	19.10%	35.10%	16.0% (7.9%, 24.0%)	0.00013	#
FIQR – Symptoms domain	-8.36 (1.173)	-16.02 (1.166)	-7.67 (1.619)	0.000002	0.44
FIQR – Function domain	-6.81 (1.207)	-12.22 (1.190)	-5.41 (1.661)	0.001	0.30
PROMIS Sleep Disturbance	-4.20 (0.564)	-8.44 (0.575)	-4.24 (0.789)	0.0000001	0.50
PROMIS Fatigue	-4.16 (0.559)	-7.18 (0.550)	-3.01 (0.768)	0.00009	0.37
Diary Sleep Quality ratings	-1.20 (0.121)	-1.77 (0.119)	-0.57 (0.168)	0.0007	0.32

*In order of statistical serial gate-keeping hierarchy to control overall Type 1 error. †PGIC was a responder analysis; difference in proportions [95% CI].

Table 3: FIQR Items* at Week 14

	TNX-102 SL (N=185)	PBO (N=179)	LS Mean (SE) Difference	95% CI	*P*-value
Please rate your level of… (past 7 days)					
Level of pain	-2.2 (0.15)	-1.2 (0.15)	-1.0	-1.4 to -0.6	<0.001
Level of energy	-1.6 (0.16)	-0.9 (0.17)	-0.8	-1.2 to -0.3	<0.001
Level of stiffness	-2.0 (0.17)	-1.2 (0.17)	-0.8	-1.3 to -0.3	<0.001
Quality of sleep	-2.9 (0.19)	-1.5 (0.19)	-1.4	-2.0 to -0.9	<0.001
Level of depression	-0.9 (0.15)	-0.2 (0.15)	-0.8	-1.2 to -0.4	<0.001
Level of memory problems	-1.3 (0.16)	-0.6 (0.17)	-0.8	-1.2 to -0.3	0.001
Level of anxiety	-1.2 (0.17)	-0.4 (0.17)	-0.8	-1.2 to -0.3	0.001
Level of tenderness to touch	-2.1 (0.18)	-1.3 (0.18)	-0.8	-1.3 to -0.3	0.001
Level of balance problems	-1.1 (0.15)	-0.6 (0.15)	-0.5	-0.9 to -0.1	0.015
Level of sensory sensitivity†	-1.8 (0.18)	-1.3 (0.18)	-0.6	-1.0 to -0.1	0.020
Over the last 7 days, fibromyalgia…					
Prevented accomplishing goals	-2.4 (0.18)	-1.6 (0.18)	-0.8	-1.3 to -0.3	0.001
Completely overwhelmed me	-2.1 (0.18)	-1.4 (0.18)	-0.7	-1.2 to -0.2	0.005

*Reported as LS mean (SE) change from baseline †To loud noises, bright lights, odors, and cold

Figure 1: Mean Change from Baseline in Weekly Averages of Daily NRS Pain Scores

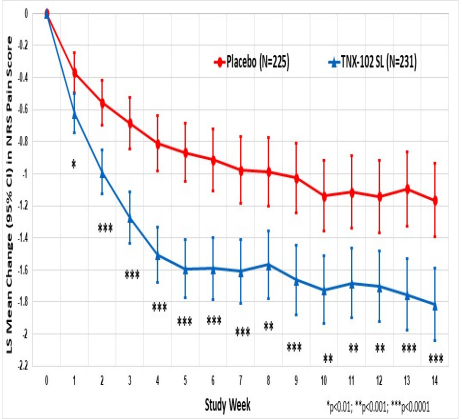
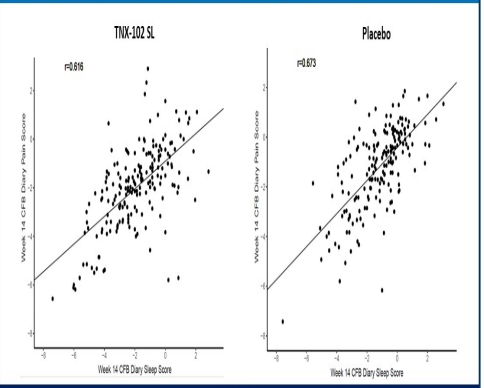


Figure 2: Correlation Between Change from Baseline in Diary Pain and Change from Baseline in Sleep Quality



SAFETY

Table 4: Treatment-Emergent Adverse Events at Rate of ≥ 3% in Either Treatment Group

System Organ Class Preferred Term	TNX-102 SL (N=231)	Placebo (N=226)	Total* (N=457)
Systemic Adverse Events			
COVID-19	10 (4.3%)	7 (3.1%)	17 (3.7%)
Somnolence	7 (3.0%)	3 (1.3%)	10 (2.2%)
Headache	7 (3.0%)	4 (1.8%)	11 (2.4%)
Oral Cavity Adverse Events			
Hypoaesthesia oral	55 (23.8%)	1 (0.4%)	56 (12.3%)
Product taste abnormal	27 (11.7%)	2 (0.9%)	29 (6.3%)
Paraesthesia oral	16 (6.9%)	2 (0.9%)	18 (3.9%)
Tongue discomfort	16 (6.9%)	0 (0.0%)	16 (3.5%)

DISCUSSION

FM is the prototypic nociplastic syndrome and COPC with central symptoms of widespread pain, unrefreshing sleep, fatigue, and cognitive dysfunction. In the current study by pharmacologically targeting unrefreshing sleep, treatment with bedtime TNX-102 SL supported this sleep/FM symptom connection by demonstrating:

Efficacy

- Significantly reduced daily pain and broad FM symptom improvement, as demonstrated by highly statistically significant improvement on the primary endpoint and all six key secondary endpoints
- Improvement in sleep quality – or target engagement – was shown by TNX-102 SL-mediated improvements over placebo on the PROMIS Sleep Disturbance instrument and broad symptom improvement shown by the FIQR Symptoms domain
- Improvement in Week 14 pain score was correlated with improvement in Week 14 sleep score in both treatment groups, suggesting TNX-102 SL treatment increases the number of responders over placebo/spontaneous remission (**Figure 2**)
- Improvements on exploratory endpoints: (1) mood and cognitive dysfunction, and (2) female sexual functioning nominally improved over the course of treatment, including the orgasm/completion domain (data not shown; also note too few males in the study to meaningfully compare on the male version of the CSFQ-14)

Safety

- Systemic treatment-emergence adverse events (TEAEs) were low, with the only AEs at ≥3% rate being headache, somnolence, and COVID-19. Among these, only somnolence rate was over two times the rate in TNX-102 SL relative to placebo
- Oral administration site reactions were the most common TEAEs, including tongue or mouth numbness or tingling and bitter aftertaste, which were typically transient, self-limited, never rated as severe, and rarely led to discontinuation

Tolerability

- High completion rate with 81.0% of the TNX-102 SL group and 79.2% of the placebo group completing 14 weeks of treatment
- Tolerability profile was favorable: No clinically meaningful weight or blood pressure change with treatment (data not shown), low rate of somnolence TEAE, and nominally improved cognitive symptoms.

Overall Conclusion

- Improvement in sleep quality mediated by TNX-102 SL appears to lead to syndromic improvement in FM
- The benefits of TNX-102 SL therapy in RESILIENT support the hypothesis that addressing sleep quality disturbance leads to syndromic improvement with favorable tolerability. Together, these findings are consistent with the concept that disturbed sleep in FM is an obstacle to recovery and pharmacological targeting may facilitate recovery.

References: [1]*Moldofsky H et al, Psychosom Med 1975;37:341-51;* [2]*Moldofsky H and Scarisbrick P. Psychosom Med 1976;38:35-44.*

Presented at IASP 2024 World Congress on Pain; Amsterdam, Netherlands; August 7, 2024