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): June 3, 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 June 3, 2024, the Company announced data from the Phase 3 RESILIENT trial of its Tonmya™ (TNX-102 SL, cyclobenzaprine HCl sublingual tablets) product candidate for the management of fibromyalgia in an oral presentation (the "Presentation") at the American Society of Clinical Psychopharmacology ("ASCP") Annual Meeting on May 29, 2024. 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 June 3, 2024, the Company announced data from the Presentation at the ASCP. The Presentation titled, *"Effects of Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl) on Mood and Anxiety Symptoms in Fibromyalgia: Results of the Phase 3 RESILIENT Trial,"* presented new data suggesting activity for improvement in depressive symptoms with Tonmya. The effect of Tonmya on depressive symptoms was studied using the Beck Depression Inventory-II ("BDI-II"). Patients started with a baseline mean (standard deviation) for placebo of 10.0 (6.72) and Tonmya of 9.6 (6.32). The BDI-II score separated at Week 2 with a nominal p-value of <0.01. By Week 14, the total BDI-II score in the TNX-102 SL group improved over placebo with a nominal p-value of 0.005 and an effect size of 0.27. In addition to the BDI-II score, in *post hoc* analyses several individual items on the Fibromyalgia Impact Questionnaire-Revised (FIQR) also improved in the Tonmya-treated group, including depression ($p < 0.001$), anxiety ($p = 0.001$), sensitivity ($p = 0.020$), memory problems ($p = 0.001$) and energy ($p < 0.001$), for which these p-values were not corrected for multiplicity. In addition, the company presented an analysis of the RESILIENT trial that compared patients who reported or who did not report adverse events of oral numbness, oral tingling, and bitter aftertaste (collectively, "Sensory AEs"). At Week 14, patients on TNX-102 SL who experienced sensory AEs separated from placebo with a p-value of <0.003 and patients on TNX-102 SL with no sensory AEs separated from placebo with a *p*-value of <0.001. Comparing the two groups, patients in the study who reported Sensory AEs, showed a

similar response to TNX-102 SL treatment in the primary endpoint of pain, compared to those with no sensory AEs ($p<0.701$). The Company believes that these findings indicate that Tonmya has broad-spectrum activity against fibromyalgia symptoms and may improve fibromyalgia at the syndromal level.

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, June 3, 2024
99.02	Effects of Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl) on Mood and Anxiety Symptoms in Fibromyalgia: Results of the Phase 3 RESILIENT Trial
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: June 3, 2024

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

EXHIBIT 99.01

Tonix Pharmaceuticals Presented New Data on Tonmya™ Suggesting Activity for Improvement in Fibromyalgia-Associated Depression Severity in an Oral Presentation at ASCP Annual Meeting

Tonmya treatment was associated with improvement in depressive symptoms as measured by the Beck Depression Inventory-II

In addition, post-hoc analyses showed improvement in depression, anxiety, memory and energy items on the Fibromyalgia Impact Questionnaire-Revised

New Drug Application (NDA) submission to the FDA on track for the second half of 2024

CHATHAM, N.J., June 3, 2024 – 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 new data from the Phase 3 RESILIENT trial of Tonmya (TNX-102 SL, cyclobenzaprine HCl sublingual tablets) for the management of fibromyalgia in an oral presentation at the American Society of Clinical Psychopharmacology (ASCP) Annual Meeting on May 29, 2024 in Miami Beach, Fla. A copy of the presentation is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

In the oral presentation titled, *"Effects of Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl) on Mood and Anxiety Symptoms in Fibromyalgia: Results of the Phase 3 RESILIENT Trial,*" Seth Lederman, MD, Chief Executive Officer, presented new data suggesting activity for improvement in depressive symptoms with Tonmya.

Depression was frequent among patients enrolled in the RESILIENT trial: ~47% reported experiencing depression within the past 6 months upon fibromyalgia diagnosis and ~25% of the intent-to-treat (ITT) population had experienced a lifetime major depressive episode (MDE). The effect of Tonmya on depressive symptoms was studied using the Beck Depression Inventory-II (BDI-II). Patients started with a baseline mean (standard deviation) for placebo of 10.0 (6.72) and Tonmya of 9.6 (6.32). The BDI-II score separated at Week 2 with a nominal p-value of <0.01. By Week 14, the total BDI-II score in the TNX-102 SL group improved over placebo with a nominal p-value of 0.005 and an effect size of 0.27.

Dr. Lederman said, "Although pain is the prototypic symptom in fibromyalgia and the validated FDA endpoint for the approval of a new drug, depression severity is also a prominent factor in the quality of life for fibromyalgia sufferers. In one study, depressive symptoms had a higher correlation with impaired quality of life than any other symptom, including pain frequency and intensity.[2] The improvement in depression observed in the Phase 3 RESILIENT was particularly striking since the mean entry score of 10 reflects mild depression. Others have struggled to show benefits of traditional antidepressants in mild depression and consequently many antidepressants have been studied in moderate or severely depressed patients and the benefits of such drugs for patients with mild depression have been inferred."

Dr. Lederman continued, "In addition to the BDI-II score, in *post hoc* analyses several individual items on the Fibromyalgia Impact Questionnaire-Revised (FIQR) also improved in the Tonmya-treated group, including : depression ($p < 0.001$), anxiety ($p = 0.001$), sensitivity ($p = 0.020$), memory problems ($p = 0.001$) and energy ($p < 0.001$), for which these p-values were not corrected for multiplicity. Together these findings indicate that Tonmya has broad-spectrum activity against fibromyalgia symptoms and may improve fibromyalgia at the syndromal level."

In the RESILIENT trial, as previously reported, Tonmya improved overall daily pain (p=0.00005), the pre-specified primary endpoint, making it the second Phase 3 study of Tonmya in the management of fibromyalgia to reach statistical significance on the pre-specified primary endpoint. Tonmya also demonstrated statistically significant and clinically meaningful results 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.."

In the RESILIENT trial, there were no new safety signals, low rates of systemic adverse events, and a favorable tolerability profile.

Tonix remains on track to submit an NDA to the U.S. Food and Drug Administration (FDA) in the second half of 2024 for Tonmya for the management of fibromyalgia and has scheduled a Type B pre-NDA meeting with FDA for the second quarter of 2024.

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 Tonmya [1], a product candidate for which two statistically significant Phase 3 studies have been completed for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction as well as fibromyalgia-type Long COVID. 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.

[1] Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration (FDA) as the tradename for TNX-102 SL for the management of fibromyalgia. Tonmya has not been approved for any indication.

[2] Offenbaecher M, et al. Pain is not the major determinant of quality of life in fibromyalgia. Rheumatology International 2021; 41:1995–2006

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

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

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.

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EXHIBIT 99.02

Effects of Bedtime TNX-102 SL (Sublingual Cyclobenzaprine HCl) on Mood and Anxiety Symptoms in Fibromyalgia:

Results of the Phase 3 RESILIENT Trial

Presented by
Seth Lederman, MD
at
American Society of Clinical Psychopharmacology
Annual Meeting, Miami, FL
May 29, 2024

Disclosures

- Authors: Gregory Sullivan[1], David Hsu[1], Mary Kelley[1], Ben Vaughn[2], Jean Engels[1] and Seth Lederman[1]
  - [1]Employees of Tonix Pharmaceuticals Holding Corp. and own stock and stock options in the company
  - [2]Employee of Rho, Inc.
- TNX-102 SL is an investigational new drug and is not approved for any indication

Characteristics of Fibromyalgia

- Symptoms include chronic **widespread pain**, **nonrestorative sleep**, **fatigue**, and **cognitive dysfunction**
- Afflicts an estimated 6-12 million US adults, majority are women
- Those with FM struggle with daily activities, have impaired quality of life (QoL), and are frequently disabled[1]
  - Main correlates for QoL in FM, explaining 56% variance, *do not include* pain intensity or frequency; rather, greatest correlates are **depression** (standardized β=-0.26), pain-related interference with everyday life (β=-0.19), general activity (β=0.13), cognitive difficulties (β=-0.12)[2]
  - Conclusion: mood symptoms have big impact on QoL in FM
- Physicians and patients report common dissatisfaction with currently marketed products

[1]Robinson RL, et al. Burden of illness and treatment patterns for patients with fibromyalgia. Pain Medicine 2012; 13(10):1366-76
[2]Offenbaecher M, et al. Pain is not the major determinant of quality of life in fibromyalgia. Rheumatology International 2021; 41:1995–2006

2016 Fibromyalgia (FM) Criteria*

- How is FM currently diagnosed? By assessing pain distribution and other core symptoms of FM:
  - **Widespread pain** index (WPI): number of areas (out of 19) with pain (**WPI range 0-19**)
  - **Symptom severity** scale (SSS) score calculated by:
    - Over past week, for following 3 symptoms rate severity 0-3 each (SSS subscore 0-9)
      - **Fatigue (0-3)**
      - **Waking unrefreshed (0-3)**
      - **Cognitive symptoms (0-3)**
    - Over previous 6 months, bothered by the following 3 symptoms (SSS subscore 0-3)
      - Headaches (0-1)
      - Pain or cramps in lower abdomen (0-1)
      - **Depression (0-1)**
    - Add two subscores for total (**SSS score range 0-12**)
  - To make the diagnosis, need:
    - **WPI ≥ 7 and SSS score ≥ 5** OR **WPI of 4-6 and SSS score ≥ 9**
    - **Generalized pain, defined as pain in 4 of 5 body regions^**
    - **Symptoms generally present for at least 3 months**

*Wolfe F, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016; 46(3):319-329.

^pain in body areas of jaw, chest, abdomen do not contribute to meeting generalized pain definition

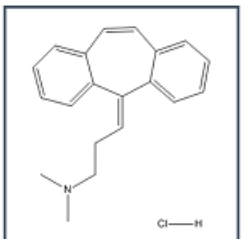
Fibromyalgia: Nonrestorative Sleep and Cyclobenzaprine

- Non-restorative sleep[1,2]
  - Harvey Moldofsky – recognition of unrefreshing/non-restorative sleep:
    - Symptom
    - Potential causative or potentiating factor
- Cyclobenzaprine[3,9]
  - Potentially the earliest drug studied in fibromyalgia as an oral swallowed agent
  - Studies showed equivocal effects and tolerability issues at "muscle spasm" doses
- Bedtime, *low-dose* cyclobenzaprine targeting non-restorative sleep[10-11]
  - Recognition of unrefreshing sleep as a target of therapy
  - Primitive oral, swallowed formulation – "flat" pharmacokinetics
- Bedtime, *sublingual transmucosal* cyclobenzaprine targeting non-restorative sleep[12]
  - Dynamic pharmacokinetic profile, rapid absorption, decrease in major metabolite, norcyclobenzaprine
  - Two studies (Phase 2 and Phase 3) at 2.8 mg; three Phase 3 studies at 5.6 mg.

[1]Moldofsky H et al. *Psychosom Med.* 1975. 37:341-51.
[2]Moldofsky H and Scarisbrick P. *Psychosom Med.* 1976. 38:35-44.
[3]Bennett RM, et al. *Arthritis Rheum* 1988. 31:1535–42.
[4]Quimby LG, et al. *J Rheumatol Suppl,* 1989 Nov;19:140–3.
[5]Reynolds WJ, et al. *J Rheumatol.* 1991.18:452–4.
[6]Santandrea S, et al. *J Int Med Res.* 1993.21:74–80.
[7]Cantini F, et al. *Minerva Med.* 1994. 85:97–100.
[8]Carette S, et al. *Arthritis Rheum.* 1994. 37:32–40.
[9]Tofferi JK, et al. *Arthritis Rheum.* 2004. 51:9–13.*1*
[10]Iglehart IW. 2003; US Patent 6,541,523.
[11]Moldofsky et al. *J Rheumatol.* 2011. 38:2653-2663
[12]Lederman S et al. *Arthritis Care Res.* 2023. 75:2359-2368.

TNX-102 SL (Sublingual Cyclobenzaprine HCl)

- Cyclobenzaprine (CBP) is a tricyclic amine close in structure to amitriptyline (AMI)*
- CBP with potent binding and antagonist activity at several receptors influencing sleep: 5-HT_{2A} serotonergic, α_1-adrenergic, H_1-histaminergic, and M_1-muscarinic receptors
- Non-restorative sleep proposed as a treatment target of pharmacotherapy[1,2]
  - TNX-102 SL hypothesized to improve pain and other FM symptoms via improvement in sleep quality
- TNX-102 SL is a proprietary formulation of CBP with unique PK profile of parent and main metabolite due to sublingual transmucosal absorption that bypasses first pass hepatic metabolism, thereby optimized for bedtime dosing and alignment with sleep period
- With this second successful phase 3 study, RESILIENT, submission of a new drug application (NDA) is targeted for 2H 2024



Cyclobenzaprine HCl

*CBP with additional double bond in central ring compared with AMI

[1]Moldofsky H. The significance of dysfunctions of the sleeping/waking brain to the pathogenesis and treatment of fibromyalgia syndrome. Rheum Dis Clin North Am. 2009;35(2):275-83.
[2]Davies KA, et al. Restorative sleep predicts the resolution of chronic widespread pain: results from the EPIFUND study. Rheumatology (Oxford). 2008;47(12):1809-13.

Phase 3 RESILIENT Study of TNX-102 SL in FM

Trial TNX-CY-F307 **ClinicalTrials.gov Identifier NCT05273749**

General study characteristics:

- Randomized, double-blind, multicenter, placebo-controlled study in fibromyalgia (FM)
- 33 U.S. sites enrolled 457 participants with FM as defined by 2016 Revisions to the 2010/2011 FM Diagnostic Criteria[1]

Primary Endpoint:

- Change from baseline to Week 14 (TNX-102 SL vs. placebo) in weekly averages of daily diary average pain intensity score

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

Key Secondary Endpoints:

- Patient Global Impression of Change
- Fibromyalgia Impact Questionnaire-Revised (FIQR) Symptoms domain and Function Domain
- PROMIS Sleep Disturbance and Fatigue instruments
- Daily diary of prior night sleep quality

Other Endpoints*:

- Beck Depression Inventory-II (BDI-II)
- Changes in Sexual Functioning Questionnaire short form (CSFQ-14)
- Individual symptom items on FIQR Symptoms domain
- Earlier timepoints for primary and key secondary endpoints

[1]Wolfe F et al. Seminars in Arthritis and Rheumatism 2016; 46:319-329.

*Uncorrected for multiple comparisons

RESILIENT Study
Demographics and Baseline Characteristics

Demographics	ITT Population	
	Placebo	TNX-102 SL
Variable	N=225	N=231
Age, Years, mean (SD)	49.5 (11.35)	49.3 (10.45)
Sex, Female, N (%)	211 (93.8%)	224 (97.0%)
Sex, Male, N (%)	14 (6.2%)	7 (3.0%)
Ethnicity, N (%)		
Hispanic or Latino	35 (15.6%)	36 (15.6%)
Race, N (%)		
Black or African American	26 (11.6%)	32 (13.9%)
White or Caucasian	192 (85.3%)	194 (84%)
Asian	5 (2.2%)	1 (0.4%)
American Indian or Alaskan Native	1 (0.4%)	2 (0.9%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)	0 (0.0%)
Multiple	1 (0.4%)	2 (0.9%)
BMI, kg/m^2, mean (SD)	31.1 (6.33)	31.1 (6.34)
Education, some college or more, N (%)	192 (85.3%)	187 (81.0%)
Employed, Yes, N (%)	150 (66.7%)	147 (63.6%)
Unable to work due to FM, N (%)	12 (5.3%)	13 (5.6%)
Duration of FM, years, mean (SD)	9.9 (9.53)	8.6 (8.44)
Concomitant Antidepressants or buspirone, N (%)	58 (25.8%)	59 (25.5%)

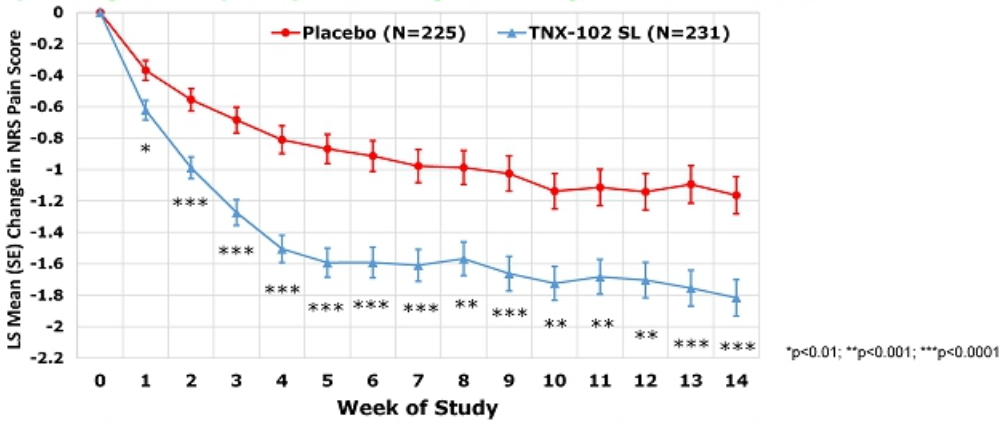
Baseline Characteristics	ITT Population	
	Placebo	TNX-102 SL
Scales	N=225	N=231
Dairy NRS Pain score, mean (SD)	5.9 (1.08)	5.9 (1.05)
PROMIS Sleep Disturbance T-score, mean (SD)	59.4 (7.16)	59.2 (6.04)
PROMIS Fatigue T-score, mean (SD)	63.9 (7.07)	63.7 (5.90)
FIQR Symptoms Domain score, mean (SD)	54.1 (14.56)	53.1 (14.86)
FIQR Function Domain score, mean (SD)	37.9 (19.08)	38.5 (19.94)
Diary NRS Sleep Quality score, mean (SD)	5.7 (1.34)	5.8 (1.30)
Depression, prior 6 months, FM Dx*, Yes, N (%)	106 (46.9%)	110 (47.6%)
BDI-II total Score, mean (SD)	10.0 (6.72)	9.6 (6.32)
Lifetime Major Depressive Episode(s), N (%)	53 (23.6%)	54 (23.4%)
Current Major Depressive Episode, N (%)	3 (1.3%)	7 (3.0%)

Abbreviations: BDI-II, Beck Depression Inventory-II; BMI, body mass index; Dx, diagnosis; FIQR, Fibromyalgia Impact Questionnaire-Revised; FM, fibromyalgia; ITT, Intention-to-Treat; N, number; NRS, numeric rating scale; Patient-Reported Outcomes Measurement Information System

*Wolfe F, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016; 46(3):319-329.

RESILIENT Primary Outcome Measure
Reduction in Widespread Pain

Weekly Average of Daily Diary NRS Ratings of Average Pain Over Prior 24 Hours



Week 14 LS mean (SE) change from baseline for TNX-102 SL -1.82 (0.12) and for placebo -1.16 (0.12); LSMD from placebo -0.65 (0.16); **p=0.00005#, Effect Size = 0.38**

#Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction. Abbreviations: LS, least squares; LSMD, least squares mean difference; NRS, numeric rating scale; SE, standard error

RESILIENT Key Secondary Outcome Measures

Six Out of the Six Key Secondary Measures Met Statistical Significance

Rating Scale*	Week 14 p-value	Met**
Patient Global Impression of Change (PGIC)	p = 0.00013^	✓
Fibromyalgia Impact Questionnaire - Symptoms	p = 0.000002#	✓
Fibromyalgia Impact Questionnaire - Function	p = 0.001#	✓
PROMIS Sleep Disturbance	p = 0.0000001#	✓
PROMIS Fatigue	p = 0.00009#	✓
Weekly average of daily Sleep Quality scores	p = 0.0007#	✓

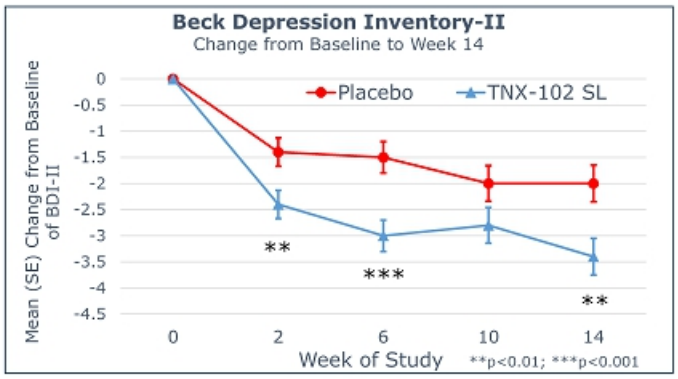
*In order of statistical serial gate-keeping hierarchy (or "waterfall") to control overall Type 1 error
**Statistical significance met

^ Based on a Pearson Chi-Squared with differences in proportions from Z-test; responders defined as subject that reply 'very much improved' or 'much improved' at Week 14; all others are non-responders
# Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction.

RESILIENT Beck Depression Inventory-II Results

	Placebo Mean (SD)	Placebo LS MCFB (SE)	TNX Mean (SD)	TNX LS MCFB (SE)	Difference in LS Means (SE)	95% CI for Difference	P-value	Effect Size
Baseline	10.0 (6.72)		9.6 (6.32)					
Week 14		-2.0 (0.35)		-3.4 (0.35)	-1.4 (0.49)	-2.3, -0.4	0.005#	0.27

- Greater reduction in total BDI-II score in TNX-102 SL group over placebo at Week 14 with p=0.005#, effect size of 0.27
  - Also separated, with p<0.01#, at Week 2 when on TNX-102 SL 2.8 mg first two weeks
  - And separated, with p<0.001#, at Week 6



#Uncorrected for multiple comparisons
SE=standard error; SD=standard deviation

RESILIENT Individual Items on FIQR
Affective Symptoms, Sensory Sensitivity, Cognition, and Energy

Selected Fibromyalgia Impact Questionnaire-Revised Symptoms Domain Item Scores

FIQ-R Item **Please rate your level of...** (past 7 days)	Week 14 LS Mean (SE) Difference from Placebo#	95% Confidence Interval#	P-value^	Effect Size
Depression	**-0.8 (0.21)**	**-1.2, -0.6**	**<0.001**	**0.35**
Anxiety	**-0.8 (0.24)**	**-1.2, -0.3**	**0.001**	**0.30**
Sensitivity to...*	**-0.6 (0.24)**	**-1.0, -0.1**	**0.020**	**0.22**
Memory problems	**-0.8 (0.23)**	**-1.2, -0.3**	**0.001**	**0.31**
Energy	**-0.8 (0.23)**	**-1.2, -0.3**	**<0.001**	**0.31**

*...loud noises, bright lights, odors, and cold

#Mixed model repeated measures analysis (no imputation); fixed categorical effects of treatment, site, study week, and treatment x study week interaction; fixed covariates of baseline value and baseline value x study week interaction
^Uncorrected for multiple comparisons

Summary of Baseline Depression BDI-II and FIQR Item Data

- While the rate of current MDE diagnosis was ~2% of the ITT, ~25% ITT had experienced a lifetime MDE, and ~47% reported past 6 month depression on FM Dx*
- Also, about 25% of the ITT enrolled on concomitant antidepressant or buspirone

- By end of treatment (Week 14), there was a greater reduction in depression severity by total BDI-II score in TNX-102 SL group compared with placebo (p=0.005)
  - And greater reduction in FIQR items for depression (p<0.001), anxiety (p=0.001), and sensory sensitivity (p=0.020) in the TNX-102 SL group compared with placebo
  - The FIQR memory item, a measure of cognitive impairment in FM, was more improved in the TNX-102 SL group than placebo (p=0.001)
  - The FIQR energy item, another indicator of less fatigue in FM, was also more improved in the TNX-102 SL group than placebo (p<0.001)
- Cohen's *d* effect sizes were between 0.27 and 0.35 for all Week 14 outcomes above except sensory sensitivity

Abbreviations: BDI-II, Beck Depression Inventory-II; Dx, diagnosis; FIQR, Fibromyalgia Impact Questionnaire-Revised; FM, fibromyalgia; ITT, Intention-to-Treat

*Wolfe F, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016; 46(3):319-329.

RESILIENT Safety

Treatment-Emergent Adverse Events (TEAEs) at Rate of ≥ 3% in Either Treatment Group

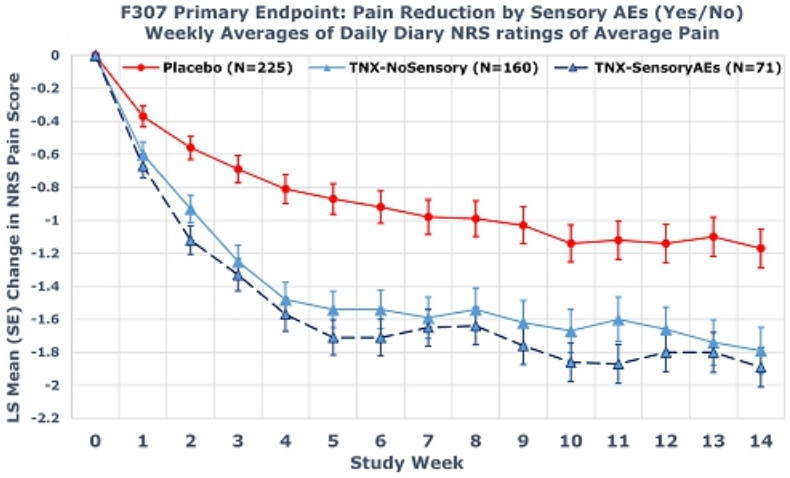
System Organ Class Preferred Term	TNX-102 SL N=231	Placebo N=226	Total* N=457
Systemic Adverse Events			
COVID-19	10 (4.3%)	7 (3.1%)	17 (3.7%)
Somnolence	7 (3.0%)	3 (1.3%)	10 (2.2%)
Headache	7 (3.0%)	4 (1.8%)	11 (2.4%)
Oral Cavity Adverse Events			
Hypoaesthesia oral	55 (23.8%)	1 (0.4%)	56 (12.3%)
Product 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%)

- Among patients randomized to TNX-102 SL and to placebo, 81.0% and 79.6%, respectively, completed the study
- No new safety signals observed; aside from COVID-19, no systemic AEs greater than 3% in TNX-102 SL group
- Events rated as mild or moderate made up 97.2% of AEs on placebo and 99.1% on TNX-102 SL
- As observed in prior studies with TNX-102 SL, oral cavity AEs were higher in TNX-102 SL than placebo, 42.9% and 10.2%, respectively
  - Most common oral AEs were oral numbness, product taste abnormal, oral tingling, and tongue discomfort (numbness and tingling believed due to weak local anesthetic properties of CBP due to sodium channel inhibition)
  - Nearly all these common oral AEs were temporally related to dosing and generally lasted <60 minutes

RESILIENT Analysis by Sensory Adverse Events (AEs)
TNX-102 SL group divided for presence/absence of 3 sensory AEs

- AEs of oral numbness, oral tingling, and bitter aftertaste named 'Sensory AEs'*
- Graph shows negligible advantage for presence of sensory AEs
- At Week 14:
  - TNX-NoSensory v Placebo
    - Diff in LS Mean (SE): -0.62 (0.179)
    - p<0.001
  - TNX-SensoryAEs v Placebo
    - Diff in LS Mean (SE): -0.72 (0.239)
    - p<0.003
  - TNX-NoSensory v TNX-SensoryAEs
    - Diff in LS Mean (SE): -0.10 (0.254)
    - p<0.701
  - Both TNX-102 SL subgroups show significantly greater pain reduction than placebo
  - The two TNX-102 SL subgroups do not significantly differ from each other

*Preferred Terms: Hypoaesthesia oral, Paraesthesia oral, Product taste abnormal



RESILIENT Safety, Continued

No Signals for Clinically Meaningful Changes in Systolic or Diastolic Blood Pressure or in Weight

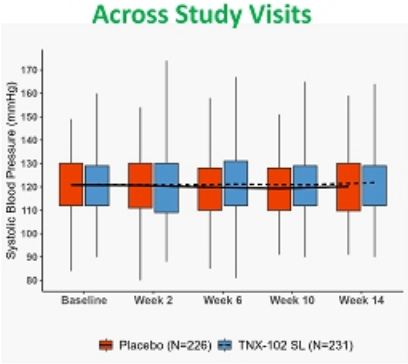
*No clinically meaningful difference in mean **systolic blood pressure** between groups*
Week 14 mean (SD) change from baseline:
TNX-102 SL = 0.7 (12.38) mmHg
Placebo = 0.5 (10.42) mmHg

*No clinically meaningful difference in mean **diastolic blood pressure** between groups*
Week 14 mean (SD) change from baseline:
TNX-102 SL = 1.1 (8.60) mmHg
Placebo = 0.2 (8.22) mmHg

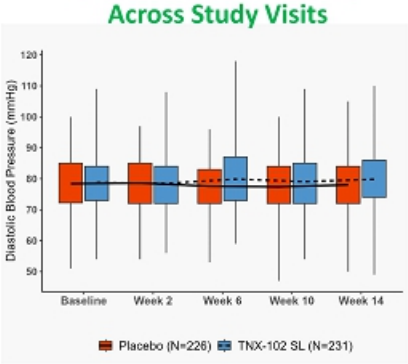
*No clinically meaningful difference in mean **weight** between treatment groups*
Week 14 mean (SD) change from baseline:
TNX-102 SL = 0.02 (2.940) kg
Placebo = 0.20 (2.932) kg

RESILIENT Safety, Continued

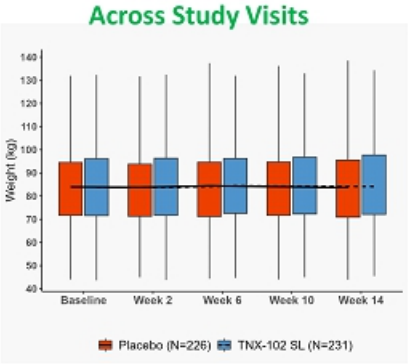
Systolic Blood Pressure Across Study Visits



Diastolic Blood Pressure Across Study Visits



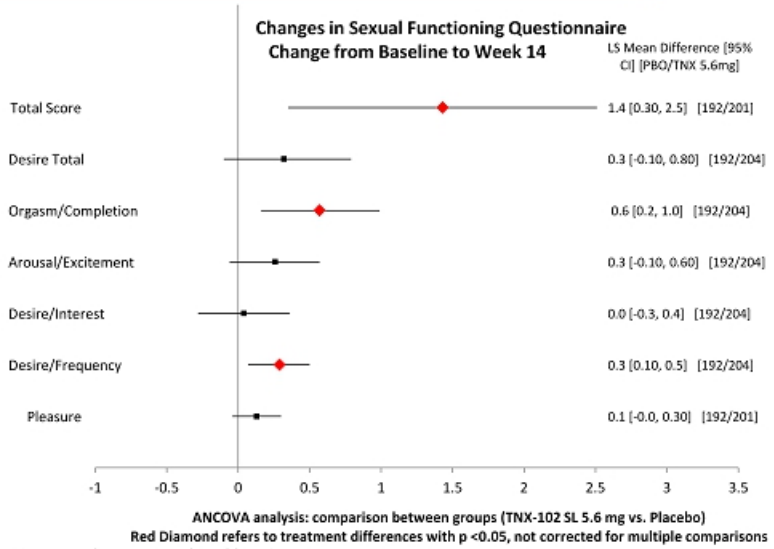
Body Weight Across Study Visits



Horizontal lines are the mean for each group; boxes are the 25th and 75th percentiles; and vertical lines begin and end at the 5th and 95th percentiles

Tolerability – Sexual Functioning

- No AEs of sexual dysfunction in RESILIENT
- Sexual functioning also systematically investigated using the Changes in Sexual Functioning Questionnaire short form (CSFQ-14) at Baseline and Week 14
- In females, *improved* scores on CSFQ-14 (indicating better sexual functioning) for TNX-102 SL group compared with placebo:
  - Total CSRQ-14 score: p=0.010
  - Orgasm/Completion item score: p=0.007
  - Desire/Frequency score item score: p=0.010
- Tolerability advantage over approved FM pharmacotherapies with serotonergic reuptake inhibition such as SNRIs
  - Most common sexual side effects of such medications are delay in orgasm or anorgasmia, the *function that was most improved* on TNX-102 SL in RESILIENT



Conclusions

- Fibromyalgia diagnostic criteria include depression (past 6 months) as part of the symptom burden, adding a point to symptom severity scale (SSS) score
- Depressive severity reported to be prominent factor for quality of life in FM
- Phase 3 RESILIENT trial demonstrated highly statistically significant effects of TNX-102 SL on pain, patient global, fibromyalgia scale symptom and function domains, sleep/sleep quality, and fatigue
- Beck Depression Inventory-II total score at Week 14 for TNX-102 SL reduced over placebo (p=0.005; effect size [ES]=0.27)
- FIQR items for depression (ES=0.35) and anxiety (ES=0.30) also reduced over placebo
- Cognitive function is the 4th core FM symptom, and FIQ-R memory item notably improved (ES=0.31), suggesting **syndromal benefit** of TNX-102 SL
- No new safety signals; low rates of systemic AEs, and high tolerability of therapy relative to currently approved FM therapies

Thank you!

QUESTIONS?