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): March 30, 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 March 30, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that Seth Lederman, M.D., Chief Executive Officer, will present an oral presentation (the "Presentation") and poster (the "Poster") at the 5th International Congress on Controversies in Fibromyalgia being held March 30-31, 2023 A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference. The Presentation and Poster, which may contain nonpublic information, are filed hereto as Exhibits 99.02 and 99.03, respectively, 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 and 99.03 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 March 23, 2023, the Company announced that Dr. Lederman will present the Poster and Presentation, entitled, "*Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results from the Randomized, Placebo Controlled RELIEF Trial*", which reports that the Company's TNX-102 SL product candidate met its pre-specified primary endpoint in the Phase 3 RELIEF trial, a potentially confirmatory registration-enabling Phase 3 trial, significantly reducing daily pain compared to placebo (p=0.01) in participants with fibromyalgia. 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.

Early discontinuation rates were similar for TNX-102 SL and placebo (17.7% and 16.5%, respectively). In addition, TNX-102 SL was well tolerated with the most common adverse event from active treatment being oral numbness or hypoaesthesia, an administration site reaction that is typically transient, was never rated as severe, and only lead to one discontinuation.

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 March 30, 2023
99.02	Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results from the Randomized, Placebo
99.03	Controlled RELIEF Trial
104	Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results from the Randomized, Placebo-Controlled RELIEF Trial 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: March 30, 2023

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

Exhibit 99-01

Tonix Pharmaceuticals Presents Positive Efficacy and Safety Data from Phase 3 RELIEF Study of TNX-102 SL for the Management of Fibromyalgia at the 5th International Congress on Controversies in Fibromyalgia

Interim Analysis of RESILIENT, a Potentially Confirmatory Registration-Enabling Phase 3 Fibromyalgia Trial of TNX-102 SL Expected Second Quarter 2023; Topline Data Expected Fourth Quarter 2023

CHATHAM, N.J., March 30, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, announced that Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals, will present an oral presentation and poster at the 5th International Congress on Controversies in Fibromyalgia being held March 30-31, 2023 at the Austria Trend Hotel Savoyen Vienna in Vienna, Austria. The presentation will take place today, Thursday, March 30, 2023 at 5:10-5:20 p.m. CET.

The presentation, titled, "Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results from the Randomized, Placebo Controlled RELIEF Trial" reports that TNX-102 SL met its pre-specified primary endpoint in the Phase 3 RELIEF trial, significantly reducing daily pain compared to placebo (p=0.01) 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.

Early discontinuation rates were similar for TNX-102 SL and placebo (17.7% and 16.5%, respectively). In addition, TNX-102 SL was well tolerated with the most common adverse event from active treatment being oral numbness or hypoaesthesia, an administration site reaction that is typically transient, was never rated as severe, and only lead to one discontinuation.

"There continues to be a pressing need for new, safe and more tolerable drugs to treat patients with fibromyalgia," said Dr. Lederman. "We are looking forward to the results of a planned interim analysis due next quarter for our RESILIENT study, a potentially pivotal confirmatory Phase 3 study of TNX-102 SL for the management of fibromyalgia."

Copies of the presentation and poster are available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com. In addition to the presentation, the Company's submitted abstract will be published in an online supplement to the journal *Clinical and Experimental Rheumatology* in a special issue on Fibromyalgia.

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.

About the Phase 3 RELIEF Study

The RELIEF study has been completed and TNX-102 SL achieved a statistically significant benefit as measured by the primary, prespecified endpoint of improvement over placebo in daily pain. The RELIEF study was a double-blind, randomized, placebo-controlled Phase 3 trial designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the management of fibromyalgia. The two-arm trial targeted enrollment of 470 participants, at approximately 40 U.S. sites. RELIEF completed final enrollment of 503 participants. The first two weeks of treatment were a run-in period in which participants start on TNX-102 SL 2.8 mg (1 tablet) or placebo. After the first two weeks, all participants had the dose increased to TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) or two placebo tablets for 12 weeks. The primary endpoint was daily diary pain severity score change (TNX-102

SL 5.6 mg vs. placebo) from baseline (using the weekly averages of the daily numerical rating scale scores), analyzed by mixed model repeated measures with multiple imputation.

Additional details about the completed RELIEF study are available at clinicaltrials.gov (NCT04172831).

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with interim data expected in the second quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition, for which a Phase 2 study was initiated in the third quarter of 2022. TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is currently enrolling with interim data expected in the fourth quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets), a once-daily formulation of tianeptine being developed as a treatment for major depressive disorder (MDD), is also currently enrolling with interim data expected in the fourth quarter of 2023. 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 second quarter of 2023. Tonix's rare disease 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 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 and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox, for which a Phase 1 study is expected to be initiated in the second half of 2023. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease portfolio also includes TNX-3900, a class of broad-spectrum small molecule oral antivirals.

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; 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. 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; 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-102 SL*

Cyclobenzaprine (Protectic®) Pipeline in a Product

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

Potent binding and antagonist activities at the serotonin-5-HT2A, α1-adrenergic, histaminergic-H1, and muscarinic-M1 receptors to facilitate restorative sleep

Innovative and proprietary PROTECTIC® Rapid drug exposure following nighttime administration

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

Patents Issued

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

Fibromyalgia

Status: Mid-Phase 3
- One positive Phase 3 study (RELIEF) completed
- Second Phase 3 study (RALLY) missed primary endpoint
- Confirmatory Phase 3 study (RESILIENT) is currently enrolling
  - >50% enrolled

Next Steps: Interim analysis results expected 2Q 2023

Long COVID

Status: Phase 2
- Phase 2 study (PREVAIL) is currently enrolling

Next Steps: Trial enrollment is in process

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TNX-102 SL: F304 (RELIEF) Phase 3 Study

- **General Study Design:** Phase 3, Randomized, Multicenter (39), Parallel Group, Double-Blind, Placebo-Controlled 14 Week Study
- **Objectives:** To evaluate efficacy and safety of bedtime TNX-102 SL in fibromyalgia (FM)
- **Investigational Product (IP):** TNX-102 SL (sublingual cyclobenzaprine) is a tricyclic drug that potently binds and antagonizes: hydroxytryptamine-2A, α1-adrenergic, H1-histaminergic, and M1-muscarinic acetylcholine receptors
- **Study Visits:** Screening, Baseline, and four treatment (Weeks 2, 6, 10 & 14/ET) visits
- **IP Dosage:** first 2 weeks on 1 tablet (TNX-102 SL 2.8 mg); at Week 2 visit the dose is increased to 2 tablets providing 5.6 mg of TNX-102 SL at bedtime for 12 weeks
- **Patient Population:** diagnosis of primary FM as defined by 2016 Revision to the 2010/2011 FM diagnostic criteria (ACR Preliminary Diagnostic Criteria)
- **Exclusionary Medications:** duloxetine, milnacipran, pregabalin, gabapentin, tramadol, tapentadol, muscle relaxants, tricyclic antidepressants, MAOIs, trazodone, narcotics/opioids, naltrexone, benzodiazepines, anticonvulsants (exception for migraine), sodium oxybate, ketamine, CGRP/CGRP-R meds, and all other cyclobenzaprine

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Demographics

Variable	Placebo N=255	TNX-102 SL N=248	Total N=503
Age, years (mean, SD)	49.3 (10.2)	50.0 (9.4)	49.6 (9.8)
Sex, female	247 (96.9%)	232 (93.5%)	479 (95.2%)
Ethnicity, Hispanic/Latino	42 (16.5%)	43 (17.3%)	85 (16.9%)
Race			
White or Caucasian	216 (84.7%)	222 (89.5%)	438 (87.1%)
Black or African American	20 (7.8%)	19 (7.7%)	39 (7.8%)
All Other	19 (7.5%)	7 (2.8%)	26 (5.9%)
BMI (kg/m^2)	31.6 (6.3)	32.4 (6.6)	32.0 (6.4)
Education, some college or greater	212 (83.1%)	205 (82.7%)	417 (82.9%)
Employed, currently	158 (62.0%)	182 (73.4%)	340 (67.6%)
Unable to work due to fibromyalgia	15 (5.9%)	16 (6.5%)	31 (6.2%)
Duration of fibromyalgia, years	9.0 (8.1)	9.2 (8.4)	9.1 (8.2)

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Primary Efficacy Endpoint Analysis

Endpoint: change from baseline to Week 14 endpoint in diary NRS weekly average of daily self-reported average pain severity

Visit Statistic	Placebo (N = 255) Value	Placebo (N = 255) Change from Baseline	TNX-102 SL (N = 248) Value	TNX-102 SL (N = 248) Change from Baseline
Baseline				
Mean (SD)	**6.0 (1.08)**		**6.1 (1.06)**	
Week 14				
LS mean (SE) [1]	4.6 (0.12)	**-1.5 (0.12)**	4.2 (0.12)	**-1.9 (0.12)**
95% CI [1]	(4.3, 4.8)	(-1.7, -1.3)	(3.9, 4.4)	(-2.1, -1.7)
Difference in LS mean (SE)				**-0.4 (0.16)**
95% CI for difference in LS mean				(-0.7, -0.1)
p-value for difference				**0.010**

* p <0.0452, adjusted p-value necessary for significance due to alpha-spend from an interim analysis; for Week 14 results, Cui, Hung, & Wang methodology used to combine p-values for interim and post-interim subjects

[1] Least squares means, differences, and CIs were based on an MMRM with fixed, categorical effects of treatment, center, study week, and treatment-by-study week interaction, as well as the fixed covariates of baseline value and baseline value-by-study week interaction. Missing values for Week 14 were imputed with multiple imputation, accounting for the reasons for study discontinuation (if due to adverse events or lack of efficacy, considered missing not-at-random. Abbreviations: CI = confidence interval; LS = least squares; MMRM = mixed model repeated measures; SD = standard deviation; SE = standard error

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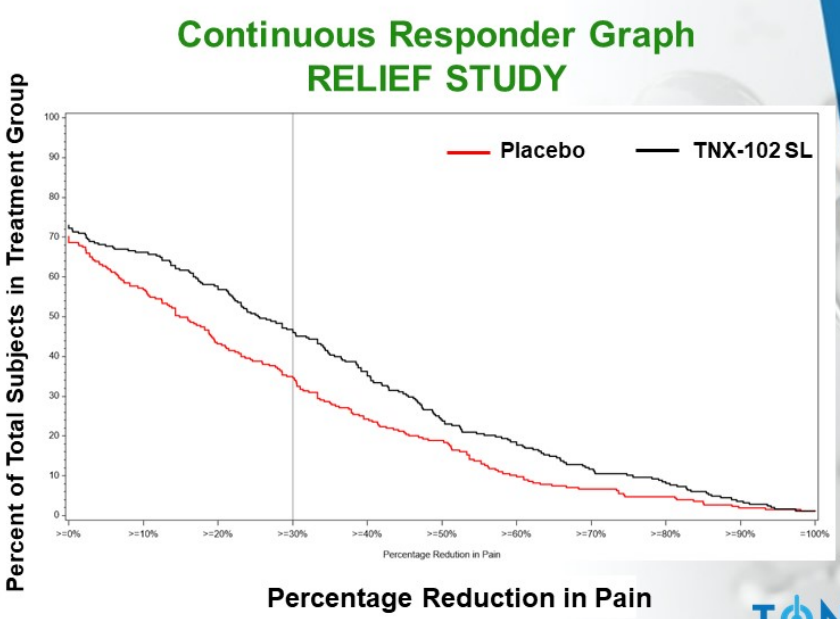
Responder Rates

Continuous Responder Graph shows a selected percent pain reduction rate (x-axis) for responder status versus percent of responders in each treatment group (y-axis)

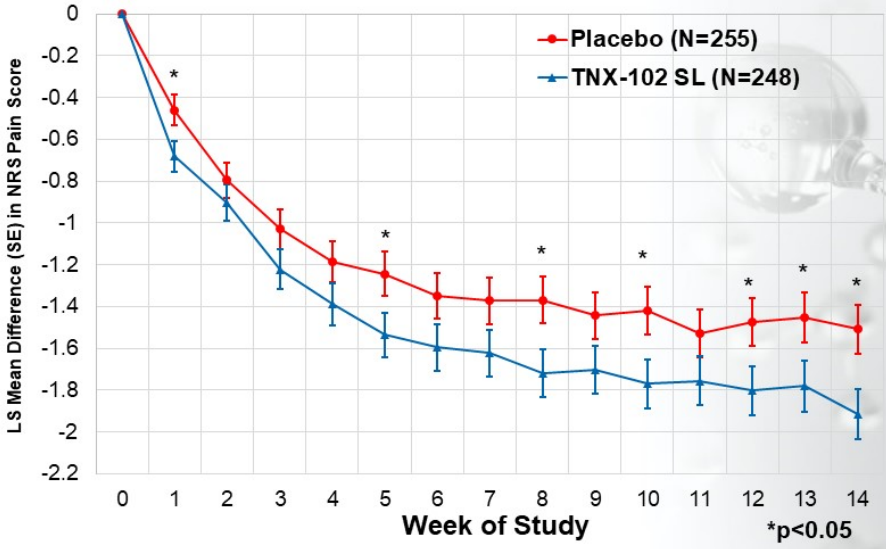
For a ≥30% Pain Reduction Responder Analysis:

- Choose ≥30% on x-axis
- On y-axis find
  - TNX-102 SL at 46.8%
  - Placebo at 34.9%
  - Logistic Regression Odds Ratio (95% CI) of **1.67 (1.16, 2.40), p=0.006**



Pain Reduction by Daily Diary Across 14 Weeks of Study

- Note: in addition to statistically significant pain reduction at Week 14, TNX-102 SL separated from Placebo at Weeks 1, 5, 8, 10, 12, & 13; all p<0.05



Key Secondary Efficacy Endpoint Analyses

- Sequential test procedure to adjust for multiplicity applied to primary and key secondary endpoints; hierarchy of key secondaries:
  - **PGIC**, responder analysis, proportion with '2' or '1' at Week 14
  - **FIQR Symptoms** domain, change from baseline at Week 14
  - **FIQR Function** domain, change from baseline at Week 14
  - **PROMIS Sleep Disturbance** (8a), change from baseline at Week 14
  - **PROMIS Fatigue** (8a), change from baseline at Week 14
  - **Sleep Quality** by daily diary, change from baseline at Week 14

TNX-102 SL was not associated with significant improvement in PGIC at week 14 but was associated with improvements in FIQR, PROMIS, and daily sleep quality.

FIQR = Fibromyalgia Impact Questionnaire – Revised; PGIC = Patient Global Impression of Change ('2' = much improved; '1' = very much improved); PROMIS = Patient-Reported Outcomes Measurement Information System

Safety

- **Exposure**
  - Mean (SD) treatment duration (days): TNX-102 SL 88.9 (26.2); Placebo 88.7 (24.9)
  - Mean (SD) study days drug taken: TNX-102 SL 77.1 (25.2); Placebo 75.9 (23.6)
- **Treatment-Emergent Adverse Events (TEAEs) Rated as Severe**
  - TNX-102 SL 4.4% of all TEAEs in group; Placebo 3.5% of all TEAEs in group
- **Incidence of Oral TEAEs**
  - TNX-102 SL 40.7%; Placebo 9.0%
- **Discontinued Study Drug Due to TEAE**
  - TNX-102 SL 8.9%; Placebo 3.9%
- **Serious Adverse Effects**
  - TNX-102 SL 2 SAEs; Placebo 5 SAEs; none deemed related to study drug
- **Completion rates**
  - TNX-102 SL 82.3%; Placebo 83.5%

Treatment Emergent Adverse Events (TEAEs)

- Well tolerated: only systemic TEAE that occurred at a rate of ≥3.0% in either arm was somnolence, sedation, and dry mouth in the TNX-102 SL arm
- Consistent with known side effects of marketed oral cyclobenzaprine

	TNX-102 SL (N=248)		Placebo (N=255)		Total (N=503)	
Systemic Adverse Events	**N**	**%**	**N**	**%**	**N**	**%**
Sedation	9	3.6	1	0.4	10	2.0
Fatigue	9	3.6	4	1.6	13	2.6
Dry Mouth	8	3.2	7	2.7	15	3.0
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Hypoaesthesia oral	43	17.3	1	0.4	44	8.7
Paraesthesia oral	14	5.6	1	0.4	15	3.0
Product taste abnormal	11	4.4	1	0.4	12	2.4
Glossodynia	9	3.6	2	0.8	11	2.2

CNS PORTFOLIO

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Conclusions

- **TNX-102 SL reduced pain in fibromyalgia significantly more than placebo** (p=0.010) over 14 weeks of treatment
- 30% pain responder analysis demonstrated greater responders with TNX-102 SL at 46.8% than with placebo at 34.9% (p=0.006)
- TNX-102 SL had **broad syndromal effects across core fibromyalgia symptoms** of widespread pain, fatigue, sleep disturbance, memory disturbance, mood disturbance, and sensory sensitivity
- Most common adverse event from active treatment is oral hypoaesthesia, a sensory administration site reaction that is **typically transient, never rated as severe**, and lead to only 1 discontinuation
- TNX-102 SL was **very well tolerated**, with the two highest rates of systemic adverse events, sedation and fatigue, both at 3.6%
- Only 17.7% of TNX-102 SL group discontinued early (16.5% on Placebo)

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Since the F304 "RELIEF" Study

- Fibromyalgia
  - F306 "RALLY"
    - Second phase 3 study similar to RELIEF
    - Enrollment was stopped at the interim
    - Excess drop-outs in both drug- and placebo-arms
      - Delta wave of the COVID-19 landscape may have contributed to terminations
  - F307 "RESILIENT"
    - Potentially confirmatory pivotal phase 3 study enrolling
    - Design is similar to RELIEF and RALLY
    - Expecting interim results in Q2 2023

- Fibromyalgia – like Long COVID
  - PA201 "PREVAIL"
  - Approximately two-thirds of Long COVID patients have multi-site pain

CNS PORTFOLIO

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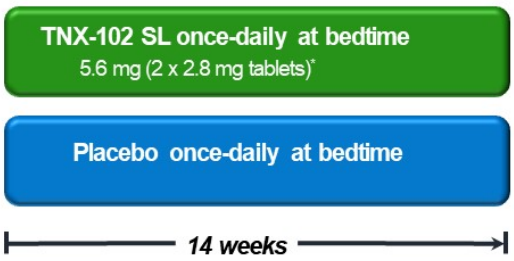
Phase 3 RESILIENT Study Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia
- U.S. sites only, expected to enroll approximately 470 patients
- One unblinded interim analysis based on 50% of randomized participants

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
  - Analyzed by mixed model repeated measures with multiple imputation (MMRM with MI)



*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)

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Phase 2 PREVAIL Fibromyalgia-Type Long COVID Study Design

CNS PORTFOLIO

Study characteristics:

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

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
  - Analyzed by mixed model repeated measures with multiple imputation (MMRM with MI)

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)"

TONIX PHARMACEUTICALS

THANK YOU

Exhibit 99-03

Efficacy and Safety of TNX-102 SL* (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results from the Randomized, Placebo-Controlled RELIEF Trial

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

INTRODUCTION

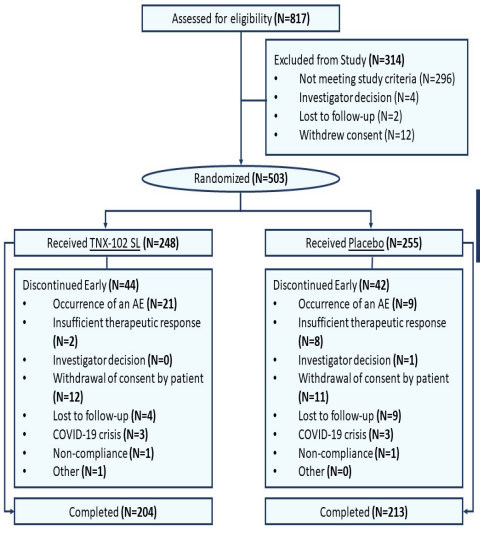
Fibromyalgia (FM) is characterized by chronic widespread pain, fatigue, and nonrestorative sleep that is linked to nociplastic pain (central sensitization). FM afflicts an estimated 6-12 million adults in the U.S., the majority of whom are women. Physicians and patients report common dissatisfaction with currently marketed products. TNX-102 SL ("TNX") is a patented sublingual tablet formulation of cyclobenzaprine HCl which provides rapid transmucosal absorption and reduced production of an active metabolite due to bypass of first-pass hepatic metabolism. TNX is a multifunctional agent with potent binding and antagonist activities at the 5-HT_{2A}-serotonergic, α_1-adrenergic, H_1-histaminergic, and M_1-muscarinic receptors. TNX is believed to work in FM by targeting improvement in sleep quality, which, in turn, reverses nociplastic pain. Previous Phase 2 and 3 trials of TNX at 2.8 mg showed signals for broad efficacy, including robust effects in sleep and other FM symptoms, but narrowly missed significance on the primary outcome of daily diary pain reduction. Accordingly, this Phase 3 trial ('RELIEF') evaluated efficacy and safety of TNX for FM at 5.6 mg.

METHODS

Phase 3 'RELIEF' was a double-blind, randomized, placebo-controlled trial designed to evaluate the efficacy and safety of TNX. Intent-to-treat sample was made up of 503 patients meeting 2016 FM diagnostic criteria who were enrolled in the 14-week trial at 39 U.S. sites. Patients received TNX 2.8 mg or placebo for 2 weeks followed by TNX 5.6 mg or placebo for 12 weeks. Primary outcome measure was change from baseline in weekly average of daily diary pain scores (0-10 NRS) at Week 14. The 1st key secondary endpoint was proportion of responders who were "much improved" or "very much improved") on Patient Global Impression of Change (PGIC). Remaining key secondaries were: Fibromyalgia Impact Questionnaire-Revised (FIQ-R) symptom domain; FIQ-R function domain; Patient Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance; PROMIS Fatigue; and daily diary NRS of sleep quality. Data were analyzed by mixed model repeated measures (MMRM) with multiple imputation for missing data or by logistic regression for PGIC. To adjust for multiplicity and control for overall type I error, a fixed sequence procedure was applied to the primary and key secondary efficacy endpoints.

RESULTS

Figure 1: CONSORT Diagram

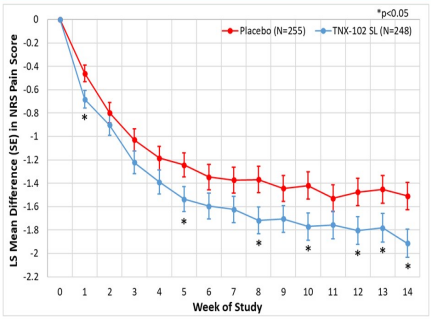


As seen in **Table 1**, no clinically important differences in baseline demographic or clinical characteristics were identified between groups.

Table 1: Demographics and Baseline Characteristics

	TNX-102 SL (N=248)	Placebo (N=255)	Total (N=503)

Figure 2: Mean Change from Baseline in Weekly Averages of Daily NRS Pain Scores



The 1st key secondary endpoint, the PGIC responder analysis trended for a greater proportion of responders (rating of "very much improved" or "much improved" at Week 14) to TNX-102 SL (37.5%) compared with placebo (29.4%), but the result was not statistically significant (p=0.058) **(Table 2)**. Due to the hierarchical statistical testing order, analyses of remaining endpoints are considered descriptive and are reported with nominal p-values.

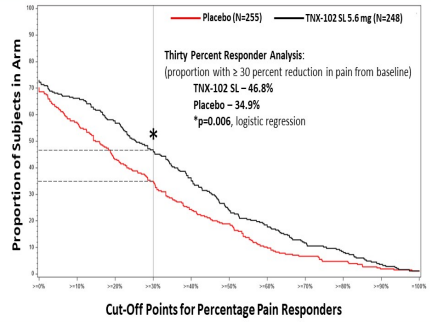
Effects on Symptoms and Functioning as Measured by FIQ-R

The syndromal activity of TNX was studied by the FIQ-R. TNX showed improvement over placebo in both the Symptom domain (LS mean difference [SE] = -4.3 [1.60] units; p=0.007) **(Figure 4)** and Function domain (-4.4 [1.69] units; p=0.009) **(Figure 5)**.

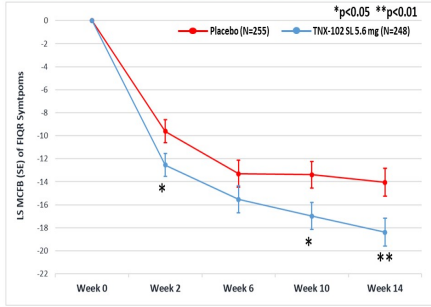
Effects on Sleep and Fatigue as Measured by PROMIS

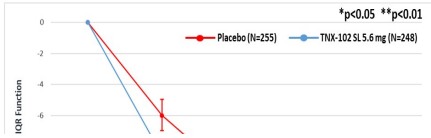
For the PROMIS Sleep Disturbance instrument, TNX substantially improved over placebo on T-scores (LS mean difference: -2.9 [0.82] units; p<0.001) **(Figure 6)**. Additionally, TNX showed improvement over placebo on the PROMIS Fatigue instrument T-scores (-1.8 [0.76] units; p=0.018) **(Figure 7)**.

Figure 3: Continuous Responder Analysis Graph



Figures 4 & 5: MCFB in FIQ-R Symptom Domain and FIQ-R Function Domain





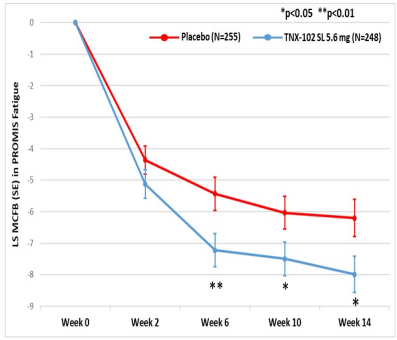


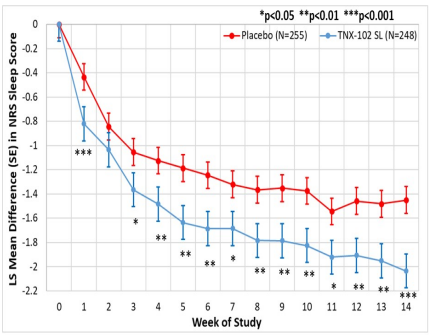
Table 2: Summary of Key Secondary Endpoints

Outcome Measure at Week 14	TNX-102 SL (N=248)	Placebo (N=255)	*P*-value
Non-Specific	%	%	
PGIC Responders	37.5%	29.4%	0.058
Fibromyalgia Syndrome-Related	**LS Mean [SE]**	**LS Mean [SE]**	
FIQ-R Symptom Domain	-18.4 [1.21]	-14.0 [1.21]	0.007#
FIQ-R Function Domain	-13.6 [1.26]	-9.3 [1.26]	0.009#
PROMIS Sleep Disturbance	-9.5 [0.64]	-6.5 [0.61]	<0.001#
PROMIS Fatigue	-8.0 [0.58]	-6.2 [0.59]	0.018#
Daily Sleep Quality Diary, NRS	-2.0 [0.12]	-1.5 [0.12]	<0.001#

nominally significant

Figure 8: Mean Change from Baseline in Weekly Averages of Daily NRS Sleep Quality Scores

For the daily diary sleep quality ratings, TNX-102 SL (-2.0 [0.12] units) compared to placebo (-1.5 [0.12] units) was nominally significant (LS mean difference: -0.6 [0.17] units; p<0.001).



TNX-102 SL was similarly well tolerated as in Phase 2 BESTFIT and Phase 3 AFFIRM studies which both studied TNX at a lower dose of 2.8 mg daily. There were no new safety signals observed in the RELIEF study at the 5.6 mg daily dose. As expected, based on prior TNX-102 SL studies, administration site reactions are the most commonly reported adverse events and were higher in the TNX-102 SL treatment group, including rates of oral or tongue numbness or tingling, bitter or unpleasant aftertaste, and tongue pain **(Table 3)**. The only systemic treatment-emergent adverse events that occurred at a rate of 3.0% or greater in the TNX arm were sedation, fatigue, and dry mouth, which are consistent with known side effects of marketed oral cyclobenzaprine. Adverse events resulted in premature study discontinuation in 8.9% of those who received TNX compared with 3.9% of placebo recipients. Among participants randomized to the TNX and placebo arms, 82.3% and 83.5%, respectively, completed the 14-week dosing period.

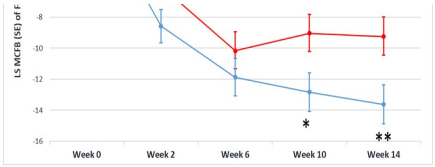
Table 3: Treatment-Emergent Adverse Events in ≥3% of Subjects Assigned to TNX

	TNX-102 SL (N=248)		Placebo (N=255)		Total (N=503)	
Systemic Adverse Events	N	%	N	%	N	%

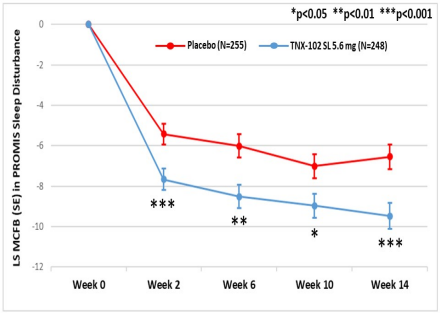
Females, %	93.5%	96.9%	95.2%
White, %	89.5%	84.7%	87.1%
Not Hispanic or Latino, %	82.7%	83.5%	83.1%
Married, %	54.4%	54.5%	54.5%
Avg. age, years	50.0	49.3	49.6
BMI (kg/m^2)	32.4	31.6	32.0
Unable to work due to FM symptoms, %	6.5%	5.9%	6.2%
Education, some college or higher, %	82.7%	83.1%	82.9%
Avg. duration of disease, years	9.2	9.0	9.1

Topline Results of the RELIEF Study

As seen in **Figure 2**, the RELIEF study achieved statistical significance on the pre-specified primary efficacy endpoint: change from baseline in weekly average of daily diary pain severity numerical rating scale (NRS) scores for TNX-102 SL 5.6 mg (LS mean [SE]: -1.9 [0.12] units) versus placebo (-1.5 [0.12] units), analyzed by MMRM with multiple imputation (LS mean [SE] difference: -0.4 [0.16] units, p=0.010). Similarly, analyzed by a responder analysis, the TNX group had a higher rate of ≥30% pain responders (p=0.006), as shown in the continuous responder analysis graph **(Figure 3).** TNX separates from placebo consistently at a higher proportion up to about ≥95% improvement in pain.



Figures 6 & 7: MCFB in PROMIS Sleep Disturbance and PROMIS Fatigue



Presented at The 5th International Congress on Controversies in Fibromyalgia, March 30-31, 2023

Sedation	9	3.6	1	0.4	10	2.0
Fatigue	9	3.6	4	1.6	13	2.6
Dry Mouth	8	3.2	7	2.7	15	3.0
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Hypoaesthesia oral	43	17.3	1	0.4	44	8.7
Paraesthesia oral	14	5.6	1	0.4	15	3.0
Product taste abnormal	11	4.4	1	0.4	12	2.4
Glossodynia	9	3.6	2	0.8	11	2.2

DISCUSSION & CONCLUSIONS

- Bedtime TNX at the 5.6 mg dose significantly reduced daily pain (p=0.010) and was associated with a higher rate of ≥30% pain responders (p=0.006).
- TNX demonstrated robustly improved daily sleep quality (**Fig. 8**), consistent with the proposed mechanism that TNX targets nonrestorative sleep to reverse symptoms of nociplastic pain
- TNX is a well tolerated, non-addictive analgesic that is not associated with common side-effects of other oral FM treatments that include weight gain, sexual dysfunction, insomnia and nausea.
- TNX improves patient global functioning by providing robust syndromal relief of FM, including improvements in pain, sleep and fatigue.