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): December 7, 2020

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.)**

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

Registrant's telephone number, including area code: (212) 980-9155

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 Global 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.

Tonix Pharmaceuticals Holding Corp (the "Company") issued a press release and held a conference call announcing positive Phase 3 RELIEF study results for its TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg product candidate for the treatment of fibromyalgia. A copy of the press release is furnished as Exhibit 99.01 hereto and incorporated herein by reference. Copies of the script of the conference call and the presentation presented during the conference call are furnished as Exhibits 99.02 and 99.03 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.01, 99.02 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 December 7, 2020, the Company announced that TNX-102 SL (cyclobenzaprine HCl sublingual tablets) met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.01) in participants with fibromyalgia in the Phase 3 RELIEF study. TNX-102 SL at 5.6 mg showed statistically significant and clinically meaningful improvement on the primary endpoint of reducing daily pain, and showed activity in improving sleep and reducing fatigue. Based on previously collected long term safety exposure data , the mature stage of the Company's Good Manufacturing Practice manufacturing processes for TNX-102 SL, and established product stability at 36 months, the Company believes that upon achieving positive results from the currently enrolling, second potential pivotal Phase 3 study, RALLY, it may potentially be in a position to submit a New Drug Application for TNX-102 SL for fibromyalgia to the U.S. Food and Drug Administration in 2022 without further addiction liability studies, with commercial manufacturing to supply to the U.S. market in 2022.

Table 1. Results of Primary and Secondary Endpoints

Outcome Measure at Week 14	Intent-to-Treat Analysis	P-value[1]
Primary Endpoint		
Daily Pain Diary, NRS	Mean Change (Primary Analysis)[2]	0.010*
Key Secondary Endpoints		
Non-specific		
Patient Global Impression of Change	Proportion "Much" or "Very Much Improved"	0.058 (LR)
Fibromyalgia Syndrome-Related		
FIQ-R Symptom Domain	Mean Change	0.007#
FIQ-R Function Domain	Mean Change	0.009#
PROMIS Fatigue	Mean Change	0.018#
Daily Sleep Quality Diary, NRS	Mean Change	<0.001#
PROMIS Sleep Disturbance	Mean Change	<0.001#

Abbreviations: FIQ-R = Fibromyalgia Impact Questionnaire - Revised; PROMIS = Patient-Reported Outcomes Measurement Information System; LR = Logistic Regression (missing data considered non-responders); NRS = Numeric Rating Scale

* statistically significant at p<0.0452

nominally significant at p<0.0452

[1] Analysis by Mixed Model Repeated Measures with Multiple Imputation unless otherwise indicated.

[2] Primary endpoint analysis for FDA approvals of Cymbalta® and Lyrica® in fibromyalgia.

SUMMARY OF TOPLINE RESULTS OF THE RELIEF STUDY

In analyzing the efficacy endpoints, a sequential test procedure was applied to the primary and six key secondary efficacy endpoints such that each endpoint had to meet the statistical significance (below a two-sided 0.0452 p-value) for all subsequent endpoints to be considered for statistical significance.

The RELIEF study achieved statistical significance on the primary efficacy endpoint: change from baseline in the 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 mixed model repeated measures with multiple imputation (LS mean [SE] difference: -0.4 [0.16] units, p=0.010, Table 1).

The statistically significant improvement in pain is further substantiated when diary pain was analyzed by another standard statistical approach, a 30 percent responder analysis, with 46.8% on active and 34.9% on placebo having a 30 percent or greater reduction in pain (logistic regression; odds ratio [95% CI]: 1.67 [1.16, 2.40]; p=0.006).

The key secondary efficacy endpoints, in sequential order, are: (1) Patient Global Impression of Change (PGIC) (responder analysis); (2) FIQ-R symptom domain score (mean change); (3) FIQ-R function domain score (mean change); (4) PROMIS Sleep Disturbance instrument T-score (mean change); (5) PROMIS Fatigue instrument T-score (mean change); and (6) daily diary NRS assessment of sleep quality (mean change). The responder analysis of PGIC trended for a greater proportion of responders (rating of “very much improved” or “much improved” at week 14) to TNX-102 SL of 37.5% compared with placebo of 29.4%, but the result did not achieve statistical significance (logistic regression; odds ratio [95% CI]: 1.44 [0.99, 2.10]; p=0.058). Therefore, because of the sequential test waterfall, the remaining key secondary endpoints only could be considered at best nominally significant. The Company believes that the ongoing COVID-19 pandemic may have affected trial participants’ sense of well-being and confounded the Patient Global Impression of Change measure, a general measure of patient self-assessed benefit that is not tied to any specific symptom of fibromyalgia. The five other key secondary endpoints all resulted in nominal p-values of less than 0.02.

Consistent with the proposed mechanism that TNX-102 SL acts in fibromyalgia through improving sleep quality, TNX-102 SL showed nominal improvement of sleep by several measures. For 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). For the PROMIS Sleep Disturbance instrument, TNX-102 SL was also nominally significant over than placebo on T-scores (LS mean difference: -2.9 [0.82] units; p<0.001). The effect sizes on the diary sleep ratings and PROMIS Sleep Disturbance instrument were 0.31 and 0.32, respectively.

TNX-102 SL showed nominal improvement over placebo on the PROMIS Fatigue instrument T-scores (-1.8 [0.76] units; p=0.018).

The syndromal activity of TNX-102 SL was studied by the Fibromyalgia Impact Questionnaire – Revised (FIQ-R). TNX-102 SL showed nominal improvement over placebo in both the symptom domain (-4.3 [1.60] units; p=0.007) and function domain (-4.4 [1.69] units; p=0.009).

SAFETY RESULTS OF THE PHASE 3 RELIEF STUDY

In the RELIEF study, TNX-102 SL was similarly well tolerated as in Phase 2 BESTFIT and Phase 3 AFFIRM studies which both studied TNX-102 SL 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. Among participants randomized to the TNX-102 SL and placebo arms, 82.3% and 83.5%, respectively, completed the 14-week dosing period. 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 tongue/mouth numbness, pain/discomfort of tongue/mouth, mouth taste impairment and tongue/mouth tingling, and taste impairment (6.5% vs. 0.4%). Tongue/mouth numbness or tingling and taste impairment were local effects nearly always temporally related to dose administration and transiently expressed (<60 minutes) in most occurrences. The only systemic treatment-emergent adverse events that occurred at a rate of 5.0% or greater in either arm was somnolence/sedation at 5.6 percent in the TNX-102 SL arm which was consistent with known side effects of marketed oral cyclobenzaprine. Adverse events resulted in premature study discontinuation in 8.9% of those who received TNX-102 SL compared with 3.9% of placebo recipients. There were a total of seven serious adverse events in the study, none of which were deemed related to investigational product; 5 in placebo arm, and two in TNX-102 SL arm. Of the two in the TNX-102 arm, one was a motor vehicle accident with multiple bone fractures, and the other was a pneumonia secondary to an infection.

Table 2. Treatment-Emergent Adverse Events at Rate of 5% or Greater in Either Treatment Arm

	TNX-102 SL (N=248)		Placebo (N=255)		Total (N=503)	
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Oral numbness	43	17.3	2	0.8	45	8.9
Oral pain/discomfort	29	11.7	5	2.0	34	6.8
Taste impairment	16	6.5	1	0.4	17	3.4
Oral tingling	14	5.6	1	0.4	15	3.0
Systemic Adverse Events	**N**	**%**	**N**	**%**	**N**	**%**
Somnolence/Sedation	14	5.6	3	1.2	17	3.4

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 results of the Phase 3 RELIEF study, 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 December 7, 2020
99.02	Conference Call Script
99.03	Presentation of the Company

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: December 7, 2020

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

Exhibit 99.01

Tonix Pharmaceuticals Announces Positive Phase 3 RELIEF Study Results for TNX-102 SL 5.6 mg in Fibromyalgia

New 5.6 mg Dose Achieved Statistically Significant Pain Reduction Over Placebo at Week 14 (Primary Endpoint, p=0.01)

TNX-102 SL Generally Well Tolerated with Adverse Event Profile Comparable to Prior Studies; No New Safety Signals Observed

Approximately 90% of Those Affected by Fibromyalgia are Women; 95% of Participants in the RELIEF Study were Women

Company to Host Conference Call Today at 8:30 a.m. EST

CHATHAM, N.J., December 7, 2020 - Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that TNX-102 SL (cyclobenzaprine HCl sublingual tablets) met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.01) in participants with fibromyalgia in the Phase 3 RELIEF study (Table 1). TNX-102 SL is a novel, non-opioid, centrally-acting analgesic, taken once daily at bedtime, being developed for the management of fibromyalgia. RELIEF was a 14-week randomized, double-blind, placebo-controlled trial of TNX-102 SL 5.6 mg, in which 503 participants with fibromyalgia were randomized in a 1:1 ratio across 39 U.S. sites. All participants received one tablet of TNX-102 SL (2.8 mg) or placebo for the first two weeks, which was increased to two tablets of TNX-102 SL (5.6 mg) or placebo for the remaining 12 weeks.

“Tonix is dedicated to improving the lives of the millions suffering from fibromyalgia, approximately 90% of whom are female, and the results of the RELIEF trial bring new hope to this community,” said Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals. “TNX-102 SL at 5.6 mg showed statistically significant and clinically meaningful improvement on the primary endpoint of reducing daily pain, as well as showed activity in key secondary endpoints of improving sleep and reducing fatigue. One of the biggest challenges in drug development is finding a dose that balances efficacy and tolerability. We are pleased with the consistent effects of TNX-102 SL 5.6 mg on the primary endpoint of daily pain as well as the tolerability of this dose in the RELIEF study. We are also pleased at the activity shown on all of the fibromyalgia specific, pre-specified secondary endpoints. We look forward to the results of the currently enrolling, second potential pivotal Phase 3 study, RALLY, for which we expect to report topline data in the second half of 2021. Based on the long term safety exposure data we have already collected, the mature stage of our Good Manufacturing Practice (GMP) manufacturing processes and the established product stability at 36 months, we believe that upon achieving positive results from the currently enrolling RALLY study, we may potentially be in a position to submit a New Drug Application (NDA) for TNX-102 SL for fibromyalgia to the U.S. Food and Drug Administration (FDA) in 2022. Additionally, we believe that our commercial manufacturing is on track to supply the U.S. market in 2022.”

Table 1. Results of Primary and Secondary Endpoints

Outcome Measure at Week 14	Intent-to-Treat Analysis	P-value[1]
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PROMIS Fatigue	Mean Change	0.018#
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Abbreviations: FIQ-R = Fibromyalgia Impact Questionnaire - Revised; PROMIS = Patient-Reported Outcomes Measurement Information System; LR = Logistic Regression (missing data considered non-responders);
NRS = Numeric Rating Scale

* statistically significant at p<0.0452

nominally significant at p<0.0452

[1] *Analysis by Mixed Model Repeated Measures with Multiple Imputation unless otherwise indicated.*
[2] *Primary endpoint analysis for FDA approvals of Cymbalta® and Lyrica® in fibromyalgia.*

"These results support the proposed mechanism in which TNX-102 SL targets disturbed sleep in fibromyalgia and that improved sleep quality leads to improvement of fibromyalgia at the syndromal level," continued Dr. Lederman. "The sleep disorder specific to fibromyalgia has been called 'non-restorative' sleep. Dr. Harvey Moldofsky, Professor emeritus of Psychiatry and Medicine at the University of Toronto, founding Director of the University of Toronto Center for Sleep and Chronobiology, and Member of the Tonix Scientific Advisory Board, first recognized the central role of non-restorative sleep in the pathogenesis of fibromyalgia[3,4]. Our program is based on the subsequent pioneering work of Dr. Iredell W. Iglehart III, Assistant Professor of Medicine, part-time, Division of Rheumatology, Johns Hopkins School of Medicine, and Member of the Tonix Scientific Advisory Board, who recognized that a sleep-focused cyclobenzaprine treatment protocol had the potential to target non-restorative sleep and lead to improvement of fibromyalgia at the syndromal level[5]. Transforming this treatment paradigm into a potential product with the clinical activity described in the RELIEF study depended on the invention of the Protectic® and Angstro® technologies. These technologies are integral to TNX-102 SL, which is a sublingual tablet designed for transmucocal delivery of cyclobenzaprine with distinctive pharmacokinetic properties that include bypassing first-pass hepatic metabolism. Teams led by Giorgio Reiner at APR Applied Pharma Research S.A. and Professor Marino Nebuloni and Patrizia Colombo at Redox Analytical Science Srl invented and developed these underlying technologies in collaboration with Tonix."

"I'm pleased that TNX-102 SL has demonstrated statistically significant treatment effects on fibromyalgia pain," said Dr. Harvey Moldofsky. "These results validate the mechanism that improving sleep quality can lead to syndromal effects on fibromyalgia. The sublingual formulation of TNX-102 SL for transmucosal absorption showed promise at the 2.8 mg dose in two prior studies, but now that the 5.6 mg dose has shown consistent efficacy, we are encouraged in the outcome of future studies."

“TNX-102 SL has the potential to be a new non-addictive, non-opiate analgesic for the management of fibromyalgia which is particularly important given that fibromyalgia is a chronic pain condition,” said Gregory Sullivan, M.D., Chief Medical Officer of Tonix. “Approximately one third of fibromyalgia patients resort to opiates out of desperation and because of dissatisfaction with available therapies. Cyclobenzaprine, the active ingredient of TNX-102 SL, has no recognized potential for addiction. Based on our previous discussions with FDA, we expect to submit an NDA without new addiction liability studies. TNX-102 SL could potentially offer fibromyalgia patients, who have multiple disabling fibromyalgia symptoms, a first-line monotherapy with broad symptom relief, and the compliance advantage of being administered once-a-day (at bedtime).”

[3] *Moldofsky H et al, Psychosom Med 1975;37:341-51.*
[4] *Moldofsky H and Scarisbrick P. Psychosom Med 1976;38:35-44.*
[5] *Iglehart IW. 2003; US Patent 6,541,523.*

SUMMARY OF TOPLINE RESULTS OF THE RELIEF STUDY

The RELIEF study included a pre-specified interim analysis that was conducted in September 2020. Due to the inclusion of the potential to stop for success for this interim analysis, positive results required a two sided p-value of 0.0452 for both primary and secondary endpoints. Based on interim results, the independent data monitoring committee (IDMC) made the non-binding recommendation that the trial continue to completion with the addition of 210 participants to the original sample size of 470 participants, which was the maximum number of participants that could be added under the interim statistical analysis plan. Given this information, the Company decided to complete the study with the 503 enrolled participants and not to add additional participants. The first cohort of the study was enrolled between December 2019 and April 2020 at a time when the COVID-19 pandemic struck the U.S. Due to the pandemic, the Company modified the protocol in accordance with FDA guidelines to ensure patient safety and minimize risk in enrolling the first cohort. The modification allowed sites to conduct remote study visits for select cases in which the COVID-19 pandemic made on-site visits unsafe or otherwise not possible. The second cohort was enrolled between last week of April and July 2020 and, by this time, the sites’ COVID-19-related safety procedures for participants’ attendance at clinic visits had become routine. At the time of the interim analysis in September 2020, there were only 15 participants still active in the study, all of whom completed their last visit by the end of October 2020.

In analyzing the efficacy endpoints, a sequential test procedure was applied to the primary and six key secondary efficacy endpoints such that each endpoint had to meet statistical significance (below a two-sided 0.0452 p-value) in order for the subsequent endpoints to be considered for statistical significance.

The RELIEF study achieved statistical significance on the pre-specified primary efficacy endpoint: change from baseline in the 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 mixed model repeated measures with multiple imputation (LS mean [SE] difference: -0.4 [0.16] units, p=0.010, Table 1).

The statistically significant improvement in pain is further substantiated when diary pain was analyzed by another standard statistical approach, a 30 percent responder analysis, with 46.8% on active and 34.9% on placebo having a 30 percent or greater reduction in pain (logistic regression; odds ratio [95% CI]: 1.67 [1.16, 2.40]; p=0.006).

The key secondary efficacy endpoints, in sequential order, were: (1) Patient Global Impression of Change (PGIC) (responder analysis); (2) FIQ-R symptom domain score (mean change); (3) FIQ-R function domain score (mean change); (4) PROMIS Sleep Disturbance instrument T-score (mean change); (5) PROMIS Fatigue instrument T-score (mean change); and (6) daily diary NRS assessment of sleep quality (mean change). The responder analysis of PGIC trended for a greater proportion of responders (rating of "very much improved" or "much improved" at Week 14) to TNX-102 SL of 37.5% compared with placebo of 29.4% , but the result did not achieve statistical significance (logistic regression; odds ratio [95% CI]: 1.44 [0.99, 2.10]; p=0.058). Therefore, because of the sequential test waterfall, the remaining key secondary endpoints only could be considered nominally significant at best.

"The results on Patient Global Impression of Change or PGIC were unexpected based on results from the prior studies. PGIC is a general measure of patient self-assessed benefit that is not tied to any specific symptom of fibromyalgia. In two prior studies of TNX-102 SL at 2.8 mg in fibromyalgia, PGIC met statistical significance in both. We speculate that the ongoing COVID-19 pandemic might have affected the participants' sense of well-being and confounded the PGIC measure," said Dr. Sullivan. "The five other key secondary endpoints all resulted in nominal p-values of less than 0.02."

Consistent with the proposed mechanism that TNX-102 SL acts in fibromyalgia through improving sleep quality, TNX-102 SL showed nominal improvement of sleep by several measures. 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). For the PROMIS Sleep Disturbance instrument, TNX-102 SL was also nominally significant over placebo on T-scores (LS mean difference: -2.9 [0.82] units; p<0.001). The effect sizes on the diary sleep ratings and PROMIS Sleep Disturbance instrument were 0.31 and 0.32, respectively.Fatigue is another cardinal symptom of fibromyalgia. TNX-102 SL showed nominal improvement over placebo on the PROMIS Fatigue instrument T-scores (-1.8 [0.76] units; p=0.018).

The syndromal activity of TNX-102 SL was studied by the Fibromyalgia Impact Questionnaire – Revised (FIQ-R). TNX-102 SL showed nominal improvement over placebo in both the symptom domain (-4.3 [1.60] units; p=0.007) and function domain (-4.4 [1.69] units; p=0.009).

SAFETY RESULTS OF THE PHASE 3 RELIEF STUDY

In the RELIEF study, TNX-102 SL was similarly well tolerated as in Phase 2 BESTFIT and Phase 3 AFFIRM studies which both studied TNX-102 SL 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. Among participants randomized to the TNX-102 SL and placebo arms, 82.3% and 83.5%, respectively, completed the 14-week dosing period. 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 tongue/mouth numbness , pain/discomfort of tongue/mouth, taste impairment, and tongue/mouth tingling (Table 2). Tongue/mouth numbness or tingling and taste impairment were local effects nearly always temporally related to dose administration and transiently expressed (<60 minutes) in most occurrences. The only systemic treatment-emergent adverse events that occurred at a rate of 5.0% or greater in either arm was somnolence/sedation at 5.6% in the TNX-102 SL arm, which was consistent with known side effects of marketed oral cyclobenzaprine.. Adverse events resulted in premature study discontinuation in 8.9%of those who received TNX-102 SL compared with 3.9%of placebo recipients. There were a total of 7 serious adverse events in the study, none of which were deemed related to investigational product; 5 in placebo arm, and 2 in TNX-102 SL arm. Of the 2 in the TNX-102 SL arm, one was a motor vehicle accident with multiple bone fractures, and the other was a pneumonia secondary to an infection.

Table 2. Treatment-Emergent Adverse Events at Rate of 5% or Greater in Either Treatment Arm

	TNX-102 SL (N=248)		Placebo (N=255)		Total (N=503)	
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Oral numbness	43	17.3	2	0.8	45	8.9
Oral pain/discomfort	29	11.7	5	2.0	34	6.8
Taste impairment	16	6.5	1	0.4	17	3.4
Oral tingling	14	5.6	1	0.4	15	3.0
Systemic Adverse Events	**N**	**%**	**N**	**%**	**N**	**%**
Somnolence/Sedation	14	5.6	3	1.2	17	3.4

Conference Call Information

Tonix Pharmaceuticals will host a live conference call and webcast with slides today at 8:30 a.m. Eastern Time to discuss the topline results of this clinical trial. The call can be accessed by dialing (866) 896-2215 (U.S. and Canada) or (617) 401-8110 (international) and referencing conference ID 9045217. Callers should dial in approximately 10 minutes prior to the start of the call. A question and answer session with the Tonix management team will follow the company's remarks. Individuals can participate in an interactive Q&A session by submitting pertinent questions via the webcast platform. To access the live webcast or the replay, visit the investor page of the Company's website at https://ir.tonixpharma.com/ir-events. The webcast will be recorded and available on the Company's website for 90 days.

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 serotonin-2A, alpha-1 adrenergic, histamine-H1, and muscarinic-M1 receptors, TNX-102 SL is in clinical development as a daily bedtime treatment for fibromyalgia, PTSD, alcohol use disorder and agitation in Alzheimer's disease. The U.S. Patent and Trademark Office (USPTO) has 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 these patents 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 and RALLY Studies

The RELIEF and RALLY studies are double-blind, randomized, placebo-controlled phase 3 trials designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets). The two-arm trials each targeted enrolling 470 participants at approximately 40 U.S. sites. For the first two weeks of treatment, there is 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 have 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 is 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).

Additional details about the ongoing RALLY study are available at clinicaltrials.gov (NCT04508621).

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing small molecules and biologics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is primarily composed of central nervous system (CNS) and immunology product candidates. The CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer and autoimmune diseases. In addition to fibromyalgia, Tonix's lead CNS candidate, TNX-102 SL**, is in development for the treatment of PTSD, agitation in Alzheimer's disease (AAD) and alcohol use disorder (AUD). The PTSD program is in Phase 3 development, while AAD and AUD are Phase 2 ready. The AAD program has FDA Fast Track designation. Tonix's programs for treating addiction conditions also include TNX-1300* (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution), which is in Phase 2 development for the treatment of life-threatening cocaine intoxication and which has FDA Breakthrough Therapy designation. TNX-601 CR** (tianeptine oxalate controlled-release tablets) is another CNS program, currently in Phase 1 development as a daytime treatment for depression while TNX-1900**, intranasal oxytocin, is in development as a non-addictive treatment for migraine and cranio-facial pain. Tonix's lead vaccine candidate, TNX-1800*, is a live replicating vaccine based on the horsepox viral vector platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects efficacy data from animal studies of TNX-1800 in the first quarter of 2021. TNX-801*, live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox. Tonix's preclinical pipeline includes TNX-1600** (triple reuptake inhibitor), a new molecular entity being developed as a treatment for PTSD; TNX-1500* (anti-CD154), a monoclonal antibody being developed to prevent and treat organ transplant rejection and autoimmune conditions; and TNX-1700* (rTFF2), a biologic being developed to treat gastric and pancreatic cancers.

*TNX-1800, TNX-801, TNX-2300, TNX-2600, TNX-1300, TNX-1500 and TNX-1700 are investigational new biologics and have not been approved for any indication.

**TNX-102 SL, TNX-601 CR, TNX-1600 and TNX-1900 are investigational new drugs and have not been approved for any indication.

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

About APR Applied Pharma Research s.a.

APR is an independent pharma company headquartered in Switzerland with subsidiaries in Italy and Germany focused, since more than 25 years, in the development and commercialization of products intended to improve the quality of life of patients and families affected with rare or debilitating diseases. APR leverages many years of experience in developing patented drug delivery technologies, which are then applied to develop innovative therapeutic solutions.

Further information about APR Applied Pharma Research can be found at www.apr.ch

About Redox - Analytical Science srl

Redox is an independent CRO company headquartered in Monza- Italy with R&D activities and customer analytical support to pharmaceutical companies for more than 30 years. From more than 25 years the analytical activities have been certified by national and international agencies (European Medicines Agency, the Italian Medicines Agency (AIFA), FDA, and etc). One of the main activities is the development of new drug products in order to improve the pharmaceutical actions and at the same time improve the stability and reducing the cost of the new drug substance. Several unique and sophisticated analytical techniques and equipment are used in support to research and development strategies with the focus to reach the best and effective pharmaceutical formulation in a short time frame. More than 30 professional people are dedicated to our efforts and many projects are ongoing in collaboration with the pharmaceutical industry as well as with Italian and international Universities.

Further information about Redox can be found at www.labredox.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 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, 2019, as filed with the Securities and Exchange Commission (the “SEC”) on March 24, 2020, 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

Tonix Pharmaceuticals

Phase 3 RELIEF Study Topline Results Conference Call

December 7, 2020

Operator

Good morning, ladies and gentlemen and welcome to Tonix Pharmaceuticals' conference call to discuss the results of the Phase 3 RELIEF study. At this time all participants are in a listen-only mode. Later we will conduct a question-and-answer session. Instructions will follow at that time. As a reminder this conference call is being recorded.

I would now like to turn the conference over to Peter Vozzo of Westwicke, investor relations for Tonix Pharmaceuticals. You may begin.

Peter Vozzo

Thank you, [*operator's name*].

Good morning everyone and thank you for joining us today. We will review results of the Phase 3 RELIEF study of TNX-102 SL for fibromyalgia.

Earlier this morning, the company issued a press release announcing the results of the study.

On the call with me today are Tonix Pharmaceuticals' president and chief executive officer, Dr. Seth Lederman; and chief medical officer, Dr. Greg Sullivan.

Today's call is being made available via the Investor Relations section of the company's website at ir.tonixpharma.com.

Following remarks by management we will open the call to questions.

Before we begin, I would like to remind everyone that this call will contain forward-looking statements, which are subject to risks and uncertainties. Any statements regarding future events, results or expectations are forward-looking statements. Please note that these forward-looking statements reflect our opinions only as of the date of this call. We undertake no obligation to revise or update these forward-looking statements in light of new information or future events, except as required by law. Information concerning factors that could cause actual results to differ materially from those contained in or implied by such forward-looking statements are discussed in greater detail in our most recent Form 10-Q and Form 10K filed with the SEC, especially under the caption Risk Factors.

I will now turn the call over to Dr. Lederman.

Seth Lederman – CEO

Thank you, Peter, and good morning to everyone joining us.

Today we are pleased to talk to you about the positive topline results of the Phase 3 RELIEF study. Today's news is a major accomplishment and milestone in the development of TNX-102 SL, and is particularly encouraging news for the millions suffering from the debilitating impact of fibromyalgia.

On today's call, I will provide a few opening remarks, and then we will spend much of the time with our Chief Medical Officer, Dr. Greg Sullivan, who will review the topline data we have reported on today. We'll then follow with Q&A.

As Greg will cover in much more detail, allow me to summarize some of the key takeaways from our topline data results. First, our new 5.6 mg dose achieved statistically significant pain reduction over placebo at Week 14, which was the primary endpoint. TNX-102 SL was generally well tolerated with an adverse event profile that was comparable to our prior studies, and with no new safety signals observed. We are very pleased with these results, and believe it validates our view that TNX-102 SL can provide a meaningful clinical benefit for patients suffering from fibromyalgia.

Slide 3 (TNX-102 SL: Potential Treatment for Fibromyalgia)

Turning to slide 3, fibromyalgia is a common and complex central nervous system condition characterized by chronic widespread pain, nonrestorative sleep and fatigue, as well as diminished cognition and mood disturbances, all of which negatively impact the quality of life for these sufferers. Around 6-12 million adults in the U.S. have fibromyalgia – 90% of whom are women. And fewer than half of those treated for fibromyalgia receive complete relief from the three FDA-approved drugs. Notably, and unfortunately, more than one-third of those with fibromyalgia use opioids, off label, as a means of treatment.

Slide 4 (Overview of TNX-102 SL)

Before we turn to the data, I would like to provide what we think is some important background information on TNX-102 SL and our clinical experience with the drug.

Turning to slide 4, TNX-102 SL is a Protectic proprietary formulation of cyclobenzaprine that after sublingual administration facilitates transmucosal absorption. By administering cyclobenzaprine sublingually, in contrast to oral formulations, unique pharmacokinetic and pharmacodynamic effects are achieved, as explained in the next slide.

Slide 5 (TNX-102 SL: Differentiation from Oral Formulations)

On slide 5 are provided the unique features, benefits and advantages of TNX-102 SL which differentiates it from oral formulations of cyclobenzaprine. As I mentioned in the previous slide, TNX-102 SL is a Protectic formulation which facilitates transmucosal absorption after sublingual administration. Sublingual administration offers several benefits in that it:

- bypasses hepatic metabolism and reduces formation of an “activating” metabolite
- generates a pharmacokinetic profile that is more favorable for fast onset and nighttime therapeutic action, while minimalizing the risk of residual undesirable daytime side effects
- allows the use of low doses of cyclobenzaprine to more selectively recruit high affinity target receptors (5HT2a, alpha1, H1 and M1)

I will now turn it over to Greg to run through the data.

Greg Sullivan – CMO

Slide 6 (Study Design: Phase 3 F304/RELIEF)

Thanks, Seth, and good morning everyone.

Turning to slide 6, the RELIEF study is a randomized, placebo-controlled trial of 503 participants with fibromyalgia at 39 U.S. clinical sites, with the goal of evaluating the potential clinical benefit and safety of using TNX-102 SL to treat fibromyalgia. For the first two weeks of treatment, there was a run-in period in which patients started on one tablet of 2.8 mg TNX-102 SL or placebo. After the first two weeks, all patients had the dose increased to TNX-102 SL 5.6 mg – two 2.8 mg tablets – or two placebo tablets for the remaining 12 weeks.

Recall, the study included a pre-specified interim analysis that was conducted in September 2020. Based on interim results, the independent data monitoring committee made the non-binding recommendation that the trial continue to completion with the addition of 210 participants to the original sample size of 470 participants, which was the maximum number of participants that could be added under the interim statistical analysis plan. Based on this information, we decided to complete the study with the 503 enrolled participants at that time and not to add additional participants.

Slides 7 (Primary Efficacy Endpoint)

Moving to slide 7,the primary endpoint in the RELIEF study is daily diary pain severity score change from baseline using the weekly averages of the daily numerical rating scale scores, comparing TNX-102 SL 5.6 mg with placebo, and analyzed by mixed model repeated measures with multiple imputation. TNX-102 SL demonstrated a statistically significant improvement on the primary endpoint, where the p-value was 0.01.

Slides 8 (Primary Efficacy Endpoint)

On slide 8, you can see the weekly change from baseline in pain for the two arms of the study, noting the progressively greater separation starting around week 4.

Slide 9 (Secondary efficacy endpoints)

On slide 9 you will see the key secondary efficacy endpoints. The Patient Global Impression of Change, trended for more responders but did not achieve significance at a p-value of 0.058 when significance required $p<0.045$. Whereas the next five secondaries demonstrated quite good separation from placebo. The Fibromyalgia Impact Questionnaire covers a broad array of fibromyalgia symptoms in one domain and function in another, both showing impressive p-values less than 0.01. Also, notable, the activity on PROMIS fatigue indicates effects on several of the core symptoms of fibromyalgia. Finally, two measures of sleep quality, the daily sleep quality diary and the PROMIS Sleep Disturbance instrument indicated robust separation from placebo, and these results are similar to our prior studies and consistent with our hypothesized mechanism of action of treating fibromyalgia by targeting the sleep disturbance that characterizes fibromyalgia.

Slide 10 (F304 Continuous Responder Analysis (CRA) Graph)

Turning to slide 10, we show a continuous responder analysis graph which typically can be included in the label of fibromyalgia products. It allows you to see the proportion of pain responders in each arm of the study over an entire range of cut-off points. So if you look at the typically used 30% or greater improvement, where there is a vertical line, you can draw a horizontal line from each arm to the Y-axis to see the proportion of responders at that level in each arm. Generally, you want to see separation of the two curves throughout the range of cut-off points, which is what you see here all the way up to about 95% or better reduction in pain.

Slides 11 and 12 (Safety/AEs/tolerability)

Moving to slide 11,regarding safety, as Seth mentioned, TNX-102 SL was generally well tolerated with an adverse event profile comparable to prior studies. There were no new safety signals observed. Here we see that oral administration site reactions were more common in the active group, with tongue/mouth numbness, technically referred to as oral hypoaesthesia, was the highest adverse event in the active arm. These oral AEs are similar to what was seen in prior studies with TNX-102 SL, although the tongue/mouth numbness in this study was only about half the rate of prior studies. These oral sensory AEs, numbness, tingling, impaired taste, are typically transient events related to dosing that usually last less than an hour, usually occur intermittently, are rarely rated as severe or lead to discontinuation from the study. We believe these are a result of the known local anesthetic properties of cyclobenzaprine, which is a tricyclic molecule that has inhibitory actions on voltage gated sodium channel pain receptors. Systemic adverse events were quite low, with somnolence/sedation being the only systemic AE that was greater than 5%, which you see was only 5.6% versus 1.2% in placebo.

Slide 12 (Safety/AEs/tolerability)

On slide 12, you will see that discontinuation rates were low for a study in fibromyalgia. Among participants randomized to the active and control arms, 82.3% and 83.5%, respectively, completed the 14-week dosing period. Also, only about 9% on active and 4% on placebo discontinued the study due to an adverse event. No SAEs were considered related to TNX-102 SL.

We will continue to analyze these data further, and look forward to presenting overall findings at a future medical conference.

Importantly, these data validate that TNX-102 SL has potential as a novel non-addictive, centrally-acting analgesic for the management of fibromyalgia. Upon completion of a second positive Phase 3 study, which is currently ongoing, we believe Tonix is well positioned to submit an NDA having already completed long-term exposure studies at this dose as well as the majority of CMC requirements for a product launch.

We want to express our gratitude to the RELIEF study participants and their families for their assistance in the development of this novel approach. We are now an important step closer to bringing a new potential treatment to the many patients suffering with the effects of fibromyalgia.

I will now turn the call back over to Seth.

Seth Lederman – CEO

Slide 13 (TNX-102 SL Intellectual Property – U.S. Protection expected until 2035)

Thank you Greg.

I would like to briefly review with you the IP estate for TNX-102 SL.

While we have international patent protection and filings, I will start with the U.S. There are five issued patents from the USPTO that cover the Protectic (eutectic) formulation in the U.S. It is expected that these patents will provide protection until 2035, not accounting for adjustments due to regulatory review time.

In addition, Tonix has filed patents in key markets, including EU, China and Japan, a number of which also have been issued.

Finally, patents have also been filed and issued in many other countries, and pending in others, which would support global commercialization.

Slide 14 (Next Steps)

Turning to slide 14, we look forward to the results of the currently enrolling, confirmatory Phase 3 RALLY study for which we expect to report topline data in the second half of 2021. We expect that based on the long term safety exposure data we have already collected, the mature stage of our GMP manufacturing processes and the established 36 month product stability, we will be in a position to submit an NDA for TNX-102 SL for fibromyalgia to the FDA in 2022, pending positive results from the ongoing Phase 3 RALLY study.

Slide 15 (Conclusion)

Moving to slide 15, TNX-102 SL at 5.6 mg showed statistically significant improvement on the primary endpoint of reduced daily pain while also showed activity in improving sleep and reducing fatigue. TNX-102 SL, with its unique efficacy and tolerability profile, could potentially address the unmet need for first-line therapies with broader symptom relief and better tolerability, as well as offer an option for those patients who do not respond or cannot tolerate existing therapies.

TNX-102 SL is a non-opioid, non-addictive, centrally-acting analgesic that could provide a new therapeutic option for fibromyalgia patients, with U.S. patent protection expected to extend through 2035.

Tonix is dedicated to improving the lives of the millions suffering from fibromyalgia, and the results of the RELIEF trial bring new hope to the fibromyalgia community in which there has been pervasive dissatisfaction with currently-approved products.

Our program would not be possible without our brave trial participants and their families, and we are tremendously grateful for their participation. I also want to congratulate the Tonix team that executed the trial so professionally.

I will now turn the call back to the operator for questions.

Question-and-Answer Session

Seth Lederman – concluding remarks

Thank you, everyone, for joining us this morning, and we look forward to updating you on our progress throughout the coming year.

END

Exhibit 99.03

TONIX PHARMACEUTICALS

Results of Phase 3 RELIEF Study in Fibromyalgia

Version P0260 12-7-2020 (Doc 0742)

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, risks related to failure to obtain U.S. Food and Drug Administration clearances or approvals and noncompliance with its regulations; our need for additional financing; delays and uncertainties caused by the global COVID-19 pandemic; substantial competition; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties. 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, 2019, as filed with the Securities and Exchange Commission (the "SEC") on March 24, 2020, 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.

TNX-102 SL: Potential Treatment for Fibromyalgia

Volkswagen Check Engine [Photograph]. (2011, October 14). Wikipedia

- Fibromyalgia is considered a central nervous system disorder with symptoms that include: chronic widespread pain, nonrestorative sleep, fatigue, diminished cognition and mood disturbances
- Believed to result from inappropriate pain signaling in central nervous system in the absence of peripheral injury[1]
- An estimated 6-12 million adults in the U.S. have fibromyalgia[2], 90% of whom are women
- Causes significant impairment in all areas of life[3]
  - Lower levels of health-related quality of life – reduced daily functioning
  - Interference with work (loss of productivity, disability)
- Fewer than half of those treated for fibromyalgia receive complete relief from the three FDA-approved drugs[4]
- Substantial off-label use of narcotic painkillers and prescription sleep aids[5]
  - Among those diagnosed, more than one-third have used prescription opioids as a means of treatment[6]

[1] Phillips K & Clauw DJ, Best Pract Res Clin Rheumatol 2011;25:141.
[2] American Chronic Pain Association (www.theacpa.org, 2019)
[3] Schaefer et al., Pain Pract, 2015.
[4] The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[5] Patient Trends: Fibromyalgia", Decision Resources, 2011.
[6] Berger A, Dukes E, Martin S, Edelsberg J, Oster G, Int J Clin Pract, 2007; 61(9):1498–1508.

Overview of TNX-102 SL*

Protectic® proprietary formulation of cyclobenzaprine that supports sublingual administration

TNX-102 SL is a non-opioid, centrally-acting analgesic that works by improving sleep quality

◇ Scientific Rationale for Protectic® Formulation ◇

- Engenders unique pharmacokinetic and pharmacodynamic properties that emphasize sleep properties of cyclobenzaprine while minimizing undesirable properties
- Potential therapeutic value in a constellation of disorders where sleep disturbances are:
  - Co-morbid
  - Involved in the onset, progression and severity of the disease

*TNX-102 SL is in clinical stage of development and not approved for any indication

TNX-102 SL: Differentiation from Oral Formulations

FEATURE	BENEFIT	ADVANTAGE
Cyclobenzaprine	40+ years as oral medication	Established safety record
Formulation: Protectic®	Allows submucosal absorption	Not achievable with oral formulation
Administration: sublingual	Bypasses gut	Avoids first-pass metabolism; reduced formation of "activating" metabolite
Pharmacokinetic profile	Rapid absorption (peak at ~4 hours, low trough levels 8-24 hours)	Desired profile for nighttime action
Dose: low (2.8 to 5.6 mg)	Recruitment of high affinity receptors (5-HT_{2A}, α_1, H_1, M_1)	Complimentary multi-modal mechanism of action with less risk of off-target interference

Study Design: Phase 3 RELIEF

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia in 39 U.S. sites (full sample size N=503)
- Adaptive Design: one unblinded interim analysis based on 50% of randomized participants

[1]Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

Primary endpoint (Week 14):

- Daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline in the weekly average as measured by the numerical rating scale (NRS), using mixed model repeated measures analysis with multiple imputation (MMRM with MI)

Key Secondary endpoints (Week 14):

- Patient Global Impression of Change responder analysis
- Fibromyalgia Impact Questionnaire - Revised (FIQ-R) Symptom Domain score
- FIQ-R Function Domain score
- PROMIS Sleep Disturbance instrument T-score
- PROMIS Fatigue instrument T-score
- Weekly average of the daily diary assessment of sleep quality

Pivotal efficacy study to support NDA approval

RELIEF Study: Primary Efficacy Endpoint[1]

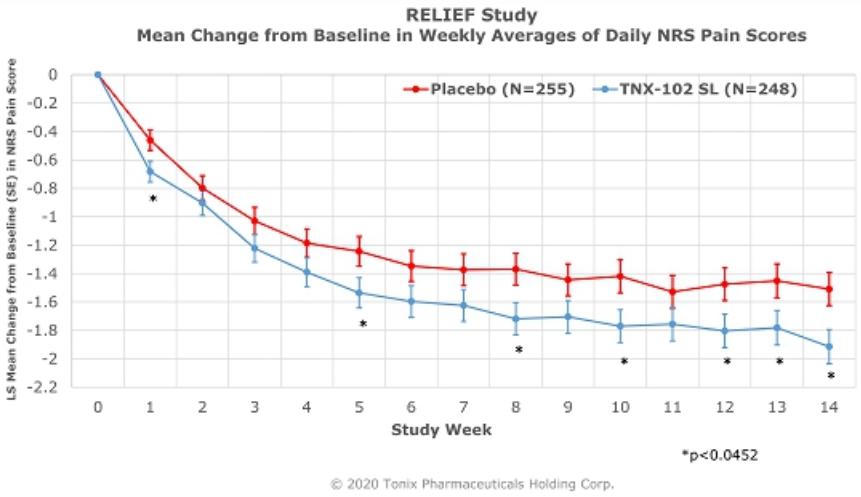
Primary Outcome Measure at Week 14	Placebo (N=255)	TNX-102 SL[2] (N=248)	Treatment Difference	P value
	LS Mean Change from Baseline (SE)	LS Mean Change from Baseline (SE)	Difference in LS Mean Change from Baseline Between TNX-102 SL and Placebo (SE)	
Daily Pain Diary, NRS	-1.5 (0.12)	-1.9 (0.12)	-0.4 (0.16)	0.010*

Statistical Method: Mixed Model Repeated Measures analysis with Multiple Imputation
*p<0.0452 (requisite p-value hurdle for full study after Interim Analysis)
[1] Same primary endpoint analysis for FDA approvals of Cymbalta® and Lyrica® in fibromyalgia
Abbreviations: LS = least squares; NRS = numeric rating scale; SE = standard error

- The successful primary efficacy analysis is also supported by an exploratory 30% responder analysis of daily diary pain, which indicated 46.8% on TNX-102 SL versus 34.9% on placebo achieved a 30 percent or greater reduction in pain (logistic regression; odds ratio [95% CI]: 1.67 [1.16, 2.40]; p=0.006)
  - 30% responder analysis was the primary analysis in F301 AFFIRM study of TNX-102 SL 2.8 mg
    - Also was the same primary endpoint analysis for FDA approval of Savella® for fibromyalgia

[2] TNX-102 SL is in clinical stage of development and not approved for any indication

RELIEF Study: Primary Efficacy Endpoint (continued)



RELIEF Study: Key Secondary Efficacy Endpoints

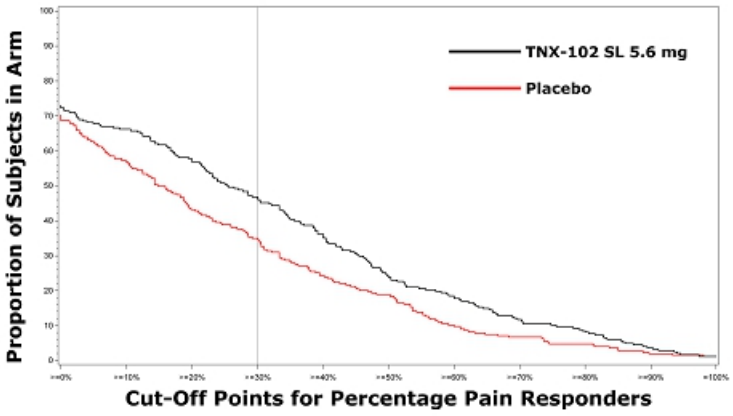
Outcome Measure at Week 14	Intent-to-Treat Analysis[1]	*P*-value
Non-Specific		
Patient Global Impression of Change	Responder Analysis: Proportion "Much Improved" or "Very Much Improved"	0.058
Fibromyalgia Syndrome-Related		
FIQ-R Symptom Domain	Mean Change from Baseline	0.007[#]
FIQ-R Function Domain	Mean Change from Baseline	0.009[#]
PROMIS Fatigue	Mean Change from Baseline	0.018[#]
Daily Sleep Quality Diary, NRS	Mean Change from Baseline	<0.001[#]
PROMIS Sleep Disturbance	Mean Change from Baseline	<0.001[#]

[#] nominally significant at p<0.0452
[1] Combined periods (pre- and post-interim analysis); responder analysis is by Logistic Regression (missing = non-responder); the five mean change analyses are by Mixed Model Repeated Measures with Multiple Imputation
Abbreviations: FIQ-R = Fibromyalgia Impact Questionnaire – Revised; NRS = numeric rating scale; PROMIS = Patient-Reported Outcomes Measurement Information System

*TNX-102 SL is in clinical stage of development and not approved for any indication

RELIEF Study: Continuous Responder Analysis (CRA) Graph

- The CRA graph allows one to see the proportion of responders over an entire range of cut-off points
- For example, >=30% improvement in pain is considered clinically meaningful in pain studies
- Looking at that vertical line at >=30% and visualizing a horizontal line to the y-axis tells you the proportion of each arm that achieved that level of pain improvement or better (47% for TNX-102 SL and 35% for placebo)
- It can be seen that TNX-102 SL separates from placebo, always at a higher proportion, up to about >=95% improvement



Adverse Events* (AEs) in RELIEF Study

	TNX-102 SL (N=248)		Placebo (N=255)		Total (N=503)	
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Tongue/mouth numbness	43	17.3	2	0.8	45	8.9
Tongue/mouth pain/discomfort	29	11.7	5	2.0	34	6.8
Taste impairment	16	6.5	1	0.4	17	3.4
Tongue/mouth tingling	14	5.6	1	0.4	15	3.0
Systemic Adverse Events	**N**	**%**	**N**	**%**	**N**	**%**
Somnolence/Sedation	14	5.6	3	1.2	17	3.4

* Table reports only AEs at rate of greater than 5% in either treatment arm

No serious and unexpected AEs in RELIEF related to TNX-102 SL

- Systemic AEs comparable with prior studies and consistent with approved oral cyclobenzaprine product labeling
- Oral AEs similar to prior studies with TNX-102 SL, although tongue/mouth numbness at about half the rate in RELIEF

Safety and Tolerability in RELIEF Study

- No new safety signals in RELIEF at TNX-102 SL 5.6 mg dose
- 82.3% in active arm and 83.5% in placebo arm completed the study
- 8.9% in active arm and 3.9% in placebo arm discontinued due to adverse events
- 7 SAEs in study: 2 in active arm and 5 in placebo arm
  - Of 2 in active arm, one was motor vehicle accident with multiple bone fractures, and other was pneumonia due to infection; both deemed unrelated to TNX-102 SL
- Similar oral administration site reactions as in prior studies with TNX-102 SL
- Overall low rates of systemic side effects, highest being somnolence/sedation at 5.6% in active group, 1.2% in placebo

TNX-102 SL Intellectual Property – U.S. Protection expected until 2035

Composition of matter (eutectic):
Protection expected to 2034/2035

- 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
- European Patent Office (EPO) issued European Patent No. 2968992 in December 2019 (validated in 37 countries). Opposition filed in October 2020 by Hexal AG
- China National Intellectual Property Administration issued Chinese Patent No. ZL 201480024011.1 in April 2019
- Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018, Patent No. 6614724 in November 2019, and Patent No. 6717902 in June 2020
- 10 granted patents (Indonesia, Saudi Arabia, New Zealand, Australia, Mexico, Taiwan, Israel, South Africa)
- 31 patent applications pending (4 being allowed in U.S., China, Israel, South Africa)

Composition of matter (sublingual):
Protection expected to 2033

- NZIPO issued New Zealand Patent No. 631144 in March 2017 and Patent No. 726488 in January 2019
- Taiwanese Intellectual Property Office issued Taiwanese Patent No. I590820 in July 2017, Patent No. I642429 in December 2018 and Patent No. I683660 in February 2020
- Australian Patent Office issued Australian Patent No. 2013274003 in October 2018 and Patent No. 2018241128 in September 2020
- JPO issued Japanese Patent No. 6259452 in December 2017
- 20 patent applications pending

Next Steps

- **Results from ongoing 2nd potential pivotal Phase 3 study, RALLY (F306), for TNX-102 SL in fibromyalgia expected in 2nd half of 2021**
  - Same protocol design as RELIEF study
  - Enrollment began in September 2020

- **Following positive results from RALLY, an NDA could potentially be filed in 2022**
  - Long term safety exposure studies completed
  - GMP manufacturing processes mature and 36-month stability established

Conclusion

- **TNX-102 SL is now mid-Phase 3 in fibromyalgia**
  - Millions suffer from this chronic condition
  - Remains an unmet need due to lack of efficacy and intolerable side effects associated with approved drugs, for many patients

- **TNX-102 SL is a differentiated compound with robust IP**
  - TNX-102 SL is a non-opioid, non-addictive, centrally-acting analgesic that could provide a new therapeutic option for fibromyalgia patients
  - Patent protection expected to extend through 2035
    - 5 patents issued in the U.S.

TONIX PHARMACEUTICALS

Q&A