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

FORM 8-K

CURRENT REPORT

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

Date of report (date of earliest event reported): November 8, 2019

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.)

509 Madison Avenue, Suite 1608, New York, New York 10022
(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 2.02 Results of Operations and Financial Condition

On November 8, 2019, Tonix Pharmaceuticals Holding Corp. (the "Company") announced its operating results for the quarter ended September 30, 2019. A copy of the press release that discusses this matter is filed as Exhibit 99.01 to, and incorporated by reference in, this report.

Item 7.01 Regulation FD Disclosure.

The Company will present data from the Phase 3 trial of its lead product candidate (the "Presentation") at the American College of Rheumatology/Association of Rheumatology Professionals (ACR/ARP) Annual Meeting on November 10, 2019. The Presentation, which may contain nonpublic information, is filed as Exhibit 99.02 hereto and incorporated herein by reference.

The information in this Current Report on Form 8-K, including Exhibits 99.01 and 99.02 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it 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.

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 Securities and Exchange Commission. 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 dated November 8, 2019, issued by the Company
99.02	Presentation by 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: November 8, 2019

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

Exhibit 99.01

Tonix Pharmaceuticals Reports Third Quarter 2019 Financial Results and Operational Highlights

50% of Enrollment Complete for Phase 3 RECOVERY Trial of Tonmya® for the Treatment of PTSD

Results from RECOVERY Interim Analysis Expected First Quarter 2020

Topline Data Expected Second Quarter 2020 Based on Currently-Planned Sample Size

NEW YORK, November 8, 2019 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced financial results for the quarter ended September 30, 2019, and provided an overview of recent operational highlights. Tonix's lead product candidate, TNX-102 SL*, is in Phase 3 development for the treatment of both posttraumatic stress disorder (PTSD) and fibromyalgia.

"We recently reported that we have enrolled over 50 percent of the current target number of participants for our Phase 3 RECOVERY study of TNX-102-SL or Tonmya®** for the treatment of PTSD," said Seth Lederman, M.D., President and Chief Executive Officer. "The first 50% of participants (n = 125) are the cohort for the interim analysis of the RECOVERY study for which we expect results in the first quarter of 2020. We also expect to report topline data from RECOVERY in the second quarter of 2020 unless the Independent Data Monitoring Committee (IDMC) recommends increasing the number of participants. In addition, we are planning to start a new Phase 3 study of TNX-102 SL in fibromyalgia, the F304 or RELIEF study."

Recent Highlights

Research and Development

TNX-102 SL (cyclobenzaprine HCl sublingual tablets)

- Based on guidance from its recent Breakthrough Therapy Type B Clinical Guidance meeting with the U.S. Food and Drug Administration (FDA), the Company plans to conduct an interim analysis for the currently-enrolling Phase 3 RECOVERY study. Pending final approval by FDA, the planned interim analysis will have three possible recommendations: 1) keep the current sample size and continue as planned; 2) provide the opportunity to increase the sample size to include up to a maximum of 120 additional participants, based on certain criteria; and 3) stop the study early for futility.
- Changed the timing of primary endpoint analysis for the currently-enrolling Phase 3 RECOVERY study from Week 4 to Week 12, to correspond to the two previous studies of TNX-102 SL in PTSD, based on guidance from the FDA.
- Initiated a single-dose, randomized, open-label, 3-way crossover study to evaluate the dose-proportionality and food-effect of TNX-102 SL in healthy subjects (TNX-CY-F110). This study is one of the requirements to support a New Drug Application (NDA) for TNX-102 SL.
- Completed long-term studies in participants with PTSD to evaluate the tolerability of TNX-102 SL 5.6 mg to support an NDA for the treatment of PTSD. The data provide Tonix with exposure data of daily dosing of TNX-102 SL 5.6 mg for at least 12 months in more than 50 individuals, and daily dosing of TNX-102 SL 5.6 mg for at least 6 months in more than 100 individuals. The data was collected in open label extension (OLE) studies of the PTSD program. Based on FDA guidance, the long-term studies in PTSD are also expected to support an NDA for the treatment fibromyalgia.
- Met with the FDA in October to discuss the development plan for TNX-102 SL as a treatment for alcohol use disorder (AUD). This new indication is expected to be developed under a separate IND. AUD is a chronic relapsing brain disease characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using.
- Met with FDA to discuss the continuation of the Breakthrough Therapy Designation (BTD) for TNX-102 for PTSD in August 2019 after receiving the "Intent to Rescind" letter in December 2018. FDA is considering the data we submitted to support the continuation of the BTD. The FDA has advised that there is no timetable for their decision on whether to withdraw the "Intent to Rescind" letter or rescind BTD or for any other action. The BTD for TNX-102 SL for PTSD and the "Intent to Rescind" letter both continue to remain in effect.
- Awarded U.S. Patent No. 10,357,465 for the composition and formulation of TNX-102 SL. This patent, "Eutectic Formulations of Cyclobenzaprine Hydrochloride," includes 14 claims directed to eutectics of cyclobenzaprine hydrochloride and mannitol and methods of making those eutectics. U.S. market exclusivity, excluding possible patent term extensions, is expected through 2035.
- Announced the upholding of the Company's European method of use patent, 2501234B1, for TNX-102 SL for use of the active ingredient in TNX-102 SL, cyclobenzaprine, for the treatment of PTSD, by the European Patent Office.

TNX-601 CR (tianeptine oxalate)

- Dosed healthy subjects in a Phase 1 study evaluating the safety, tolerability and pharmacokinetics (PK) of controlled release (CR) formulations of TNX-601 (tianeptine oxalate). TNX-601 is being developed as a potential daytime treatment for PTSD. Data from this study are expected by the end of 2019. Expected to be Phase 2 ready for ex-US study and IND-ready in the US in 2020.
- Awarded U.S. patent No. 10,449,203 for crystalline tianeptine oxalate salt, the active ingredient of TNX-601.This patent "Tianeptine Oxalate Salts and Polymorphs," includes claims directed to crystalline tianeptine oxalate salts, and disclosures directed to methods of using those crystalline forms and their compositions. U.S. market exclusivity, excluding possible patent term extensions, is expected through December 28, 2037.

TNX-1700 (recombinant trefoil factor 2, or rTFF2)

- Obtained an exclusive license from Columbia University for the development of a biologic, TNX-1700 (recombinant trefoil factor 2, or rTFF2), for the treatment of gastric and pancreatic cancers. The licensed assets were invented and developed, in part, by Dr. Timothy C. Wang, Chief, Division of Digestive and Liver Diseases, and Director of the Gastrointestinal and Pancreas Cancer Program and Tumor Biology and Microenvironment (TBM) program in the Herbert Irving Cancer Center at Columbia University.

TNX-1500 (monoclonal antibody anti-CD154)

- Entered into a research collaboration with Massachusetts General Hospital to develop TNX-1500, Tonix's internally developed, proprietary anti-CD154 (or CD40-ligand) monoclonal antibody that targets CD154 for the prevention and treatment of organ transplant rejection. TNX-1500 is also a potential treatment for autoimmune conditions.

*TNX-1300*** *(double-mutant cocaine esterase)*

- Met with FDA to discuss and reach agreement on the design of toxicology studies for TNX-1300 to support a Phase 2 clinical study.

TNX-1600 (triple reuptake inhibitor)

- Obtained an exclusive license for a triple reuptake inhibitor, TNX-1600, to treat PTSD and potentially other CNS disorders. The transaction was a license agreement with Wayne State University and an asset acquisition from TRImaran Pharma, Inc.

TNX-801 (live virus vaccine for percutaneous [scarification] administration)

- Joined the Alliance for Biosecurity, a coalition of biopharmaceutical companies and laboratory/academic partners that promotes a strong public-private partnership to ensure medical countermeasures are available to protect public health and enhance national health security.

Financial

Raised $5.4 million in gross proceeds in an underwritten public offering in July 2019.

Third Quarter 2019 Financial Results

Research and development expenses for the third quarter of 2019 totaled $5.1 million, compared to $3.3 million for the same period in 2018. This increase is primarily due to timing of activities related to the PTSD RECOVERY study, ramp-up of work related to TNX-601, and an increase in non-clinical expenses related to development of the pipeline.

General and administrative expenses for the third quarter of 2019 totaled $2.8 million, compared to $2.3 million for the same period in 2018. The modest increase is primarily due to an increase in patent prosecution costs and higher insurance premiums.

Net loss was $7.8 million, or $5.69 per share, for the third quarter of 2019, compared to net loss of $5.5 million, or $54.99 per share, for the third quarter of 2018. The weighted average common shares outstanding were 1,377,857 for the third quarter of 2019 and 99,640 for the third quarter of 2018, which amounts have been retroactively restated to reflect a 1-for-10 reverse stock split of our issued and outstanding shares that was effectuated on November 1, 2019.

At September 30, 2019, Tonix had $10.0 million of cash and cash equivalents, compared to $25.0 million as of December 31, 2018. Cash used in operations was $6.6 million for the third quarter of 2019, compared to $4.9 million for the same period last year.

About the Phase 3 RECOVERY Study

The RECOVERY Phase 3 study is a double-blind, randomized, placebo-controlled study of Tonmya 5.6 mg (2 x 2.8 mg sublingual tablets) over 12 weeks of treatment for civilian and military-related PTSD. The RECOVERY Phase 3 study restricts enrollment of study participants to individuals with PTSD who experienced an index trauma within nine years of screening. Two previous PTSD studies of Tonmya by the Company (P201 and P301) restricted enrollment to participants who experienced traumas during military service since 2001. The primary efficacy endpoint is the Week 12 mean change from baseline in the severity of PTSD symptoms as measured by CAPS-5 between those treated with Tonmya and those receiving placebo. The CAPS-5 is a standardized structured clinical interview and serves as the standard in research for measuring the symptom severity of PTSD. A formal unblinded interim analysis will be completed when approximately 50 percent (n=125) of participants have been randomized and have completed or discontinued the 12-week course of treatment with bedtime Tonmya 5.6 mg or placebo sublingual tablets. The Company expects to report the results of the interim analysis and the recommendation of the IDMC in the first quarter of 2020. If the current projected population of 250 study participants remains unchanged, the Company expects to report topline data in the second quarter of 2020.

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering and developing small molecules and biologics to treat psychiatric, pain and addiction conditions. Tonix's lead product candidate, TNX-102 SL, is in development for posttraumatic stress disorder (PTSD), fibromyalgia, agitation in Alzheimer's disease and alcohol use disorder (AUD). TNX-102 SL is in Phase 3 development as a bedtime treatment for PTSD (trade name Tonmya) and fibromyalgia. The Phase 3 RECOVERY trial (P302) in PTSD is currently enrolling and results from an interim analysis are expected in the first quarter of 2020 and topline data are expected in the second quarter of 2020 if the sample size remains the same. The Company is planning the Phase 3 RELIEF trial (F304) in fibromyalgia. The agitation in Alzheimer's disease program is Phase 2 ready and the development for AUD is in the pre-Investigational New Drug (IND) application stage. Tonix is advancing two other PTSD therapeutic programs in the pre-IND stage, with different mechanisms than TNX-102 SL and designed for daytime dosing: TNX-601 (tianeptine oxalate-CR tablets) and TNX-1600 (a triple reuptake inhibitor). TNX-601 is in clinical formulation testing outside of the U.S and is expected to be IND-ready in 2020. Tonix's programs for treating addiction conditions also include TNX-1300 (double-mutant cocaine esterase), which is in Phase 2 development for the treatment of cocaine intoxication. Tonix's preclinical pipeline includes 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. Finally, TNX-801 (live virus vaccine for percutaneous [scarification] administration) to potentially prevent smallpox and TNX-701 (undisclosed small molecule) to prevent radiation effects are being advanced as medical countermeasures to improve biodefense.

**TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication.*

***Tonmya has been conditionally accepted by the U.S. Food and Drug Administration (FDA) as the proposed trade name for TNX-102 SL for the treatment of PTSD.*

****TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication.*

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

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; 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, 2018, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2019, 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.

Tonix Pharmaceuticals Reports Third Quarter 2019 Financial Results

TONIX PHARMACEUTICALS HOLDING CORP.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Costs and expenses				
Research and development	$ 5,052	$ 3,264	$ 12,502	$ 12,501
General and administrative	2,839	2,277	7,592	6,171
Total costs and expenses	7,891	5,541	20,094	18,672
Operating loss	(7,891)	(5,541)	(20,094)	(18,672)
Interest income, net	53	62	183	171
Net loss	$ (7,838)	$ (5,479)	$ (19,911)	$ (18,501)
Net loss per common share, basic and diluted	$ (5.69)	$ (54.99)	$ (23.93)	$ (195.51)
Weighted average common shares outstanding, basic and diluted*	1,377,857	99,640	832,050	94,628

* All per share amounts and number of shares in the condensed consolidated financial statements have been retroactively restated to reflect the reverse stock split.

TONIX PHARMACEUTICALS HOLDING CORP.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands)
(Unaudited)

	September 30, 2019	December 31, 2018(1)
Assets		
Cash and cash equivalents	$ 10,024	$ 25,034
Prepaid expenses and other	1,529	1,022
Total current assets	11,553	26,056
Other non-current assets	719	263
Total assets	$ 12,272	$ 26,319
Liabilities and stockholders' equity		
Total liabilities	$ 2,417	$ 2,655
Stockholders' equity	9,855	23,664
Total liabilities and stockholders' equity	$ 12,272	$ 26,319

(1) The condensed consolidated balance sheet for the year ended December 31, 2018 has been derived from the audited financial statements but does not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements.

Jessica Morris (corporate)
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(212) 980-9159

Scott Stachowiak (media)
Russo Partners
scott.stachowiak@russopartnersllc.com
(646) 942-5630

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

Exhibit 99.02

A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) for the Treatment of Fibromyalgia (FM):

Evidence for a Broad Spectrum of Activity on the FM Syndrome

Gregory Sullivan, MD
Chief Medical Officer
Tonix Pharmaceuticals Inc

presenting at

American College of Rheumatology
Annual Meeting, Atlanta, GA
November 10, 2019

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, substantial competition; 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 risks related to failure to obtain U.S. Food and Drug Administration clearances or approvals and noncompliance with its regulations. 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, 2018, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2019, 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.

Disclosure Statements

- Gregory Sullivan MD is an employee of Tonix Pharmaceuticals Inc and owns stock and stock options in the company
- The co-authors on this work are employees or consultants of Tonix Pharmaceuticals Inc
- TNX-102 SL is an investigational new drug and has not been approved for any indication

TNX-102 SL for the Treatment of Fibromyalgia
Rationale for Targeting Sleep Quality

- Inter-relationship between poor sleep quality and fibromyalgia (FM) described almost 50 years ago[1]
  - Moldofsky & Smythe identified anomalous alpha-rhythms in stage 4 NREM EEG delta wave sleep in patients with "fibrositis syndrome" (a former name for fibromyalgia)
  - In healthy volunteers, stage 4 sleep deprivation results in temporary appearance of myalgia, tenderness, and fatigue comparable to that in fibromyalgia (FM)
    - Suggests sleep disturbance in FM may not only be a consequence of pain but also pathogenic in the disorder
- Sleep deprivation impairs descending pain inhibition pathways involved in controlling/coping with pain[2]
  - Poor sleep quality is a risk factor for the development of widespread pain through central sensitization
  - Reduced slow wave sleep (SWS) in FM may indicate impairment in homeostatic mechanisms of pain control
  - Serotonergic (5-HT) and noradrenergic (NA) systems mediate descending inhibitory pain pathways in FM
    - Dysfunction in descending inhibitory activity plays a role in central sensitization in FM and the maladaptive pain expression
    - Enhancement of restorative sleep via modulation of 5-HT and NA pathways may allow homeostatic plastic changes in pain processing circuitry and recovery from FM
- Proof of concept study showed clinical and pharmacodynamic benefit of low dose cyclobenzaprine in FM[3]
  - 8-week RCT with polysomnography (PSG) demonstrated improvement in core FM symptoms
  - Cyclobenzaprine treatment associated with a decreased pathological arousal pattern in the SWS EEG

[1] Moldofsky & Smythe. *Psychosomatic Medicine*. 1975; **37**(4):341–351. [2] Choi EHS. *Nat Rev Rheumatol* 2015; **11**:513–520. [3] Moldofsky et al. *J Rheumatol* 2011; **38**:2653-63.
CNS, central nervous system; EEG, electroencephalogram; RCT, randomized clinical trial

Non-restorative Sleep is Common in Fibromyalgia and May Contribute to Pain Symptoms[1]

Sleep problems and non-restorative sleep have been reported in >90% of fibromyalgia patients[2-5]

- Prolonged time to sleep onset (latency)

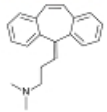
- Increased number of arousals leading to fragmented sleep

- Non-restorative sleep or waking feeling unrefreshed
  - Diffuse stiffness, aching and fatigue, even after 6-8 hours sleep

[1] Oswald I. *Proc R Soc Med.* 1962; 55:910-912; [2] Bigatti SM, et al. *Arthritis Rheum* 2008; 59:961-967; [3] Russell IJ & Bieber CS in *Wall and Melzack's Textbook of Pain* 5th edn Ch. 44 (eds McMahon SB & Koltzenburg M) 669-682, Elsevier, 2006. [4] Moldofsky H. *Joint Bone Spine* 2008; 75:397-402. [5] Yunus MB et al. *Arthritis Rheum* 1991; 34:15-21; Illustrations from: Stahl SM. *Stahl's Illustrated Chronic Pain and Fibromyalgia*. New York, NY: Cambridge University Press; 2009.

What is TNX-102 SL?

- **TNX-102 SL is a sublingual eutectic formulation[1] of cyclobenzaprine (CBP) for transmucosal absorption**
  - CBP is a tricyclic molecule with high affinity for target receptors that play key roles in sleep physiology and restorative sleep-related pain processing
  - *In vitro* studies[2] show potent binding and functional antagonism at each of
    - 5-HT_{2A}
    - α_1-adrenergic
    - Histamine-H_1
  - Non-narcotic, centrally-acting analgesic with no recognized risk of addiction



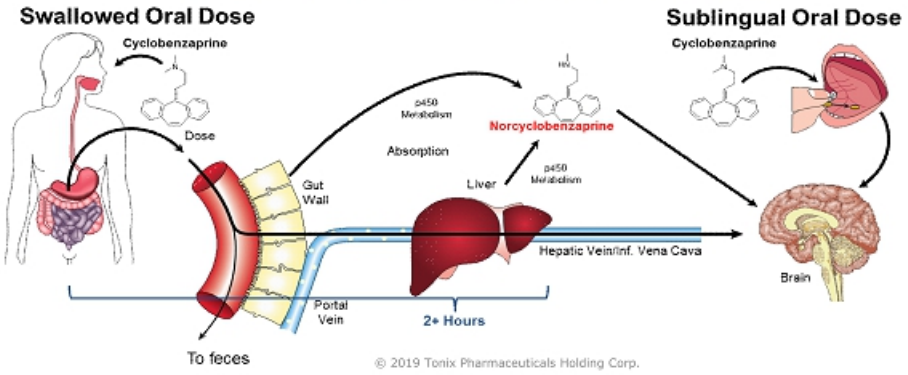
[1] Notice of Allowance for Eutectic Proprietary Protectic™ Formulation Patent issued by the U.S. Patent and Trademark Office; [2] Daugherty et al. Society of Biological Psychiatry (SOBP) 70th Annual Scientific Convention, May 14-16, 2015 Toronto, Ontario, Canada.

- **TNX-102 SL is designed for bedtime administration with desirable nighttime pharmacokinetic profile and pharmacodynamics effects[3]**
  - Rapid systemic exposure and increased plasma concentration and AUC during sleep period
  - Avoids first-pass metabolism reducing exposure to long-lived active metabolite, norcyclobenzaprine (nCBP)
    - $t_{1/2}$~72 hours
    - Less selective for target receptors -> undesirable off-target functional activities
    - Exposure (AUC_{0-48}) for CBP/nCBP of 1.9 for TNX-102 SL vs. 1.2 for oral IR tablet[2]
    - Multi-dose (20-day) PK of TNX-102 SL compared to simulated multi-dose oral IR CBP shows flipped nighttime exposure ratio: higher CBP to nCPB with TNX-102 SL; higher nCBP to CBP with oral IR CBP[4]

[3] Lederman et al. European Congress of Rheumatology, June 2015, , Rome, Italy; 4 Sullivan et al. American Society of Clinical Psychopharmacology (ASCP), May 28-31, 2019, Scottsdale, AZ; IR, immediate-release;

TNX-102 SL: Sublingual Cyclobenzaprine Tablet

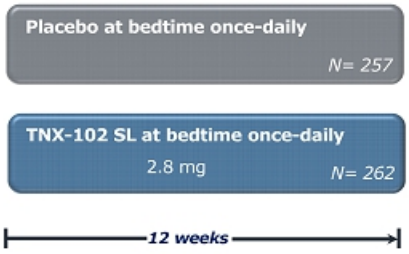
- **Faster Absorption**
- **Bypasses "First-Pass" Hepatic Metabolism**
  - **Reduced metabolism of parent CBP to active metabolite nCBP**



Phase 3 AFFIRM Study of TNX-102 SL 2.8 mg in Fibromyalgia

General Study Characteristics:

- 12-week, randomized, double-blind, placebo-controlled study in fibromyalgia conducted at 45 U.S. sites
- TNX-102 SL 2.8 mg at bedtime nightly for 12 weeks
- Daily diary reporting of average pain severity over prior 24 hours



Primary Endpoint

- Response defined as a ≥ 30% improvement from baseline to Week 12 in the weekly average of the daily self-reported average NRS pain severity (Logistic Regression[1])

Key Secondary Endpoints

- Patient's Global Impression of Change (PGIC) responder analysis at Week 12
- Fibromyalgia Impact Questionnaire - Revised (FIQR) Symptom Domain score at Week 12
- FIQR Function Domain score at Week 12
- Weekly average of the daily diary assessment of sleep quality at Week 12
- Patient Reported Outcomes Measurement Information System (PROMIS) Short Form score for sleep disturbance at Week 12
- PROMIS Short Form score for fatigue at Week 12
- Weekly average of the daily self-reported average pain severity score at Week 12

[1] subject's with missing data considered non-responders

AFFIRM Study Results:
Primary Analysis

- Primary Analysis of Pain Response in FM (TNX-102 SL N=262; Placebo N=257)
  - Logistic regression (LR) responder analysis (≥30% pain reduction); all discontinuations considered non-responders
  - TNX-102 SL **28.6%**; Placebo **22.6%**; Odds Ratio (95% CI) of 1.41 (0.94, 2.10), p=0.095, **NS**
  - AFFIRM Study did not meet its primary endpoint

CI, confidence interval; LR, logistic regression; N, number; NS, not significant; OR, odds ratio

AFFIRM Study Results:
Pre-Planned Sensitivity Analyses Assessed Impact of Missing Data Handling on Primary Efficacy Outcome

- **Sensitivity Analysis 1 – Treatment of missing data** (TNX-102 SL N=262; Placebo N=257)
  - Responder analysis by LR; discontinuations due to LOE/AE treated as non-responders, all others as LOCF
  - TNX-102 SL **33.6%**; Placebo **23.7%**; OR (95% CI) of 1.65 (1.12, 2.42), **p=0.012**
  - **Conclusion: treating non-LOE/non-AE discontinuations as non-responders in the primary analysis reduced response rate more for TNX-102 SL (by 5%) than for placebo (by 1.1%), compared to LOCF**

- **Sensitivity Analysis 2 – Treatment of missing data** (TNX-102 SL N=262; Placebo N=257)
  - Responder analysis by LR; discontinuations due to LOE/AE treated as non-responders; all others with values imputed using quadratic fit on within-subject observed pain scores
  - TNX-102 SL **39.3%**; Placebo **26.1%**; OR (95% CI) of 1.87 (1.28, 2.72), **p=0.001**
  - **Conclusion: treating non-LOE/non-AE discontinuations as non-responders in primary analysis reduced response rate more for TNX-102 SL (by 10.7%) than for placebo (by 3.5%), compared to within-subject quadratic fitting**

AE, adverse event; CI, confidence interval; LOCF, Last Observation Carried Forward; LOE, Lack of Efficacy; LR, logistic regression; N, number; OR, odds ratio

AFFIRM Study Results:

Pre-Planned Sensitivity Analyses Indicated Treatment of Missing Data May Have Had Adverse Impact on Primary Efficacy Outcome

- Unexpected imbalance in patient discontinuations for reasons unrelated to efficacy or tolerability (eg, patient relocating) created a negative bias in the primary responder analysis because any patient who left the study for any reason, prior to completion, was labeled a non-responder despite their results up to that point

- 'Withdrawal of Consent' utilized as discontinuation reason when a patient informs a site she/he can no longer participate due to moving away from site or starting school or job incompatible with study visits. Note imbalance in this reason in disposition table.

- AFFIRM disposition table:

Discontinuation Reason	TNX-102 SL	Placebo
Occurrence of an AE	20 (7.6%)	11 (4.3%)
Withdrawal of Consent	**15 (5.7%)**	**3 (1.2%)**
Investigator Decision	6 (2.3%)	0 (0.0%)
Lack of Efficacy	6 (2.3%)	5 (1.9%)
Lost to Follow-up	11 (4.2%)	15 (5.8%)
Other	1 (0.4%)	1 (0.4%)
Total	59 (22.5%)	35 (13.6%)

AFFIRM Study Results:
Supporting Primary Efficacy Analyses

- Primary Analysis in Per Protocol (PP) Population (TNX-102 SL N=179; Placebo N=200)
  - Responder analysis in PP population; all discontinuations are non-responders (like primary analysis)
  - PP population includes all randomized patients with no major protocol violations who are at least 70% compliant with investigational product and who have non-missing Week 12 pain data
  - TNX-102 SL **38.5%**; Placebo **26.0%**; OR (95% CI) of 1.81 (1.17, 2.82), **p=0.008**
  - **Conclusions:**
    - **Compared with the ITT population, the PP population showed a higher response rate (by 9.9%) to TNX-102 SL than the higher rate to placebo (by 3.4%), and there was a positive (p<0.01) efficacy signal**
    - **Major protocol violations and/or poor compliance with IP also adversely affected efficacy signal in the ITT population**

AFFIRM Study Results:
Primary Efficacy Analysis by an Additional Standard Statistical Approach to Pain and Overall Conclusions on the Negative Primary Outcome

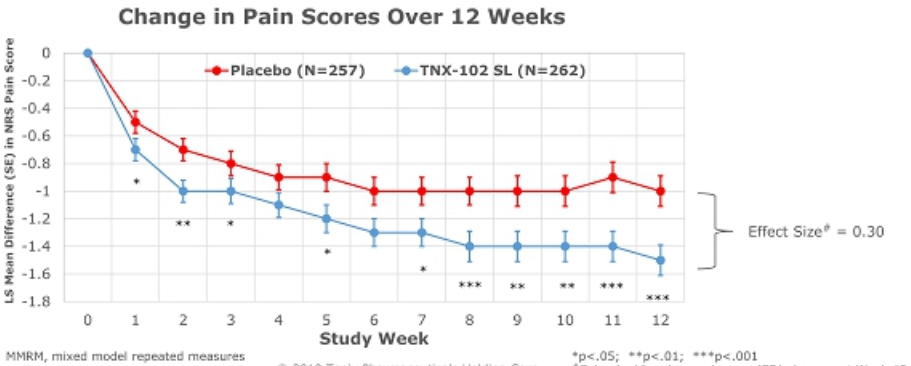
- ≥50% Responder Analysis (all discontinuations treated as non-responders)
  - TNX-102 SL **14.5%**; Placebo **8.6%**; OR (95% CI) of 1.82 (1.04, 3.17), **p=0.035**

- Overall Conclusion On Negative Outcome of the Primary Efficacy Analysis:
  - Unexpected imbalance in discontinuations unrelated to efficacy or tolerability, i.e., in the 'withdrawal of consent' category
  - Imbalance created negative bias in primary responder analysis since any patient who left the study for any non-LOE/non-AE reason prior to completion was labeled a non-responder despite their results up to that point

MCFB, Mean Change from Baseline; MMRM, Mixed Models Repeated Measures; MAR, Missing-at-Random

AFFIRM Study Results:
Graphical Display of Primary Endpoint Analyzed by Mean Pain MMRM

- Mean Pain Analysis (MMRM with no imputation) (TNX-102 SL N=262; Placebo N=257)
  - Difference in LS Mean (SE): **-0.6** (0.15); 95% CI (-0.8, -0.3); **p<0.001**

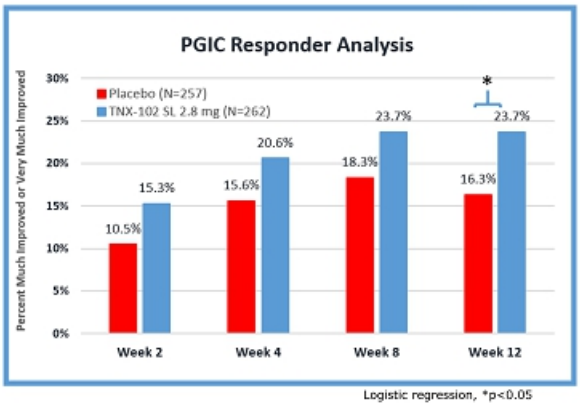


MMRM, mixed model repeated measures

*p<.05; **p<.01; ***p<.001
#Cohen's *d* for observed mean (SD) changes at Week 12

AFFIRM Study Results:
Patient Global Impression of Change (PGIC)

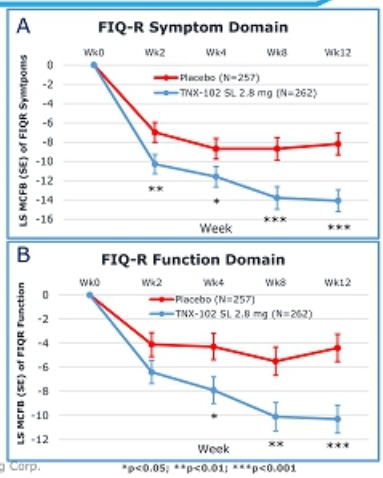
- Responder status defined as a patient rating of 2 ('much improved') or 1 ('very much improved')
- Significantly greater percentage of responders to TNX-102 SL 2.8 mg than placebo at Week 12 (p=0.038)
- Activity of TNX-102 SL 2.8 mg in FM cross-validated by significant effect on Week 12 PGIC



Logistic regression, *p<0.05

AFFIRM Study Results:
Fibromyalgia Impact Questionnaire – Revised (FIQ-R)

- Robust effect of TNX-102 SL 2.8 mg on FIQ-R Symptoms domain (see figure A)
  - Early onset significant by Week 2
- Similarly robust effect TNX-102 SL 2.8 mg on FIQ-R Function domain by Week 12 (see figure B)
  - Functional improvement trails onset of FM symptom improvement, with first significant function timepoint at Week 4
- FIQ-R Total score was significantly more improved at Week 2 (p=0.023), Week 8 (p<0.001) and Week 12 (p<0.001)
- Significant and clinically-meaningful effects of TNX-102 SL on FIQ-R symptom, function, and total score also cross-validate the activity in FM

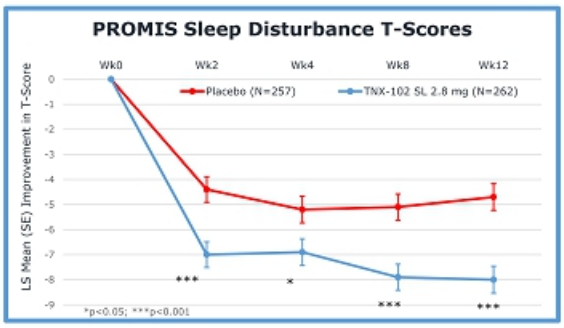


*p<0.05; **p<0.01; ***p<0.001

AFFIRM Study Results:
Early Effects on Sleep Quality of TNX-102 SL

PROMIS Sleep Disturbance

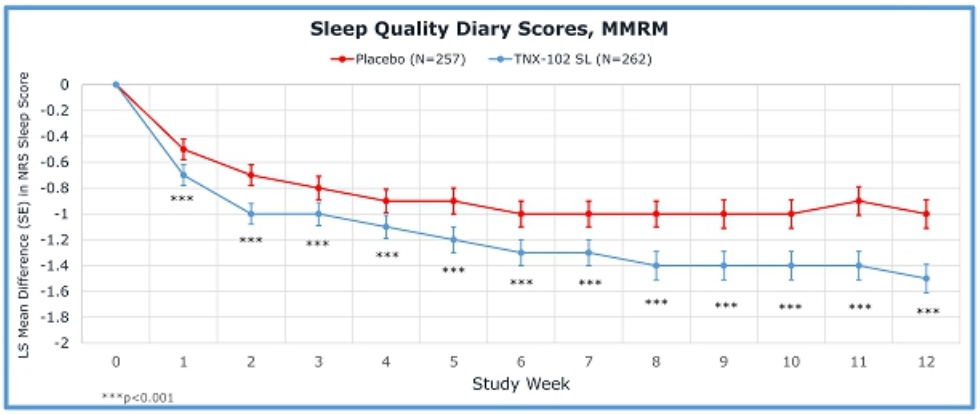
- Baseline Mean (SD) T-Scores:
  - Placebo group: 59.9 (6.8)
  - TNX-102 SL group: 59.0 (6.6)
- PROMIS Sleep Disturbance instrument showed positive effects on sleep quality that began separating early, by Week 2



Daily Sleep Quality Diary NRS

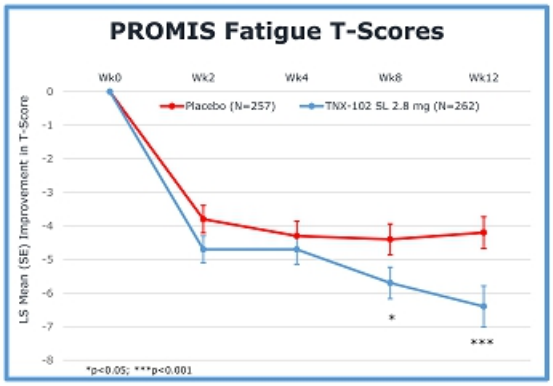
- Sleep quality on the daily diary showed greater improvement for TNX-102 SL 2.8 mg over placebo for every week of the study (all $p<0.001$; see figure on next slide)

AFFIRM Study Results:
TNX-102 SL Effects on Sleep Quality as Recorded on Daily Diary



AFFIRM Study Results: TNX-102 SL Effects on Fatigue in FM

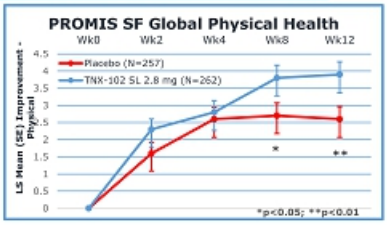
- Fatigue is a core FM symptom
  - Fatigue is 1 of 3 symptoms that, if experienced over the past week, can contribute up to 3 points to the symptom severity score for diagnosis[1]
- TNX-102 SL 2.8 mg had a statistically significant improvement on fatigue by Week 8 that continued through Week 12
- The steep slope down for the TNX-102 SL group for fatigue improvement from Week 4 onward contrasts with the relatively flat effect of placebo over the same period

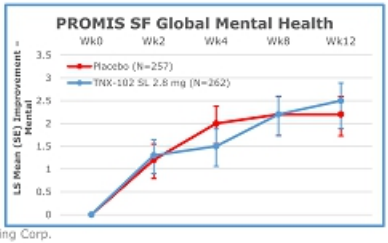


[1]Wolfe et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Seminars in Arthritis and Rheumatism 2016; 46:319-329.

AFFIRM Study Results: PROMIS Global Health – Short Form

- Higher scores reflect improved health on PROMIS Global Health
- TNX-102 SL 2.8 mg improved Global Physical Health domain by last four weeks of study, at Weeks 8 and 12
- TNX-102 SL 2.8 mg had no effect on Global Mental Health domain





AFFIRM Study Results:
Safety and Tolerability

- Trial Completion Rates: 86.4% Placebo; 77.5% TNX-102 SL 2.8 mg
- TNX-102 SL was well-tolerated in AFFIRM and AEs reported were similar to other TNX-102 SL studies
- Total of 7 serious adverse events (SAEs) were reported: 4 in placebo group and 3 in TNX-102 SL group. No new safety signals observed; multiple causal factors involved in each SAE, and all resolved quickly and without sequelae
- Table of systemic AEs and local administration site reactions (at rate of ≥3% in TNX-102 SL group:

Systemic Adverse Events	Placebo N=256	TNX-102 SL 2.8 mg N=262	Total N=518*
Fatigue	2.3%	5.7%	4.1%
Headache	3.9%	3.4%	3.7%
Somnolence	1.6%	3.1%	2.3%
Local Administration Site Reactions			
Hypoaesthesia oral*	0.8%	40.1%	20.7%
Glossodynia	1.6%	9.2%	5.4%
Paraesthesia oral	1.2%	7.6%	4.4%
Product taste abnormal	0.8%	6.1%	3.5%
Oral discomfort	0.0%	3.1%	1.5%

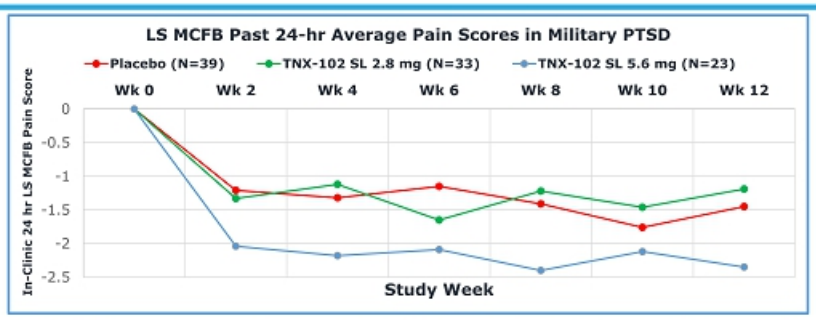
*Oral hypoaesthesia (tongue numbness) was most common AE, generally transient (<60 minutes), rated mild in 87% and moderate in 13% on TNX-102 SL, and rarely (0.8%) associated with discontinuation; *Safety Population (N=518)

What was learned about dose and tolerability from studies of TNX-102 SL in PTSD?

- For overall PTSD symptoms, TNX-102 SL 5.6 mg showed an efficacy signal, whereas the 2.8 mg dose did not
- The most common AE with TNX-102 SL, oral hypoaesthesia, occurred at similar rates with 2.8 mg (39%) and 5.6 mg (36%) in AtEase, and 5.6 mg (37%) in HONOR.
  - Rate of oral hypoaesthesia does not appear to be dose dependent
- TNX-102 SL 5.6 mg was well tolerated with only systemic AE of somnolence at a consistently higher rate (at ~16%) than in 2.8 mg
- In-clinic Past 24-hr average NRS pain ratings were collected at each visit in the military PTSD study AtEase (P201; data on next slide)

Evidence from Military PTSD Study of Higher Dose Requirement for Pain

Dose Effect on Past 24-hr Average Pain in PTSD Patient with Baseline Pain ≥4



- TNX-102 SL 5.6 mg dose with greater effect on pain in PTSD patients (with baseline pain ≥4) than 2.8 mg dose, which was similar to placebo on pain
- Cohen's *d* effect size for Week 12 (on observed mean [SD] differences from baseline) between 5.6 mg and placebo = 0.34
- At least for the types of pain experienced in this military PTSD population, only the 5.6 mg dose had numerically greater effect than placebo on pain (LS mean difference from placebo = 0.9 units at Week 12)

LS, least squares; MCFB, mean change from baseline; PTSD, posttraumatic stress disorder

Conclusions

- The AFFIRM Study in fibromyalgia (FM) did not achieve significance on the primary endpoint
  - While the study was not significant base on the pre-specified pain responder analysis, it was significant by other standard pain analysis techniques
  - Results were highly sensitive to methods used to handle missing data
- Significant effects on PGIC and FIQ-R cross-validated the activity of TNX-102 SL in FM
- Improved effects on sleep quality, present within the 1st week and throughout treatment, support the mechanistic hypothesis that TNX-102 SL has positive effects on FM mediated by improvements in sleep quality
- Broad based effects on FM symptoms also evident from statistically significant effects on PROMIS Fatigue Scale and Global Physical Health domain
- Studies with TNX-102 SL at 2.8 mg and 5.6 mg in PTSD suggested higher dose more effective on pain, and the 5.6 mg dose is generally well-tolerated
- Therefore, the planned next phase 3 study of TNX-102 SL in FM will utilize the 5.6 mg dose with the expectation of a larger effect on FM pain and symptoms than the 2.8 mg dose used in AFFIRM

Co-Authors: R. Michael Gendreau, Gendreau Consulting
Judith Gendreau, Gendreau Consulting
Ashild Peters, Tonix Pharmaceuticals Inc
Perry Peters, Tonix Pharmaceuticals Inc
Seth Lederman, Tonix Pharmaceuticals Inc

Thank you!