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 2, 2018

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 306, 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))

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 8.01 Other Events.

On November 3, 2018, Tonix Pharmaceuticals Holding Corp. (the "Company") presented a poster entitled *Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL*, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301)* (the "Poster Presentation"), which includes results and retrospective analyses from the Phase 3 P301 study for the Company's lead product candidate, at the 2018 CNS Summit. The Poster Presentation and the press release that discusses this matter are filed as Exhibits 99.01 and 99.02, respectively, to, and incorporated by reference in, this report.

On November 2, 2018, the Company presented a poster entitled *Differential Treatment Effects of TNX-102 SL*, a Sublingual Formulation of Cyclobenzaprine, on Dissociative Symptoms of Derealization and Depersonalization in a Military-Related PTSD Population: Retrospective Analysis of a Double-Blind Randomized Study* (the "Retrospective Analysis Poster Presentation") at the 2018 CNS Summit. A copy of the Retrospective Analysis Poster Presentation is filed as Exhibit 99.03 to, and incorporated by reference in, this report.

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	Poster Presentation
99.02	Press Release dated November 6, 2018, issued by the Company
99.03	Poster Presentation

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 6, 2018

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

Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL*, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301)

Gregory Sullivan, MD[1], R Michael Gendreau, MD, PhD[2], Judy Gendreau, MD[1], Ashild Peters, RN[1], Perry Peters[1], Jean Engels, MS[3], Seth Lederman, MD[1]

[1] Tonix Pharmaceuticals, Inc., New York, NY 10022; [2] Gendreau Consulting, Poway, CA 92064; [3] Engels Statistical Consulting, Minneapolis, MN 55044

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

INTRODUCTION

Trial P301 (the 'HONOR' study) was a Phase 3 randomized clinical trial of TNX-102 SL (TNX) in military-related PTSD. Participants who experienced index traumas during military service in 2001 or later, received TNX 5.6 mg or placebo (PBO) for 12 weeks. TNX is a sublingual formulation of cyclobenzaprine designed for nightly bedtime use. TNX was previously studied in a Phase 2 trial, P201 ('AtEase'), in 2015-2016 with participants randomized 2:2:1 to placebo (N=92), TNX 2.8 mg (N=90), and TNX 5.6 mg (N=49) (topline reported 5/2016). The primary endpoint comparing the 2.8 mg dose and placebo at Week 12 was not met, but secondary analysis showed the 5.6 mg dose had a strong trend for difference from PBO in mean change from baseline (MCFB) on CAPS-5 (mixed model repeated measures (MMRM), P=0.053). The present Phase 3 trial, P301, was conducted two years later in 2017-2018 and compared TNX 5.6 mg and placebo. P301 was stopped (7/2018) after an interim analysis (IA) of the first 274 randomized participants showed the primary endpoint did not meet a pre-specified continuation threshold at Week 12. The results of pre-planned and retrospective analyses of P301 are presented, and relevant analyses supporting the design of the upcoming Phase 3 trial are discussed.

METHODS

The Phase 3 P301 study was a multicenter, double-blind, placebo-controlled, 12-week trials conducted in the US. Participants meeting PTSD diagnosis, assessed by Clinician-Administered PTSD Scale for DSM-5 (CAPS-5), were randomized to TNX 5.6 mg or PBO treatment groups. Study P301 required PTSD DSM-5 Criterion A-qualifying trauma(s) incurred during military service since 2001; free of antidepressants ≥ 2 months; free of or washed off other psychotropics. Excluded were severe suicide risk (intent or plan; attempt within 1 year); substance use disorders (SUDs) within 6 months; lifetime bipolar, psychotic, obsessive-compulsive, or antisocial personality disorders.

RESULTS

At the time of IA, there were 274 randomized participants (mITT=252) in P301. **Table 1** provides the demographic and baseline characteristics. As shown in **Table 2**, the primary analysis at Week 12 was not significant (LS mean [standard error] difference -1.0 [1.88], p=0.60, MMRM with MI), yet, there was notable separation from placebo on the primary at Week 4 (-3.6 [1.51], p=0.019). Retrospective analyses were performed to better understand how to design future studies and identify the potential group of responders for enrichment design.

Table 1. Participant Demographics and Characteristics

	P301 mITT Population	
Variable	Placebo N=127	TNX-102 SL 5.6 mg N=125
Females, %	13.4%	8.0%
Avg age, yrs.	35.5	35.9
Body Mass Index, kg/m^2	29.3	29.9
Employment (current), %	63.0%	55.2%
Unable to work due to PTSD symptoms, %	12.6%	16.8%
Education, some college or higher, %	85.1%	82.4%
Tobacco Use (current), %	31.5%	33.6%
THC use (current), %	26.8%	26.4%
Alcohol use (current), %	75.6%	69.6%
Active Duty/Veterans (at time of study), No.	17/110	9/116
Time since trauma, mean years	9.2	9.1
Time since trauma, median years	9.3	9.5
Combat index trauma, %	77.2%	83.2%
Deployments, mean number	3.0	2.6
Baseline CAPS-5 Scores, mean	42.4	42.0
Baseline BDI-II Scores, mean	23.0	25.6

BDI-II=Beck Depression Inventory-II; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; THC=tetrahydrocannabinol

Table 2. P301 Study Primary Analysis in mITT Population in P301

	Placebo		TNX-102 SL 5.6 mg		Primary Analysis	
Visit	N=127		N=125		MMRM with MI	
Statistic	CAPS-5 Value	MCFB	CAPS-5 Value	MCFB	Difference	p-value
Week 4						
LS Mean (SE)	31.0 (1.62)	-11.2 (1.62)	27.5 (1.73)	-14.7 (1.73)	-3.6 (1.51)	**0.019**
Week 8						
LS Mean (SE)	29.4 (1.76)	-12.8 (1.76)	27.6 (1.86)	-14.6 (1.86)	-1.8 (1.77)	0.321
Week 12						
LS Mean (SE)	28.0 (1.80)	-14.2 (1.80)	27.0 (1.90)	-15.2 (1.90)	-1.0 (1.88)	0.602

BOLD, p<0.05; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; LS=least squares; MCFB=mean change from baseline; MI=multiple imputation; mITT=modified Intent-to-Treat sample; MMRM=mixed model repeated measures; SE=standard error

Retrospective Analysis on Time-Since-Trauma (TST)

The median TST in P301 was approximately 9 years. When P301 participants are divided into two subgroups (**Table 3**), one with index trauma within 9 years of screening (≤9 year) and the other with index trauma >9 years prior to screening (>9 year), a treatment response is evident in the TST ≤9 year group (CAPS-5 improvement at Week 12 of -5.9 points, p=0.039). In contrast, in the TST >9 year group TNX 5.6 mg did not separate from placebo at Week 12 (numerical increase in CAPS-5 of +1.8 points, p=0.509). The lack of separation between TNX 5.6 mg and PBO in the TST >9 year group was in large part attributable to a high placebo response at Week 12 (least squares mean change from baseline of -14.1 points).

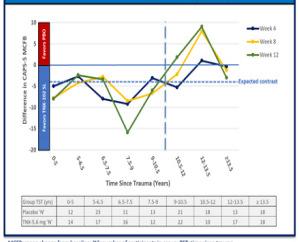
Table 3. CAPS-5 – TST ≤9 & >9 Years in P301

	Time Since Index Trauma ≤9 Years						Time Since Index Trauma >9 Years					
Visit	Placebo (N=60)		TNX-5.6 mg (N=61)		MMRM with MI		Placebo (N=67)		TNX-5.6 mg (N=64)		MMRM with MI	
Statistic	Value	MCFB	Value	MCFB	Diff	p-value	Value	MCFB	Value	MCFB	Diff	p-value
Week 4												
LS Mean	34.2	-7.8	27.3	-14.7	-6.9	**0.004**	33.1	-9.3	30.7	-11.7	-2.4	0.300
Week 8												
LS Mean	32.4	-9.6	27.2	-14.8	-5.2	0.069	31.5	-10.9	31.3	-11.1	-0.2	0.940
Week 12												
LS Mean	33.2	-8.8	27.3	-14.7	-5.9	**0.039**	28.3	-14.1	30.1	-12.3	1.8	0.509

BOLD, p<0.05; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; Diff=difference; LS=least squares; MCFB=mean change from baseline; MI=multiple imputation; MMRM=mixed model repeated measures; SE=standard error; TNX-5.6=TNX-102 SL 5.6 mg

Dividing the mITT sample into groups based on TST (1.5-2 years each as well as 0-5 years and ≥13.5 years groups), the CAPS-5 differences in MCFB between TNX 5.6 mg and PBO are displayed in **Figure 1** for Weeks 4, 8, and 12 post-baseline timepoints. The figure shows that for TST <10.5 years, TNX 5.6 mg showed good separation from PBO (left side of vertical 10.5 year line). "Expected contrast" dashed line indicates observed effect from Phase 2. Separation of TNX 5.6 mg from PBO in TST >10.5 years group was either small or worked in the favor of PBO (right side of vertical 10.5 year line).

Figure 1. CAPS-5 Mean Change from Baseline Difference from Placebo of TNX-102 SL 5.6 mg in TST Subgroupings

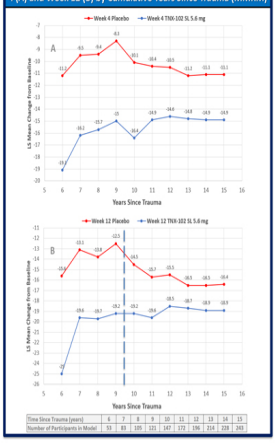


Group TST (yrs)	0-5	5-6.5	6.5-7.5	7.5-9	9-10.5	10.5-12	12-13.5	≥ 13.5
Placebo 'N'	12	23	11	13	21	18	13	18
TNX-5.6 mg 'N'	14	17	16	12	22	19	17	18

MCFB=mean change from baseline; 'N'=number of participants in group; TST=time since trauma

An alternate way to look at the efficacy of TNX 5.6 mg is CAPS-5 change from baseline for TNX 5.6 mg and PBO as a function of cumulative years since index trauma within each time range, starting with ≤6 years TST, through to ≤15 years TST. The results of this exploratory analysis are presented in **Figure 2A and 2B** for the Week 4 and Week 12 timepoints, respectively. The total number of participants included in the model for each time range is provided in the table following the figure. Note in **Figure 2B** for Week 12 the increasing response to PBO with the additions of participants >9 years TST (see vertical dashed line). In contrast, the response to TNX 5.6 mg is relatively constant (in range of -19.5 to -18.5 CAPS-5 improvement) with the additions of participants >6 years TST.

Figure 2A & 2B. CAPS-5 Total Score Change from Baseline at Week 4 (A) and Week 12 (B) by Cumulative Years Since Trauma (MMRM)



Time Since Trauma (years)	6	7	8	9	10	11	12	13	14	15
Number of Participants in Model	53	83	105	121	147	172	196	214	228	243

Secondary Efficacy Evaluations in mITT Population and ≤9 Year Subgroup

In **Table 4**, the results of the mITT population and the TST ≤9 years subgroup are presented for the key secondary endpoints of CGI-I and SDS, and the other secondaries of PGIC, PROMIS SD, and BDI-II for Week 4 and Week 12. Of these five secondary endpoints, only in BDI-II did TNX differ from PBO at Week 8 in the TST ≤9 year subgroup (data not shown). Note that for TST ≤9 subgroup, all five secondary endpoints showed a p-value <0.05 at Week 12, indicating possible global and functional recovery, and improved sleep quality and mood after 12 weeks of TNX 5.6 mg compared with PBO.

Table 4. Weeks 4 & 12 Secondary Endpoints for mITT & TST ≤9 Years Subgroup

		P301 mITT				P301 ≤9 Year Subsample			
		PBO (N=127) v. TNX-5.6 (N=125)				PBO (N=60) v. TNX-5.6 (N=61)			
		Week 4		Week 12		Week 4		Week 12	
	Analysis	LSMD	p-value	LSMD	p-value	LSMD	p-value	LSMD	p-value
CGI-I	MMRM	-0.3	**0.015**	-0.1	0.403	-0.6	**0.002**	-0.5	**0.021**
SDS	MMRM	-0.2	0.785	-1.6	0.101	-1.8	0.167	-4.3	**0.007**
PGIC	MMRM	-0.2	0.238	-0.3	**0.020**	-0.4	**0.045**	-0.6	**0.007**
PROMIS SD	MMRM	-3.1	**0.015**	-2.7	0.082	-4.5	**0.029**	-5.0	**0.042**
BDI-II	MMRM	-1.1	0.330	-1.4	0.255	-5.2	**0.008**	-6.6	**0.001**

BOLD, p<0.05; BDI-II=Beck Depression Inventory-2; CGI-I=Clinical Global Impressions – Improvement scale; MMRM=mixed model repeated measures; PBO=placebo; PGIC, Patient Global Impression of Change scale; PROMIS SD=Patient-Reported Outcome Measures Information System Sleep Disturbance; SDS=Sheehan Disability Scale; TNX 5.6=TNX-102 SL 5.6 mg

Supported by P301 TNX 5.6 mg Response in Female and Non-Combat Subgroups and Clinically Meaningful Week 4 CAPS-5 Score Reduction, Next Phase 3 Trial Will Study Mixed Civilian and Military Population with Week 4 Primary:

Based on preliminary agreement received at a recent Breakthrough Therapy Clinical Guidance meeting with the US Food and Drug Administration, Tonix plans to study a mixed civilian and military-related PTSD population in the upcoming Phase 3, potential pivotal study of TNX 5.6 mg for PTSD. The primary endpoint will be Week 4 change from baseline in CAPS-5 in TNX 5.6 mg compared with placebo, with one of the key secondary endpoints of Week 12 CAPS-5 change from baseline. As shown in **Table 5**, in P301, although groups are small, females and participants with non-combat traumas (males and females) in the TST ≤9 years subgroup trended for clinically-meaningful reductions in CAPS-5 for TNX 5.6 mg relative to placebo.

Table 5. Weeks 4 & 12 CAPS-5 MCFB in P301 Female & Non-Combat Subsamples

		Difference in CAPS-5 MCFB from Placebo	
Subsample	Numbers Per Arm	Week 4	Week 12
Females (mITT)	PBO N= 17; TNX-5.6 N=10	-11.5	-9.1
Non-combat (≤9 yr TST)	PBO N=14; TNX-5.6 N=10	-4.8	-4.4

CAPS-5=Clinician-Administered PTSD Scale for DSM-5; MCBF=mean change from baseline; mITT=modified Intent-to-Treat sample; PBO=placebo; TNX-5.6=TNX-102 SL 5.6 mg; TST=time since trauma

Safety

There were no serious and unexpected adverse events (AEs) in P301. The AEs observed (**Table 6**) in P301 were comparable to prior studies with TNX 5.6 mg. Most frequent AE was oral hypoaesthesia (tongue/mouth numbness), related to the site of administration of TNX, which was transient (<60 min post administration) and never rated as severe. The most common systemic AE was somnolence, also never rated as severe. Two participants on PBO and 8 participants on TNX 5.6 mg had at least one AE leading to study discontinuation.

Table 6. Adverse Events in P301 at Rate ≥5% in TNX 5.6 mg Group

Category of Adverse Reaction Preferred Term	Placebo (N=134*)	TNX-102 SL 5.6 mg (N=134*)
Systemic Adverse Events		
Somnolence	9.0%	15.7%
Local Administration Site Reactions		
Hypoaesthesia oral	1.5%	37.3%
Product Taste Abnormal	3.0%	11.9%
Paraesthesia oral	0.7%	9.7%

* Safety Population

DISCUSSION AND CONCLUSIONS

- Study P301 was discontinued at a pre-planned unblinded interim analysis after a pre-specified Week 12 continuation threshold was not met.
- TNX 5.6 mg improved CAPS-5 at Week 4 (p=0.019) in the mITT population which was a pre-specified secondary endpoint.
- Retrospective analyses identified a subgroup based on TST ≤9 years in which TNX 5.6 mg separated from PBO showing a strong treatment effect.
- The lack of separation in the >9 years TST subgroup appeared to be due to a high placebo response in this subgroup.
- In the TST ≤9 years subgroup, secondary endpoints including CGI-I, PGIC, PROMIS SD and BDI-II were all p<0.05 at Weeks 4 and 12; and SDS was p=0.007 at Week 12.
- Results informed design of a new Phase 3 study with a primary endpoint at Week 4 in a mix of civilian and military PTSD.
- Analysis of subgroup of female participants and of non-combat traumas in the TST ≤9 years subgroup suggests clinically meaningful separation from PBO at Weeks 4 and 12 in these subgroups, although the numbers are small in these subgroups

ClinicalTrials.gov Identifier: NCT03062540

Presented at CNS Summit in Boca Raton, FL November 1-4, 2018; Poster 8A, Friday Nov. 2, 5:00-7:00 PM EDT, Reception and Poster Session, and abstract published in *Innovations in Clinical Neuroscience*, November-December 2018;15(11-12, suppl):S10.

Exhibit 99.02

Tonix Pharmaceuticals Presented Results and Retrospective Analyses of Phase 3 P301 "HONOR" Study in Poster Presentation at CNS Summit 2018

Retrospective Analysis Revealed Clinically Meaningful Response to Tonmya® in Female PTSD Participants Overall and for Non-Combat-Related Traumas Experienced Within Nine Years Prior to Screening

Results from Phase 3 P301 HONOR Study Retrospective Analyses Inform Design of a New Phase 3 Trial of Tonmya, which is Expected to Commence First Quarter 2019

NEW YORK, November 6, 2018 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company) presented a poster at CNS Summit 2018 held November 1-4, 2018, in Boca Raton, Fla. A poster, entitled "Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL*, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301)" includes results and retrospective analyses from the Phase 3 P301 study ("HONOR"). TNX-102 SL, or Tonmya*, is being developed for the treatment of posttraumatic stress disorder (PTSD). The poster can be found on the Scientific Presentations page of Tonix's website.

The poster presentation reports that a retrospective analysis revealed a treatment effect in participants who experienced trauma less than or equal to nine years prior to screening (approximately 50% of the modified intent-to-treat population). For this subgroup, the p-value of the primary endpoint at Week 12, using mixed model repeated measures with multiple imputation (MMRM with MI), was 0.039. In contrast, there was no benefit relative to placebo in the participants who experienced trauma more than nine years prior to screening.

A retrospective analysis of female participants overall, and of military participants with non-combat index traumas experienced less than or equal to nine years from screening, suggests clinically meaningful separation from placebo at Weeks 4 and 12 in these specific subgroups. The female subgroup (n = 27) experienced an 11.5 point improvement in CAPS-5 at Week 4 and 9.1 point improvement at Week 12, while the non-combat participant subgroup (n = 24) experienced a 4.8 point improvement at Week 4 and 4.4 point improvement at Week 12. In addition, the Week 4 assessment of CAPS-5 in the Phase 3 HONOR study showed clinically meaningful improvement at this time point in the entire modified intent-to-treat population (difference from placebo of -3.6 CAPS-5 points, $p = 0.019$).

Furthermore, for study participants who experienced trauma less than or equal to nine years prior to screening, all five secondary measures showed a p-value of <0.05 at the Week 12 endpoint, indicating possible global and functional recovery, and improved sleep quality and mood after 12 weeks of Tonmya treatment compared with placebo.

Based on these findings and following a recent Breakthrough Therapy Type B Clinical Guidance meeting with the U.S. Food and Drug Administration (FDA), the Company plans to incorporate several new design features into the new Phase 3 study, including restricting enrollment of study participants to individuals with PTSD who experienced an index trauma within nine years of screening; enrolling participants who have experienced civilian traumas, in addition to those with military-related traumas; and a CAPS-5 primary endpoint assessed at Week 4 instead of at Week 12.

Dr. Seth Lederman, CEO of Tonix commented, "Data analyses from our Phase 3 HONOR study, as well as recent feedback from the FDA, has informed and strengthened the next Phase 3 trial design which increases the probability of success as a potential pivotal efficacy study to support the Tonmya NDA approval for PTSD. The innovative Phase 3 study design has preliminary acceptance from the FDA and will be initiated in the first quarter of 2019."

Dr. Gregory Sullivan, Chief Medical Officer of Tonix commented, “The findings of P301 show that in PTSD, time since trauma is important in the treatment response to Tonmya. In addition, the primary and secondary efficacy results from females and military personnel with non-combat index traumas in the Phase 3 HONOR study supports the expansion of our next Phase 3 study to include civilians with PTSD, the majority of whom are female.”

There were no serious and unexpected adverse events (AEs) in the HONOR/P301 study with TNX-102 SL 5.6 mg. The AEs observed in both PTSD studies, P301 and previously in Phase 2 P201, were comparable and also consistent with the experience in prior studies with TNX-102 SL 2.8 mg in fibromyalgia. Observed systemic AEs were consistent with those described in approved oral cyclobenzaprine product labels. Similar severity and incidence of oral hypoesthesia (tongue/mouth numbness) has been observed across studies (37% in P301; 36% in P201) for TNX-102 SL or Tonmya 5.6 mg.

**Tonmya has been conditionally accepted by the U.S. Food and Drug Administration (FDA) as the proposed trade name for TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the treatment of PTSD. TNX-102 SL is an investigational new drug and has not been approved for any indication.*

The Phase 3 HONOR Study (P301)

The HONOR study was a randomized, placebo-controlled study that was planned to enroll 550 participants with military-related PTSD at 44 U.S. clinical sites. The primary efficacy endpoint was the 12-week 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 structured clinical interview and serves as the standard in research for measuring the symptom severity of PTSD. A planned, unblinded interim analysis was completed in July 2018 when approximately 50 percent (n=274) of planned participants were randomized and completed 12 weeks of treatment with either bedtime sublingual Tonmya 5.6 mg (2 x 2.8 mg tablets) or placebo sublingual tablets. Based on a pre-specified study continuation threshold at Week 12, the study was discontinued due to inadequate separation from placebo in the primary efficacy endpoint. Meaningful improvement in overall PTSD symptoms was observed at Week 4, at which time the Tonmya treated group separated from placebo in CAPS-5 ($p = 0.019$) and in the Clinical Global Impression – Improvement (CGI-I) scale ($p = 0.015$), a key secondary endpoint. Also, at Week 4, sleep quality improved as measured by both the PROMIS Sleep Disturbance scale and the CAPS-5 sleep disturbance item, supporting the proposed mechanism of action of Tonmya. Retrospective analysis of the discontinued Phase 3 P301 Study revealed clinically meaningful response to Tonmya in PTSD participants with trauma experienced within nine years prior to screening but not in participants with trauma experienced greater than nine years prior to screening. Additional details of the HONOR study are available at https://clinicaltrials.gov/ct2/show/NCT03062540.

About Tonmya and PTSD

Tonmya or TNX-102 SL is a sublingual transmucosal tablet formulation of cyclobenzaprine. PTSD is a serious condition that affects approximately 11 million U.S. adults, and is characterized by chronic disability, inadequate treatment options, especially for military-related PTSD, and an overall high utilization of healthcare services that contributes to significant economic burdens.

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering and developing pharmaceutical products to treat serious neuropsychiatric conditions and biological products to improve biodefense through potential medical counter-measures. Tonix is developing Tonmya, which has been granted Breakthrough Therapy designation, as a bedtime treatment for PTSD. Tonix is also developing TNX-102 SL as a bedtime treatment for agitation in Alzheimer's disease under a separate IND to support a Phase 2, potential pivotal, efficacy study and has been granted Fast Track designation by the FDA for this indication. TNX-601 (tianeptine oxalate) is in the pre-IND application stage, also for the treatment of PTSD but by a unique mechanism and designed for daytime dosing. Tonix's lead biologic candidate, TNX-801, is a potential smallpox-preventing vaccine based on a live synthetic version of horsepox virus, currently in the pre-IND application stage.

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; 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, 2017, as filed with the Securities and Exchange Commission (the "SEC") on March 9, 2018, 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.

Contacts

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

Differential Treatment Effects of a Sublingual Formulation of Cyclobenzaprine (TNX-102 SL*) on Dissociative Symptoms of Derealization and Depersonalization in a Military-Related PTSD

Gregory M. Sullivan[1], Kimmons Wilson[1],R. Michael Gendreau[2], Judy Gendreau[1], Ashild Peters[1], Perry Peters[1], Amy Forst[1], Jean Engels[3], Seth Lederman[1]
[1]Tonix Pharmaceuticals, Inc., New York, NY 10022; [2]Gendreau Consulting, Poway, CA 92064; [3]Engels Statistical Consulting, Minneapolis, MN 55044

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

INTRODUCTION

Dissociative phenomena involve the experience of detachment from reality. Symptoms of dissociation are often associated with trauma-related disorders such as posttraumatic stress disorder (PTSD). Prominent in PTSD are symptoms that include depersonalization (DP), a sense of being detached from, or an outside observer of, one's body, and derealization (DR), a sense of the world as unreal, dreamlike, distant, or distorted.

DSM-5 introduced a dissociative subtype of PTSD (D-PTSD) to account for symptoms of DR and/or DP that develop with the disorder, and it is estimated that 15-30% of PTSD patients qualify for D-PTSD.[1,2] Dissociative symptoms are reported to correlate with arousal and reactivity in PTSD,[3] are associated with increased severity of substance abuse,[4] and have been found to be more common in young men.[5] Sleep disturbances appear to worsen dissociation.[6]

DP and DR arise in several psychiatric disorders including PTSD, panic disorder, social anxiety disorder, and generalized anxiety disorder, and treatment of these symptoms has generally focused on treatment of the underlying disorder. Yet, there are some reports of treatment focused specifically on dissociative symptoms, in particular DP; with reports of improvement in symptoms with transcranial magnetic stimulation,[7,8] combination of selective serotonin reuptake inhibitors (SSRIs) and lamotrigine,[9,10] as well as cognitive therapy.[11] In absence of more treatment data from research focused on DP and DR, psychotherapies are currently considered to have the best outcomes when addressing both DP and DR, although pharmacotherapy with desipramine[12] was previously suggested to have a role in the treatment of DP. Current treatments for D-PTSD mostly involve cognitive-behavioral therapies and pharmacotherapy with SSRIs, the same as current guidelines for the treatment of PTSD in general.[13]

Here we report on the effects of pharmacotherapy with TNX-102 SL on dissociative symptoms of DP and DR in participants of a 12-week, Phase 2, randomized clinical trial, the 'AtEase' study, which tested the safety and efficacy of TNX-102 SL in military-related PTSD.

METHODS

The 'AtEase' study was a randomized, double-blind, placebo-controlled, multi-center 12-week safety and efficacy study of TNX-102 SL in military-related PTSD. Participants meeting the diagnosis of PTSD, as assessed by the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5), were randomized in a 2:2:1 ratio placebo, TNX-102 SL 2.8 mg, or TNX-102 SL 5.6 mg. Eligible participants had to meet the following criteria: **Inclusions**: males and females; ages 18-65; PTSD DSM-5 Criterion A trauma(s) incurred during military service since 9/11/2001; baseline total CAPS-5 score ≥ 29; free of antidepressants ≥ 2 months; free of or washed off of other psychotropics; not participating in a trauma-focused psychotherapy during study or within one month prior. **Exclusions**: severe suicide risk; substance use disorders within 6 months; lifetime bipolar 1 or 2, psychotic, obsessive-compulsive, or antisocial personality disorders.

Efficacy: The primary efficacy endpoint was mean change from baseline (MCFB) in CAPS-5 score between TNX-102 SL and placebo at Week 12 using mixed model repeated measures (MMRM) analysis. Key secondary endpoints included Clinical Global Impression–Improvement (CGI-I), Sheehan Disability Scale (SDS), PROMIS Sleep Disturbance (SD). Each CAPS-5 evaluation included the first 20 items as well as item 29 (depersonalization, DP) and 30 (derealization, DR). The scores of these two items were independent of the total CAPS-5 severity score, which was the sum of severities from the first 20 items. All analyses of continuous variables used MMRM. Correlations of dissociative symptoms with other variables use Spearman's *rho*.

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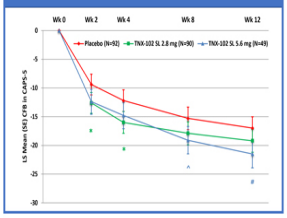
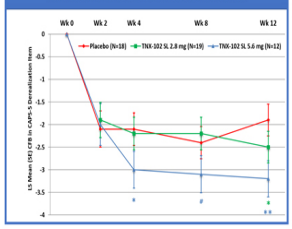
Figure 1. CAPS-5 Least Squares MCFB Over 12 Weeks of Treatment with TNX-102 SL



#p=0.053, ^p=0.094, comparing TNX-102 SL 5.6 mg to placebo, MMRM; *p<0.05, comparing TNX-102 SL 2.8 mg to placebo

Figure 2. Derealization Least Squares MCFB Over 12 Weeks of Treatment with TNX-102 SL



**p=0.001, *p=0.026, #p=0.076, comparing TNX-102 SL 5.6 mg to placebo, MMRM; *p=0.046, comparing TNX-102 SL 2.8 mg to placebo, MMRM

RESULTS

As previously reported, the TNX-102 SL 2.8 mg group (N=90) did not separate significantly on MCFB of CAPS-5 total severity score from placebo (N=92) at Week 12 (least squares mean ± standard error, -2.2 ± 1.94 points; p=0.259). But, as shown in **Figure 1**, the 2.8 mg group did separate from placebo at earlier timepoints, at Week 2 (-3.2 ± 1.55 points; p=0.040) and Week 4 (-3.8 ± 1.76 points; p=0.030). Secondary analysis of the TNX-102 SL 5.6 mg group (N=49) showed a strong trend for separation from placebo at Week 12 on MCFB of CAPS-5 (-4.5 ± 2.31 points; p=0.053; effect size of 0.36).

- On the CAPS-5 derealization item (Item 30), 21.2% of the mITT were rated >0 at baseline
  - As shown **in Figure 2**, both doses of TNX-102 SL showed a significant effect for reducing derealization over 12 weeks compared to the placebo (N=18)
    - TNX-102 SL 2.8mg→ -0.6 ± 0.30; N=19; p<0.05
    - TNX-102 SL 5.6mg→ -1.3 ± 0.37; N=12; p=0.001
- On the CAPS-5 depersonalization item (Item 29), 20.4% of the mITT scored >0 at baseline
  - Neither doses decreased depersonalization scores over 12 weeks compared to placebo (N=24)
    - TNX-102 SL 2.8mg→ 0.0 ± 0.33; N=12; p=0.92
    - TNX-102 SL 5.6mg→ 0.5 ± 0.39; N=11; p=0.23
- Participants with the dissociative subtype (DP, DR, or both), 31.2% of the mITT, failed to respond to TNX-102 SL treatment in terms of total CAPS-5 symptom severity reduction compared with the placebo (N=33)
  - TNX-102 SL 2.8mg→ 0.0 ± 4.20 points; N=22; p=0.99
  - TNX-102 SL 5.6mg→ -2.4 ± 4.76 points; N=17; p=0.62
- Baseline depersonalization (Item 29) in participants with >0 depersonalization correlated with baseline:
  - Sleep disturbance (Item 20) score → rho=0.32, p=0.026
  - Arousal and reactivity cluster (Cluster E) score → rho=0.34, p=0.019
  - CAPS-5 total score → rho=0.51, p<0.001
- Baseline derealization (Item 30) in participants with >0 derealization correlated with baseline:
  - Sleep disturbance (Item 20) score → rho=0.29, p=0.046
  - Arousal and reactivity cluster (Cluster E) score → rho=0.42, p=0.002
  - CAPS-5 total score → rho=0.42, p=0.002

Safety

Overall TNX-102 SL was well tolerated. Adverse events occurring at > 5% rate in either TNX-102 SL group are summarized in **Table 1**.

Table 1. Adverse Events at Rate of ≥5% in TNX-102 SL Arms

Systemic Adverse Events	Placebo (N=94)*	TNX-102 SL 2.8 mg (N=93)*	TNX-102 SL 5.6 mg (N=50)*
Somnolence	6.4%	11.8%	16.0%
Dry Mouth	10.6%	4.3%	16.0%
Headache	4.3%	5.4%	12.0%
Insomnia	8.5%	7.5%	6.0%
Sedation	1.1%	2.2%	12.0%
Administration Site Reactions			
Hypoaesthesia oral#	2.1%	38.7%	36.0%
Paraesthesia	3.2%	16.1%	4.0%
Glossodynia	1.1%	3.2%	6.0%

#Oral hypoaesthesia (tongue numbness) was the most common AE, was generally transient (<60 minutes), and rated as mild in 89% and moderate in 11% on TNX-102 SL;
*Safety population (N=237)

CONCLUSIONS

- The finding that 31.2% of this military PTSD population expressed the dissociative subtype (D-PTSD) is consistent with the limited epidemiology of dissociative symptoms in PTSD.
- Both derealization symptoms and depersonalization symptoms were correlated with sleep disturbance and hyperarousal, as reported in the literature
- The D-PTSD subgroup a poorer response to treatment with TNX-102 SL, in terms of improvement in CAPS-5 total score, compared with the mITT population, consistent with literature suggesting D-PTSD is less treatment responsive.
- TNX-102 SL 5.6 mg may be an effective treatment specifically for derealization symptoms but not for depersonalization symptoms
  - Yet caution interpreting this treatment effect is warranted due to the small group numbers with derealization symptoms expressed at baseline, and replication in a larger population is needed
- The differential treatment effect observed suggests derealization and depersonalization may be separate and distinct neurobiological constructs.

ClinicalTrials.gov Identifier: NCT02277704 (P201)

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