**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 21, 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. ☐

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**Item 7.01 Regulation FD Disclosure.**

Tonix Pharmaceuticals Holding Corp (the "Company") issued a press release announcing topline results from its Phase 3 RECOVERY study of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6mg product candidate for the treatment of posttraumatic stress disorder ("PTSD") and outlined future development plans. A copy of the press release is furnished as Exhibit 99.01 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.01 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 21, 2020, the Company announced topline results from its Phase 3 RECOVERY study of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg for the treatment of civilian and military-related PTSD. The RECOVERY study did not achieve statistical significance in the prespecified primary efficacy endpoint of change from baseline to Week 12 in the Clinician-Administered PTSD Scale for DSM-5 ("CAPS-5") between TNX-102 SL and placebo (p=0.343) (Table 1). In the primary analysis, TNX-102 SL subjects achieved a 20.7 unit reduction in CAPS-5 versus 18.5 units for placebo. TNX-102 SL separated from placebo in the first key secondary endpoint, Clinical Global Impression – Severity (CGI-S) scale (p=0.024) (Table 1) and in the Patient Global Impression of Change (PGIC), (p=0.007). TNX-102 SL also trended for improvement on the PROMIS Sleep Disturbance scale (p=0.055), consistent with the proposed mechanism of targeting the PTSD sleep disturbance (Table 1). Among completers, there was a 58% observed mean reduction in symptoms in the active group compared to 49% in the placebo group, as measured by CAPS-5 total. TNX-102 SL is generally well tolerated and no new safety signals were observed.

Given the complexity of PTSD as a syndrome and the demonstrated potential of TNX-102 SL to improve sleep quality in PTSD, the Company plans to meet with the U.S. Food and Drug Administration ("FDA") to discuss a proposed new indication: TNX-102 SL for the treatment of sleep disturbance associated with PTSD. Sleep disturbance is a core symptom of PTSD and believed to play roles in onset, consolidation and chronicity. Treating sleep disturbance is recognized as a clinically valid approach for addressing global improvement in PTSD. This new direction is supported by consistent results observed from all three registration-quality studies of TNX-102 SL in PTSD showing trends or nominal benefits in treating sleep disturbance, global improvement by patient self-rating or by clinician-rating. These results included female-predominant, civilian PTSD in the RECOVERY study and male-predominant, military-related PTSD in the Phase 2 AtEase and Phase 3 HONOR studies.

TNX-102 SL's tolerability profile has been expanded by the RECOVERY study, and treatment with TNX-102 SL was not associated with weight gain or sexual side effects, and TNX-102 SL treatment notably trended towards improvement of female sexual function in RECOVERY (Table 3). This tolerability profile has the potential to differentiate TNX-102 SL from the reported tolerability of the two SSRIs that are currently FDA-approved for PTSD.

**Table 1. RECOVERY study: Primary and Secondary Efficacy Endpoints**

| | TNX-102 SL (N=80) | | Placebo (N=83) | | TNX-102 SL v. Placebo | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Wk 12 Outcome Measure** | **LS Mean** | **SE** | **LS Mean** | **SE** | **LSMD** | **SE** | **95% CI** | **p-value*** | **ES** |
| **CAPS-5 CFB[#]** | -20.7 | 1.97 | -18.5 | 1.9 | -2.2 | 2.3 | -6.7, 2.3 | 0.343 | 0.15 |
| **CGI-S score CFB** | -2 | 0.18 | -1.5 | 0.17 | -0.5 | 0.22 | -0.9, -0.1 | 0.024 | 0.36 |
| **PGIC score** | 2.3 | 0.16 | 2.8 | 0.16 | -0.5 | 0.19 | -0.9, -0.1 | 0.007 | 0.43 |
| **PROMIS SD T-score CFB** | -13 | 1.57 | -9.4 | 1.51 | -3.5 | 1.82 | -7.1, 0.1 | 0.055 | 0.30 |
| **CAPS-5 item E6/SD CFB** | -1.3 | 0.19 | -0.9 | 0.19 | -0.4 | 0.23 | -0.8, 0.1 | 0.086 | 0.28 |

Abbreviations: CAPS-5 = Clinician-Administered PTSD Scale; CFB = change from baseline; CGI-S = Clinical Global Impression – Severity; CI = confidence interval; ES = effect size; LS = least squares; LSMD = least squares mean difference; N = number; PGIC = Patient Global Impression of Change; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = sleep disturbance; SE = standard error; Wk = week.

[#] **Primary efficacy endpoint**

*All secondary p-values are descriptive

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**Table 2. RECOVERY study: Changes in Weight, Blood Pressure and Heart Rate Between Baseline and Last Assessment**

| | TNX-102 SL (N=80) | | Placebo (N=84) | |
|---|---|---|---|---|
| **Change in Outcome Measure** | **Mean** | **95% CI** | **Mean** | **95% CI** |
| **Weight (kg)** | 0.03 | -0.48, 0.54 | 0.58 | -0.01, 1.16 |
| **Systolic blood pressure (mmHg)** | 1.8 | -0.8, 4.5 | 1.3 | -1.4, 4.0 |
| **Diastolic blood pressure (mmHg)** | 1.5 | -0.5, 3.5 | -0.2 | -2.3, 1.9 |
| **Heart rate (beats per minute)** | 1.8 | -1.0, 4.5 | 1.5 | -1.1, 4.0 |

Abbreviations: CI = confidence interval; N = number

**Table 3. RECOVERY study: Changes in Sexual Functioning Questionnaire Short Form**

| | TNX-102 SL (N=65) | | Placebo (N=64) | | TNX-102 SL v. Placebo | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Wk 12 Outcome Measure** | **LS Mean** | **SE** | **LS Mean** | **SE** | **LSMD** | **SE** | **95% CI** | **p-value**** | **ES** |
| **CSFQ-14 CFB* (female)** | 4.6 | 0.84 | 2.4 | 0.86 | 2.2 | 1.21 | -0.2, 4.6 | 0.07 | 0.32 |

*higher score on CSFQ-14 indicates better sexual functioning

** p-value is descriptive

Abbreviations: CSFQ-14 = Changes in Sexual Functioning Questionnaire short form: CI = confidence interval; ES = effect size; LS = least squares; LSMD = least squares mean difference; N = number; SE = standard error; Wk = week.

**RECOVERY STUDY**

**Full cohort topline analysis:**

In the full cohort topline analysis, 163 of the 192 participants enrolled in the RECOVERY study were included in the modified intent to treat ("mITT ") population. TNX-102 SL did not achieve statistical significance in the prespecified primary efficacy endpoint of change from baseline in CAPS-5 (p=0.343; Table 1).

TNX-102 SL separated from placebo in the first key secondary endpoint, CGI-S scale, by least squares ("LS") mean (SE) of -0.5 units (p=0.024) (Table 1). The CGI-S measures how clinicians rate the severity of PTSD in study participants over the preceding week and is not tied to any theoretical construct of disease recovery such as the assumptions inherent in the CAPS-5 items. Previous studies of TNX-102 SL, the AtEase and HONOR studies, used the Clinical global impression of improvement (CGI-I), which is similar to CGI-S, but is based on a "lookback" to patient baseline, rather than 7 days.

TNX-102 SL also separated from placebo in the PGIC analyzed as a continuous measure with a least squares mean difference (standard error) -0.5 (0.19), p=0.007 by Mixed Models Repeated Measures ("MMRM"). Similarly to previous TNX-102 SL studies (AtEase and HONOR), in RECOVERY TNX-102 SL separated in the PGIC by responder analysis, with TNX-102 SL treatment resulting in 51.3% responders relative to 34.9% on placebo, odds ratio 1.88 [1.00, 3.54], p=0.049 by Cochran-Mantel-Haenszel test. The PGIC measures how study participants themselves rate how they feel; it is not tied to any theoretical construct of disease recovery such as the assumptions inherent in the CAPS-5 items.

The placebo response elicited on CAPS-5 in the RECOVERY study was more pronounced than that reported by CGI-S and PGIC. Similar results were observed in the two previous studies. The high levels of PTSD symptom improvement of placebo-treated trial participants detected by CAPS was not reported by the patients themselves as measured by PGIC, nor by the clinicians by CGI-S in the RECOVERY study or by CGI-I in the AtEase or HONOR studies. The Company believes that the high levels of CAPS-5 improvement in the placebo groups of these trials do not correspond to the clinical challenges of treating moderate-to severe PTSD patients in practice, which suggests a measurement problem. Although significant efforts were devoted to CAPS-5 rater-training, certification and monitoring, the CAPS-5 data from these studies have not tracked patient and clinician perceptions of global improvement, which are typically anchors for observable units of improvement on disease symptom-specific scales.

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**Effects of TNX-102 SL on Sleep Quality**

Similar to prior studies, TNX-102 SL at 5.6 mg in RECOVERY demonstrated trends on measures of sleep quality including the PROMIS Sleep Disturbance inventory, which at Week 12 showed a LS mean difference (SE) from placebo of -3.5 (1.82), p=0.055 (Table 1). Although the early stop of enrollment due to the interim analysis outcome resulted in an underpowered sample size for detecting effects on sleep at $p<0.05$, the effect size of 0.30 on PROMIS SD suggests significant effects might have been detected by the originally planned sample of N=250. Similarly, the CAPS-5 sleep item E6 showed TNX-102 SL trended towards improvement over placebo by LS mean difference (SE) of -0.4 (0.23), p=0.086, with an effect size of 0.28. Mechanistically, TNX-102 SL is considered to improve PTSD through pharmacodynamic effects on CNS receptors that mediate sleep quality, and, as a result, improve sleep-dependent emotional memory processing necessary to recovery from PTSD. Replication of the effects on sleep in the

predominantly civilian PTSD sample of RECOVERY along with the patient and clinician rated global improvement suggests this mechanism is also operational in a mostly female sample with non-military PTSD.

**Female Sexual Dysfunction (Changes in Sexual Functioning Questionnnaire Short Form)**
The Changes in Sexual Functioning Questionnaire Short Form (CSFQ-14), which has female and male versions, was administered at baseline and Week 12 in RECOVERY. In female participants, the TNX-102 SL group (N=65) trended for greater improvement in CSFQ-14 total score compared with placebo (N=64), with a Least Squares Mean Difference (LSMD) of 2.2 units, p=0.070 (Table 3). The number of male subjects in the study in the TNX-102 SL group (N=15) and placebo group (N=19) precluded meaningful statistical comparison. These results suggest TNX-102 SL may potentially improve sexual functioning in females with PTSD, which contrasts with the approved drugs for PTSD which can have impairing effects on sexual functioning.

**Safety and Tolerability**
TNX-102 SL was well-tolerated and the adverse events reported were similar to those seen in prior TNX-102 SL studies (Table 4). There were three participants with serious adverse events ("SAEs") reported during the study: two in the placebo group and one in the active group (osteomyelitis of left great toe). None were deemed related to study drug. Administration site reactions were similar in profile to prior studies with TNX-102 SL, with oral numbness (hypoaesthesia) at the highest rate, 29.2% in the TNX-102 SL arm versus 1.1% in the placebo arm. These oral sensory adverse events ("AEs"), oral numbness, oral tingling, and tongue discomfort were always temporally-related to dosing and tended to be rated as mild and transient (<60 min) in the majority of cases. Only one of these oral sensory AEs lead to study discontinuation (in a participant who took only one dose and reported oral numbness, nausea, and emesis). Systemic AEs at a rate of ≥ 5% in the TNX-102 SL group were dry mouth (8.3 v. 3.3%) and upper respiratory tract infections (5.2 v. 4.4%). Discontinuations due to AEs were at a rate of 6.3% in the TNX-102 SL group versus 2.2% on placebo. The safety population had an overall completion rate of 65.8%, which was numerically higher in the placebo group (70.3%) than in the TNX-102 SL 5.6 mg group (61.5%). No new safety signals were observed.

**Table 2. Treatment Emergent Adverse Events at Rate of ≥ 5% in the TNX-102 SL Group**

| | TNX-102 SL (N=96) | | Placebo (N=91) | | Overall (N=187) | |
|---|---|---|---|---|---|---|
| **Administration Site Reactions** | N | % | N | % | N | % |
| Oral numbness | 28 | 29.2 | 1 | 1.1 | 29 | 15.5 |
| Oral tingling | 7 | 7.3 | 1 | 1.1 | 8 | 4.3 |
| Tongue discomfort | 5 | 5.2 | 0 | 0.0 | 5 | 2.7 |
| **Systemic Adverse Events** | N | % | N | % | N | % |
| Dry Mouth | 8 | 8.3 | 3 | 3.3 | 11 | 5.9 |
| Upper respiratory tract infection | 5 | 5.2 | 4 | 4.4 | 9 | 4.8 |

*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 21, 2020 |

**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 21, 2020

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

**Exhibit 99.01**

**CONFIDENTIAL – NOT FOR DISTRIBUTION**

**Tonix Pharmaceuticals Reports Topline Results from Phase 3 RECOVERY Study of TNX-102 SL in PTSD and Outlines Future Development Plans**

*Primary Endpoint For Full Cohort of Enrolled Participants Did Not Achieve Statistical Significance (P=0.343), Consistent with Previously Reported Interim Analysis*

*Encouraging Activity of TNX-102 SL Observed in Secondary Endpoints: Clinical Global Impression – Severity (P=0.024), Patient Global Impression of Change (P=0.007) and PROMIS Sleep Disturbance (P=0.055)*

*Participants were 94% Civilian PTSD and 79% Female: Global Impression and Sleep Results Similar to Prior Studies of TNX-102 SL in Predominanly Male, Military-Related PTSD Studies*

*TNX-102 SL Generally Well Tolerated; No New Safety Signals Observed: No Change in Weight or Blood Pressure*

*Total CAPS-5 Decreased by 58% in Treatment Group and 49% in Placebo Group*

*Planning Development of TNX-102 SL for Treatment of PTSD Sleep Disturbance Indication, Pending FDA Discussion*

CHATHAM, N.J., December 21, 2020 - Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced topline results from its Phase 3 RECOVERY study[1] of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg for the treatment of civilian and military-related posttraumatic stress disorder (PTSD). The RECOVERY study did not achieve statistical significance in the prespecified primary efficacy endpoint of change from baseline to Week 12 in the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) between TNX-102 SL and placebo (p=0.343) (Table 1). In the primary analysis, TNX-102 SL subjects acheived a 20.7 unit reduction in CAPS-5 versus 18.5 units for placebo. TNX-102 SL separated from placebo in the first key secondary endpoint, Clinical Global Impression – Severity (CGI-S) scale (p=0.024) (Table 1) and in the Patient Global Impression of Change (PGIC), (p=0.007). TNX-102 SL also trended for improvement on the PROMIS Sleep Distubance scale (p=0.055), consistent with the proposed mechanism of targeting the PTSD sleep disturbance (Table 1). Among completers, there was a 58% observed mean reduction in symptoms in the active group compared to 49% in the placebo group, as measured by CAPS-5 total. TNX-102 SL is generally well tolerated and no new safety signals were observed.

“As expected from the futility result at the interim analysis in the first quarter of 2020, TNX-102 SL did not separate on the primary endpoint of CAPS-5 at Week 12,” said Seth Lederman, M.D., President and Chief Executive Officer. “Given the complexity of PTSD as a syndrome and the demonstated potential of TNX-102 SL to improve sleep quality in PTSD, we plan to meet with the U.S. Food and Drug Administration (FDA) to discuss a proposed new indication: TNX-102 SL for the treatment of sleep disturbance associated with PTSD. Sleep disturbance is a core symptom of PTSD and believed to play roles in onset, consolidation and chronicity. Treating sleep disturbance is recognized as a clinically valid approach for addressing global improvement in PTSD[2-5]. This new direction is supported by consistent results observed from all three registration-quality studies of TNX-102 SL in PTSD (nearly 800 participants randomized across three placebo-controlled trials) showing trends or nominal benefits in treating sleep disturbance, global improvement by patient self-rating or by clinician-rating. These results included female-predominant, civilian PTSD in RECOVERY and male-predominant, military-related PTSD in the Phase 2 AtEase[6] and Phase 3 HONOR[7] studies. The FDA-approved insomnia drugs of the benzodiazepine or non-benzodiazepine classes are DEA-Schedule IV, have not been shown useful in PTSD and have the potential to impair sleep-dependent memory processing at high doses or when combined with alcohol.”

Greg Sullivan, M.D., Chief Medical Officer, said, “We are encouraged by TNX-102 SL’s activity on the sleep disturbance in PTSD and on the clinician-rated and patient self-rated global measures of clinical improvement, CGI-S and PGIC, in this predominantly female and civilian PTSD sample. Pending discussion with the FDA, we intend to pursue TNX-102 SL as a treatment for the sleep disturbance that is integral to the development and maintance of PTSD. PTSD is a memory processing disorder, and adequate quality and quantity of deep slow wave sleep and rapid eye-movement sleep are known to be important for emotional memory processing necessary for recovery from trauma. Although treatment of the PTSD sleep disturbance would be a new indication, instruments like sleep quality assessments can be validated by patient- and clinician-perception of global improvement. Therefore, the discriminatory power of CGI-S and PGIC on TNX-102 SL’s activity in PTSD support such a development. TNX-102 SL is mechanistically distinct from the two FDA approved PTSD drugs; both are SSRIs, and neither target the sleep disturbance.

Dr. Sullivan continued, “We are also encouraged by the tolerability profile that has been expanded by the RECOVERY study. TNX-102 SL treatment was not associated with weight gain or sexual side effects, and TNX-102 SL treatment notably trended towards improvement of female sexual function in RECOVERY (Table 3). This tolerability profile has the potential to differentiate TNX-102 SL from the reported tolerability of the two SSRIs that are FDA-approved for PTSD.”

“Tonix has worked diligently to develop a treatment for PTSD, a serious and disabling condition affecting nearly 12 million civilian and veteran adults in the U.S.,” said Dr. Lederman. “The demographics of the RECOVERY study participants, 94% civilians and 79% female, largely reflect the real-world metrics of those living with PTSD in which the vast majority are civilians and, among diagnosed civilians, approximately two-thirds are female. We are grateful for the contributions from all our study participants and their families in helping advance this program.”

**Table 1. RECOVERY study: Primary and Secondary Efficacy Endpoints**

| | TNX-102 SL (N=80) | | Placebo (N=83) | | TNX-102 SL v. Placebo | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Wk 12 Outcome Measure** | **LS Mean** | **SE** | **LS Mean** | **SE** | **LSMD** | **SE** | **95% CI** | **p-value*** | **ES** |
| **CAPS-5 CFB[#]** | -20.7 | 1.97 | -18.5 | 1.9 | -2.2 | 2.3 | -6.7, 2.3 | 0.343 | 0.15 |
| **CGI-S score CFB** | -2 | 0.18 | -1.5 | 0.17 | -0.5 | 0.22 | -0.9, -0.1 | 0.024 | 0.36 |
| **PGIC score** | 2.3 | 0.16 | 2.8 | 0.16 | -0.5 | 0.19 | -0.9, -0.1 | 0.007 | 0.43 |
| **PROMIS SD T-score CFB** | -13 | 1.57 | -9.4 | 1.51 | -3.5 | 1.82 | -7.1, 0.1 | 0.055 | 0.30 |
| **CAPS-5 item E6/SD CFB** | -1.3 | 0.19 | -0.9 | 0.19 | -0.4 | 0.23 | -0.8, 0.1 | 0.086 | 0.28 |

Abbreviations: CAPS-5 = Clinician-Administered PTSD Scale; CFB = change from baseline; CGI-S = Clinical Global Impression – Severity; CI = confidence interval; ES = effect size; LS = least squares; LSMD = least squares mean difference; N = number; PGIC = Patient Global Impression of Change; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = sleep disturbance; SE = standard error; Wk = week.

[#] **Primary efficacy endpoint**

*All secondary p-values are descriptive

**Table 2. RECOVERY study: Changes in Weight, Blood Pressure and Heart Rate Between Baseline and Last Assessment**

| | TNX-102 SL (N=80) | | Placebo (N=84) | |
|---|---|---|---|---|
| **Change in Outcome Measure** | **Mean** | **95% CI** | **Mean** | **95% CI** |
| **Weight (kg)** | 0.03 | -0.48, 0.54 | 0.58 | -0.01, 1.16 |
| **Systolic blood pressure (mmHg)** | 1.8 | -0.8, 4.5 | 1.3 | -1.4, 4.0 |
| **Diastolic blood pressure (mmHg)** | 1.5 | -0.5, 3.5 | -0.2 | -2.3, 1.9 |
| **Heart rate (beats per minute)** | 1.8 | -1.0, 4.5 | 1.5 | -1.1, 4.0 |

Abbreviations: CI = confidence interval; N = number

**Table 3. RECOVERY study: Changes in Sexual Functioning Questionnaire Short Form**

| | TNX-102 SL (N=65) | | Placebo (N=64) | | TNX-102 SL v. Placebo | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Wk 12 Outcome Measure** | **LS Mean** | **SE** | **LS Mean** | **SE** | **LSMD** | **SE** | **95% CI** | **p-value**** | **ES** |
| **CSFQ-14 CFB* (female)** | 4.6 | 0.84 | 2.4 | 0.86 | 2.2 | 1.21 | -0.2, 4.6 | 0.07 | 0.32 |

*higher score on CSFQ-14 indicates better sexual functioning
** p-value is descriptive
Abbreviations: CSFQ-14 = Changes in Sexual Functioning Questionnaire short form: CI = confidence interval; ES = effect size; LS = least squares; LSMD = least squares mean difference; N = number; SE = standard error; Wk = week.

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**RECOVERY STUDY**
The RECOVERY study was a double-blind, randomized, placebo-controlled, adaptive design study evaluating the efficacy and safety of TNX-102 SL 5.6 mg over 12 weeks of treatment for civilian and military-related PTSD. The study enrolled 192 participants across 29 clinical sites in the U.S. Enrollment was restricted to individuals with PTSD who experienced an index trauma within nine years of screening. The primary efficacy endpoint was the mean change from baseline in the severity of PTSD symptoms as measured by the CAPS-5 between those treated with TNX-102 SL 5.6 mg and those receiving placebo.

Interim Analysis
A pre-specified interim analysis (IA) was conducted by an unblinded Independent Data Monitoring Committee (IDMC) after half the target population was enrolled and evaluable in Q1 2020. The Company announced it stopped enrollment in RECOVERY following a non-binding recommendation to stop the trial for futility by the IDMC (N=112; IA modified Intent-to-Treat (mITT) population). The Company chose to discontinue new enrollment but continue all currently enrolled participants at that time to completion. The IDMC decision to discontinue enrollment in the study was not related to safety of TNX-102 SL; the blinded safety data from the IA did not reveal any serious and unexpected adverse events.

**Full cohort topline analysis:**
In the full cohort topline analysis, 163 of the 192 participants enrolled were included in the modified mITT population. TNX-102 SL did not achieve statistical significance in the prespecified primary efficacy endpoint of change from baseline in CAPS-5 (p=0.343; Table 1). The CAPS-5 is a standardized structured clinical interview and serves as the standard in research for measuring the symptom severity of PTSD, although it was developed as a diagnostic instrument. The CAPS-5 assesses 20 items by rating severity (a function of intensity and frequency of each symptom) on a 5 point Likert scale (0-4), so the total scores range from 0 to 80. Earlier versions of the CAPS, which assessed 17 items from the DSM-IV or earlier by recording intensity and frequency as separate 5 point Likert scales (total score range 0 to 136), were used to support the approval of the two currently marketed PTSD treatments.

TNX-102 SL separated from placebo in the first key secondary endpoint, CGI-S scale, by LS mean (SE) of -0.5 units (p=0.024) (Table 1). The CGI-S measures how clinicians rate the severity of PTSD in study participants over the preceding week and is not tied to any theoretical construct of disease recovery such as the assumptions inherent in the CAPS-5 items. Previous studies of TNX-102 SL, AtEase and HONOR, used the Clinical global impression of improvement (CGI-I), which is similar to CGI-S, but is based on a “lookback” to patient basline, rather than 7 days.

TNX-102 SL also separated from placebo in the PGIC analyzed as a continuous measure with a least squares mean difference (standard error) -0.5 (0.19), p=0.007 by Mixed Models Repeated Measures (MMRM). Similarly to previous TNX-102 SL studies (AtEase and HONOR), in RECOVERY TNX-102 SL separated in the PGIC by responder analysis, with TNX-102 SL treatment resulting in 51.3% responders relative to 34.9% on placebo, odds ratio 1.88 [1.00, 3.54], p=0.049 by Cochran-Mantel-Haenszel test. The PGIC measures how study participants themselves rate how they feel; it is not tied to any theoretical construct of disease recovery such as the assumptions inherent in the CAPS-5 items.

Dr. Sullivan said, “In RECOVERY, the placebo response elicited on CAPS-5 was more pronounced than that reported by CGI-S and PGIC. Similar results were observed in our two previous studies. The high levels of PTSD symptom improvement of placebo-treated trial participants detected by CAPS, was not reported by the patients themselves as measured by PGIC, nor by the clinicians by CGI-S in the RECOVERY study or by CGI-I in the AtEase or HONOR studies. We believe that the high levels of CAPS-5 improvement in the placebo groups of these trials do not correspond to the clinical challenges of treating moderate-to severe PTSD patients in practice, which suggests a measurement problem. Although we devoted significant efforts to CAPS-5 rater-training, certification and monitoring, the CAPS-5 data from these studies have not tracked the patient and clinician perceptions of global improvement, which are typically anchors for observable units of improvement on disease symptom-specific scales.”

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**Effects of TNX-102 SL on Sleep Quality**
Similar to prior studies, TNX-102 SL at 5.6 mg in RECOVERY demonstrated trends on measures of sleep quality including the PROMIS Sleep Disturbance inventory, which at Week 12 showed a least squares (LS) mean difference (SE) from placebo of -3.5 (1.82), p=0.055 (Table 1). Although the early stop of enrollment due to the interim analysis outcome resulted in an underpowered sample size for detecting effects on sleep at $p<0.05$, the effect size of 0.30 on PROMIS SD suggests significant effects might have been detected by the originally planned sample of N=250. Similarly, the CAPS-5 sleep item E6 showed TNX-102 SL trended towards improvement over placebo by LS mean difference (SE) of -0.4 (0.23), p=0.086, with an effect size of 0.28. Mechanistically, TNX-102 SL is considered to improve PTSD through pharmacodynamic effects on CNS receptors that mediate sleep quality, and, as a result, improve sleep-dependent emotional memory processing necessary to recovery from PTSD. Replication of the effects on sleep in the predomininantly civilian PTSD sample of RECOVERY along with the patient and clinician rated global improvement suggests this mechanism is also operational in a mostly female sample with non-military PTSD.

**Female Sexual Dysfunction (Changes in Sexual Functioning Questionnnaire Short Form)**

The Changes in Sexual Functioning Questionnaire Short Form (CSFQ-14), which has female and male versions, was administered at baseline and Week 12 in RECOVERY. In female participants, the TNX-102 SL group (N=65) trended for greater improvement in CSFQ-14 total score compared with placebo (N=64), with a Least Squares Mean Difference (LSMD) of 2.2 units, p=0.070 (Table 3). The number of male subjects in the study in the TNX-102 SL group (N=15) and placebo group (N=19) precluded meaningful statistical comparison. These results suggest TNX-102 SL may potentially improve sexual functioning in females with PTSD, which contrasts with the approved drugs for PTSD which can have impairing effects on sexual functioning.

**Safety and Tolerability**

TNX-102 SL was well-tolerated and the adverse events reported were similar to those seen in prior TNX-102 SL studies (Table 4). There were three participants with serious adverse events (SAEs) reported during the study: two in the placebo group and one in the active group (osteomyelitis of left great toe). None were deemed related to study drug. Administration site reactions were similar in profile to prior studies with TNX-102 SL, with oral numbess (hypoaesthesia) at the highest rate, 29.2% in the TNX-102 SL arm versus 1.1% in the placebo arm. These oral sensory adverse events (AE), oral numbness, oral tingling, and tongue discomfort were always temporally-related to dosing and tended to be rated as mild and transient (<60 min) in the majority of cases. And only one of these oral sensory AEs lead to study discontinuation (in a participant who took only one dose and reported oral numbness, nausea, and emesis). Systemic AEs at a rate of ≥ 5% in the TNX-102 SL group were dry mouth (8.3 v. 3.3%) and upper respiratory tract infections (5.2 v. 4.4%). Discontinuations due to AE were at a rate of 6.3% in the TNX-102 SL group versus 2.2% on placebo. The safety population had an overall completion rate of 65.8%, which was numerically higher in the placebo group (70.3%) than in the TNX-102 SL 5.6 mg group (61.5%). No new safety signals were observed.

**Table 2. Treatment Emergent Adverse Events at Rate of ≥ 5% in the TNX-102 SL Group**

| | TNX-102 SL (N=96) | | Placebo (N=91) | | Overall (N=187) | |
|---|---|---|---|---|---|---|
| **Administration Site Reactions** | N | % | N | % | N | % |
| Oral numbness | 28 | 29.2 | 1 | 1.1 | 29 | 15.5 |
| Oral tingling | 7 | 7.3 | 1 | 1.1 | 8 | 4.3 |
| Tongue discomfort | 5 | 5.2 | 0 | 0.0 | 5 | 2.7 |
| **Systemic Adverse Events** | N | % | N | % | N | % |
| Dry Mouth | 8 | 8.3 | 3 | 3.3 | 11 | 5.9 |
| Upper respiratory tract infection | 5 | 5.2 | 4 | 4.4 | 9 | 4.8 |

**About TNX-102 SL**

TNX-102 SL is a proprietary 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. TNX-102 SL recently showed a statistically significant improvement in the pre-specified primary pain endpoint in a Phase 3 study of fibromyalgia, called RELIEF (F304). A confirmatory Phase 3 trial, called RALLY is currently enrolling. Topline data from RALLY are expected in the fourth quarter of 2021. The U.S. Patent and Trademark Office has issued a patent (U.S. Patent No. 9,636,408) protecting the composition and manufacture of the unique formulation. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in the patent are important elements of Tonix's proprietary TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.The United States Patent and Trademark Office (USPTO) issued United States Patent No. 9,636,408 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.

**About Posttraumatic Stress Disorder (PTSD)**

PTSD can develop from witnessing or experiencing a traumatic event in which there was the severe threat of, or actual occurrence of, grave physical harm or death. PTSD affects approximately 12 million Americans and is a chronic and severely debilitating condition in which patients re-experience the horrific traumas that resulted in the condition in the forms of intrusive memories, flashbacks, and nightmares. PTSD typically is characterized by disrupted sleep, anxiety, agitation, avoidance, emotional numbness and estrangement from family and friends, guilt or negative beliefs about self, and sometimes is associated with clinical depression and suicidal thinking. Individuals who suffer from PTSD usually have significant impairment in social functioning, occupational disability, and an overall poor quality of life. PTSD is sometimes associated with substance abuse and unpredictable violent or suicidal behaviors.

Additional details about the RECOVERY study are available at clinicaltrials.gov (NCT03841773)

**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. Tonix's lead CNS candidate, TNX-102 SL*, is in mid-Phase 3 development for the management of fibromyalgia since positive data on the RELIEF Phase 3 trial were recently reported. The Company expects topline data in the Phase 3 RALLY study in the fourth quarter of 2021. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer, and autoimmune diseases. 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.

[1]ClinicalTrials.gov Identifier: NCT02277704

[2]ClinicalTrials.gov Identifier: NCT03668041

[3]Germain, A et al, *Current Opinion in Psychology* 2017, 14:84–89, http://dx.doi.org/10.1016/j.copsyc.2016.12.004

[4]Krystal J et al, *Biological Psychiatry* 2017; 82:e51–e59, http://dx.doi.org/10.1016/j.biopsych.2017.03.007

[5]Bajor, LA et al., *Harv Rev Psychatry* 2011;19:240–258, http://dx.doi.org/10.3109/10673229.2011.614483

[6]ClinicalTrials.gov Identifier: NCT03841773

[7]ClinicalTrials.gov Identifier: NCT03062540

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

**TNX-1800 and TNX-801 are investigational new biologics and have not been approved for any indication.

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

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**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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