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

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# 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 1, 2019**

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**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))

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. ☐
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 |

**Item 7.01 Regulation FD Disclosure.**

The Company updated its investor presentations, which are used to conduct meetings with investors, stockholders and analysts and at investor conferences, and which the Company intends to place on its website, which may contain nonpublic information. Copies of the presentations are filed as Exhibit 99.01 and 99.02 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 9.01 Financial Statements and Exhibits.**

(d)

| Exhibit No. | Description. |
|---|---|
| 99.01 | Corporate Presentation by the Company for November 1, 2019 (Abbreviated Form) |

**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 1, 2019

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

**Exhibit 99.01**

# 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.

# Free Writing Prospectus Statement



This presentation highlights basic information about us and the offering to which this communication relates. Because it is a summary, it does not contain all of the information that you should consider before investing in our securities.

We have filed a registration statement (including a prospectus, which currently is in preliminary form) with the U.S. Securities and Exchange Commission ("SEC") for the offering to which this presentation relates. The registration has not yet become effective. Before you invest, you should read the preliminary registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and this offering. You may access these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov.

The preliminary prospectus, dated October 18, 2019, is available on the SEC Web site at www.sec.gov/Archives/edgar/data/.

Alternatively, we or any underwriter participating in the offering will arrange to send you the preliminary prospectus and, when available, the final prospectus and/or any supplements thereto if you contact A.G.P./Alliance Global Partners, 590 Madison Avenue, 36th Floor, New York, NY 10022 or via telephone at 212-624-2006 or email: presentation@allianceg.com.

This presentation shall not constitute an offer to sell, or the solicitation of an offer to buy, nor will there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such state or jurisdiction. The offering will only be made by means of a prospectus pursuant to a registration statement that is filed with the SEC after such registration statement becomes effective.

# Offering Summary



| Issuer | Tonix Pharmaceuticals Holding Corp. |
|---|---|
| Exchange / Ticker | NASDAQ / TNXP |
| Offering Size | Approximately $15 million (100% Primary) |
| Over Allotment | 15% (100% Primary) |
| Use of Proceeds | • To fund Phase 3 development of our lead product candidate, TNX-102 SL<br>• To advance development of our other product candidates, including in-licensed product candidates<br>• To repurchase shares of our common stock pursuant to a stock buyback program<br>• Working capital and other general corporate purposes |
| Lead Book-Runner | A.G.P. / Alliance Global Partners |

**Who we are:**

- A clinical stage biopharmaceutical company dedicated to developing innovative treatments for patients and making meaningful contributions to society
- Focusing on small molecules and biologics to treat psychiatric, pain and addiction conditions, to improve biodefense through potential medical counter-measures and to prevent and treat organ transplant rejection

**What we do:**

- Target therapeutic areas with high need for improvement
  - Conditions with no, or inadequate, treatments
  - Significant patient populations not well served by existing therapies
- Develop innovative treatment options
  - Scientifically unique and innovative
  - Strong scientific rationale supported by preliminary clinical evidence and published literature
  - Proven regulatory pathways and established clinical endpoints
  - Built on a foundation of proprietary intellectual property

# Management Team



**Seth Lederman, MD**
President & CEO

TARGENT Fusilev vela

**Gregory Sullivan, MD**
Chief Medical Officer

Columbia University Department of Psychiatry | New York State Psychiatric Institute

**Bradley Saenger, CPA**
Chief Financial Officer

Shire | VERTEX | Seward | pwc

**Jessica Morris**
Chief Operating Officer

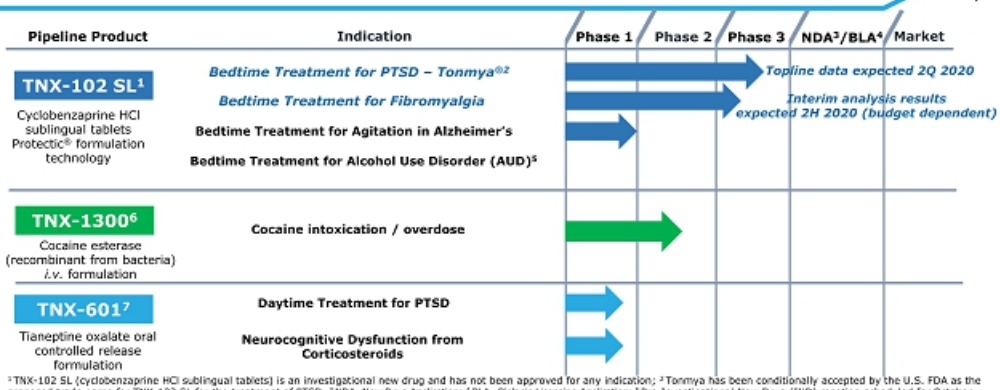
Deutsche Bank | svb Silicon Valley Bank | American Capital

# CNS Candidates in Clinical Development

## Psychiatry, Pain and Addiction

***TNX-102 SL and TNX-601 owned outright with no royalties due***






¹TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication; ²Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL for the treatment of PTSD. ³NDA- New Drug Application; ⁴BLA -Biologic Licensing Application; ⁵Pre-Investigational New Drug (IND) meeting scheduled for October with FDA. Upon receiving FDA clearance of an IND application, TNX-102 SL for AUD will be Phase 2 ready as it is expected to qualify for the 505(b)(2) pathway for approval; ⁶TNX-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; ⁷TNX-601 is in the pre-IND stage in the U.S., and a Phase 1 study for formulation development is currently being conducted outside of the U.S.

# Preclinical Pipeline[1]



| Pipeline Product | Indication(s) | Category |
|---|---|---|
| **TNX-1600**<br>Triple reuptake inhibitor[2] | Daytime Treatment for PTSD | Psychiatry |
| **TNX-1500**[3]<br>Anti-CD154 monoclonal antibody | Prevention and treatment of organ transplant rejection | Transplant |
| | Potential treatment for autoimmune conditions including systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis | Autoimmunity |
| **TNX-1700**<br>rTFF2[4] | Treatment for gastric and pancreatic cancers | Oncology |
| **TNX-801**[3]<br>Live horsepox virus (HPXV) vaccine from cell culture | Potential smallpox-preventing vaccine | Biodefense |
| **TNX-701**[3]<br>Radioprotection drug oral capsules | Protection from radiation injury | Biodefense |

[1] (Experimental new medicines and biologics, not approved for any indication
[2] (2S,4R,5R)-5-({[2-aminobenzo[d]thiazol-6-yl]methyl}amino)-2-(bis(4-fluorophenyl)methyl)tetrahydro-2H-pyran-4-ol) is an inhibitor of reuptake of three monoamine neurotransmitters (serotonin, norepinephrine and dopamine)
[3] Programs owned outright with no royalties due
[4] recombinant Trefoil Family Factor 2

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



| | |
|---|---|
| **Composition of matter (eutectic):** **Protection expected to 2034/2035** | •United States Patent and Trademark Office (USPTO) issued U.S. Patent No. 9636408 in May 2017, U.S. Patent No. 9956188 in May 2018, U.S. Patent No. 10117936 in Nov 2018, and U.S. Patent No. 10,357,465 in July 2019<br>•China National Intellectual Property Administration issued Chinese Patent No. ZL 201480024011.1 in April 2019<br>•Indonesian Patent Office issued Indonesian Patent No. IDP000055516 in January 2019<br>•Saudi Arabian Patent Office issued Saudi Patent No. 6088 in September 2018<br>•Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018<br>•New Zealand Intellectual Property Office (NZIPO) issued New Zealand Patent No. 631152 in August 2017<br>•35 patent applications pending (5 being allowed in U.S, Australia, Europe, Taiwan, South Africa) |
| **Composition of matter (sublingual):** **Protection expected to 2033** | • NZIPO issued New Zealand Patent No. 631144 in March 2017 and Patent No. 726488 in January 2019<br>• Taiwanese Intellectual Property Office issued Taiwanese Patent No. I590820 in July 2017 and Patent No. I642429 in December 2018<br>• Australian Patent Office issued Australian Patent No. 2013274003 in October 2018<br>• JPO issued Japanese Patent No. 6259452 in Dec 2017<br>• 21 patent applications pending |
| **Method of use (PTSD) for cyclobenzaprine:** **Protection expected to 2030** | • Hong Kong Patent Office issued Hong Kong Patent No. HK1176235 in September 2018<br>• USPTO issued U.S. Patent 9918948 in March 2018<br>• European Patent Office (EPO) issued European Patent No. 2501234B1 in Sept 2017 (validated in 37 countries). In response to an opposition filed in June 2018, EPO's Opposition Division determined in October 2019 that it will uphold this patent.<br>• 1 patent application pending |

# Prevalence of PTSD Among Civilians and Veterans



**4.7%**
Adult population[1]

**19-31%**
Vietnam veterans[2]

**>19%**
Iraq/Afghanistan[3]

**12 million** American adults annually[1]

**Women** more likely to develop than men[1]

[1] Goldstein et al., 2016 (adjusted for 2019); [2] Norris, PTSD Res Quar. 2013;
[3]Analysis of VA Health Care Utilization among Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn Veterans, from 1st Qtr FY 2002 through 2nd Qtr FY 2015, Washington, DC; Among 1.9M separated OEF/OIF/OND veterans, 1.2M have obtained VA healthcare; 685k evaluated by VA with possible mental disorder, and 379k diagnosed with PTSD.

# Unmet Need for Effective and Safe Therapies for Treatment of PTSD



**No FDA-approved products for PTSD since Pfizer's Zoloft® (sertraline) in 1999 and GSK's Paxil® (paroxetine) in 2001**

- Neither has shown efficacy in military-related PTSD
- Side effects relating to sexual dysfunction, sleep disruption and weight gain are commonly reported

**PTSD is signature wound of last 25 years of war**

- Affects servicemember health and performance, force readiness, and retention
- Believed to be the underlying cause of suicide in many cases
- Male PTSD patients often unresponsive or intolerant of current treatments

**Civilian PTSD is more prevalent than military**

- Results from physical and sexual assault trauma, vehicular accidents, natural disasters
- Significant cause of morbidity

# Potential Therapeutic Advantages of TNX-102 SL



**TNX-102 SL is believed to treat PTSD by improving sleep *quality***

- The brain naturally processes memories during sleep
- PTSD sufferers' emotionally charged memories disturb sleep and disrupt the natural processing of memories during sleep
- TNX-102 SL is believed to normalize memory processing and facilitate extinction consolidation (breaking the link between "triggers" and PTSD symptoms)

**Cyclobenzaprine, active ingredient of TNX-102 SL, is *NEITHER* a benzodiazepine nor a narcotic**

- Does **NOT** interact with the same receptors as traditional hypnotic sleep drugs associated with retrograde amnesia and is **NOT** an opiate

**TNX-102 SL is non-addictive**

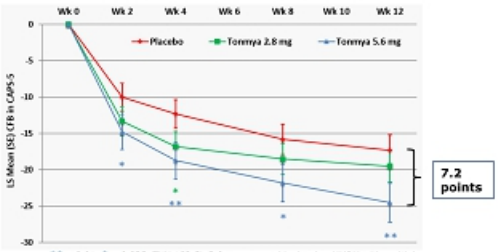
- Cyclobenzaprine is the active ingredient of an orally ingested immediate release tablet (Flexeril®), approved 40 years ago; Flexeril's current labeling indicates no abuse and dependence concern at higher doses than TNX-102 SL (15-30 mg/day v. 5.6 mg/day)
- TNX-102 SL NDA can be filed without drug abuse and dependency assessment studies

**Once-daily sublingual dose taken at bedtime enhances patient adherence and transmucosal absorption aligns bioavailability of drug with sleep cycle**

# TNX-102 SL Phase 2 Dose-Effect in Military-Related PTSD[1]

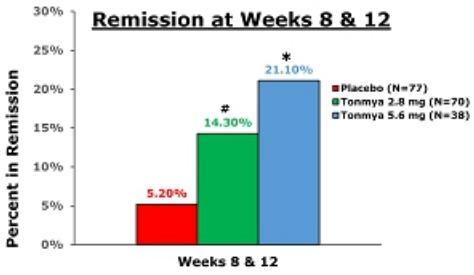


## PTSD Symptoms (CAPS-5[2] Score)




**p<0.01, *p<0.025, TNX-102 SL 5.6 mg group with placebo, MMRM with multiple imputation (MI); *p=0.018, TNX-102 SL 2.8 mg group with placebo, MMRM with MI

## Remission at Weeks 8 & 12




Remission = Loss of Diagnosis and CAPS-5 < 11
Asterisk and hashmark represent pairwise comparisons between TNX-102 SL and Placebo; #p=0.08, Odds Ratio 3.01 (0.89, 10.18)
*p=0.02, Odds Ratio 4.60 (1.27, 16.66); logistic regression

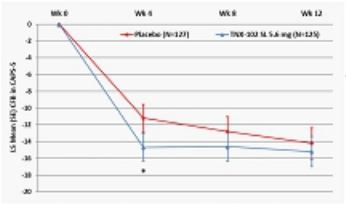
[1] Completed Phase 2 P201/AtEase study: Retrospective analysis of TNX-102 SL 5.6 mg on CAPS-5 ≥33 (high-moderate) subgroup. Primary analysis of P201/AtEase, based on TNX-102 SL 2.8 mg in participants with entry CAPS-5 ≥29 (moderate PTSD severity), was not statistically significant.
[2] CAPS-5 = Clinician administered PTSD Scale for DSM-5

# Primary Outcome (CAPS-5) in Phase 3 Study: mITT and ≤9 Years Time Since Trauma Subgroup



## Phase 3 P301/HONOR Study[1]

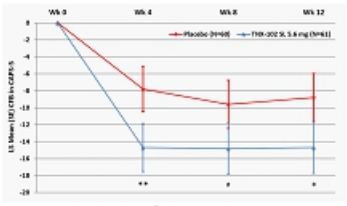
### Modified intent to treat (mITT) population



*p=0.019, TNX-102 SL 5.6 mg group v. placebo, using mixed model repeated measures (MMRM) with multiple imputation (MI)

~50% mITT Population

### *Time Since Trauma (TST) ≤9 yrs*



**p=0.004, *p=0.039, #p=0.069, TNX-102 SL 5.6 mg group v. placebo, using MMRM with MI

[1] Phase 3 P301/HONOR study: stopped in July 2018. Separation on primary endpoint did not cross pre-specified study continuation threshold at Week 12 in the interim analysis at ~50% randomization; no safety or tolerability issues discovered.

# Adverse Events (AEs) in P201/AtEase and P301/HONOR Studies



| Category of Adverse Reaction<br>Preferred Term | P201<br>Placebo (N=94) | P201<br>TNX 2.8 mg (N=93) | P201<br>TNX 5.6 mg (N=50) | P301<br>Placebo (N=134) | P301<br>TNX 5.6 mg (N=134) |
|---|---|---|---|---|---|
| Systemic Adverse Events*# | | | | | |
| Somnolence | 6.4% | 11.8% | 16.0% | 9.0% | 15.7% |
| 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% | | |
| Local Administration Site Reactions*# | | | | | |
| Hypoaesthesia oral | 2.1% | 38.7% | 36.0% | 1.5% | 37.3% |
| Paraesthesia oral | 3.2% | 16.1% | 4.0% | 0.7% | 9.7% |
| Glossodynia | 1.1% | 3.2% | 6.0% | | |
| Product Taste Abnormal | | | | 3.0% | 11.9% |

*only adverse events (AEs) are listed that are at a rate of ≥ 5% in any TNX-treated group
#no values in a row for either study means the AE in the active group(s) in that study was at a rate of <5%

**No serious or unexpected AEs in P201 or P301 related to TNX-102 SL**

- Systemic AEs comparable between studies and also consistent with those described in approved oral cyclobenzaprine product labeling
- Severity and incidence of oral hypoesthesia (oral numbness) are not dose related and similar in both studies

# TNX-102 SL for PTSD: Phase 3 P302/RECOVERY Study
## Expecting Topline Data in 2Q 2020



### General study characteristics:

- Randomized, double-blind, placebo-controlled study with baseline CAPS-5[1] ≥ 33 in approximately 30 U.S. sites
- Enrollment restricted to study participants with PTSD who experienced an index trauma ≤ 9 years from the date of screening
- Both civilian and military-related PTSD to be included


### Primary endpoint:

- CAPS-5[1] mean change from baseline at Week 4 (TNX-102 SL 5.6 mg vs. placebo)

### Key Secondary endpoints include:

- CAPS-5 mean change from baseline at Week 12 (TNX-102 SL 5.6 mg vs. placebo)
- Change from baseline Clinical Global Impression – Severity scale
- Change from baseline Sheehan Disability Scale total score

**Potential pivotal efficacy study to support NDA approval**

[1]CAPS-5 = Clinician-Administered PTSD Scale for DSM-5

# Opportunities for TNX-102 SL in Other Potential Indications



**Role of sleep disturbance more established in common psychiatric and neurological/pain disorders**

- Recognized as a core symptom of many of these disorders
- Traditional sleep medications, which increase sleep quantity, may not provide benefit (benzodiazepines in major depression) or are contraindicated (benzodiazepines in PTSD)

**Psychiatric Disorders**

- Stress Disorders (PTSD)
- Mood Disorders
- Anxiety Disorders
- Addiction (Alcohol Use Disorder)

**Psychiatric Symptoms of Neurological Disorders**

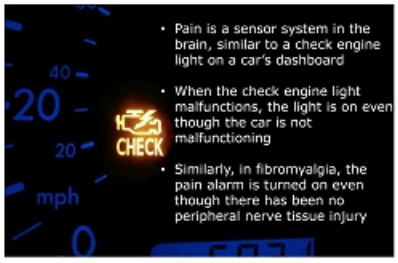
- Agitation in Alzheimer's
- Psychosis in Parkinson's, Alzheimer's and other dementias

**Chronic Pain States**

- Chronic wide-spread pain (fibromyalgia)
- Osteoarthritis

# TNX-102 SL: Potential Treatment for Fibromyalgia






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

- Fibromyalgia is considered a neurobiological disorder characterized by[1]: chronic widespread pain, non-restorative sleep, fatigue, diminished cognition
- Believed to result from inappropriate pain signaling in central nervous system in the absence of peripheral injury[1]
- An estimated 6-12 million adults in the U.S. have fibromyalgia[2]
- Causes significant impairment in all areas of life[3]
  - Lower levels of health-related quality of life – reduced daily functioning
  - Interference with work (loss of productivity, disability)
- Fewer than half of those treated for fibromyalgia receive complete relief from the three FDA-approved drugs[4]
- Inflicts substantial strain on the healthcare system
  - Average patient has 20 physician office visits per year[5]
  - Annual direct medical costs are twice those of non-fibromyalgia individuals[6]

[1] Phillips K & Clauw DJ, Best Pract Res Clin Rheumatol 2011;25:141.
[2] American Chronic Pain Association (www.theacpa.org, 2019)
[3] Schaefer et al., Pain Pract, 2015.
[4] The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[5] Robinson et al, Pain Medicine 2013;14:1400.
[6] White et al, J Occupational Environ Med 2008;50:13.

# Large Need for New Fibromyalgia Therapies that Provide Broad Symptom Improvement with Better Tolerability



- Currently-approved medications may have side effects that limit long-term use[1]
  - Many patients skip doses or discontinue altogether within months of treatment initiation
- Medication-related side effects may be similar to fibromyalgia symptoms
- High rates of discontinuation, switching and augmentation
  - Attempts to treat multiple symptoms and/or avoid intolerable side effects
  - Average of 2-3 medications used simultaneously[2]
  - Typical patient has tried six different medications[3]
- Substantial off-label use of narcotic painkillers and prescription sleep aids[3]
  - Among those diagnosed, more than one-third have used prescription opioids as a means of treatment[4]
- TNX-102 SL is a non-opioid, centrally-acting analgesic that could provide a new therapeutic option for fibromyalgia patients

[1] Nuesch et al, Ann Rheum Dis 2013;72:955-62.
[2] Robinson RL et al, Pain Medicine 2012;13:1366.
[3] Patient Trends: Fibromyalgia", Decision Resources, 2011.
[4] Berger A, Dukes E, Martin S, Edelsberg J, Oster G, Int J Clin Pract, 2007; 61(9):1498–1508.

# TNX-102 SL 2.8 mg for Fibromyalgia:
## Summary of Completed Phase 3 Study F301 and Results



**General study characteristics:**

- Randomized, 12-week, double-blind, placebo-controlled Phase 3 study of TNX-102 SL 2.8 mg (half the dose being developed for PTSD) taken daily at bedtime (n=519)
- Patients had to satisfy the 2010 ACR Preliminary Diagnostic Classification Criteria
- **Primary endpoint:** Weekly average pain improvement as a 30% responder analysis
- **Secondary endpoints:** PGIC, FIQ-R Symptom Domain, FIQ-R Function Domain, Daily Sleep Quality Diary, PROMIS Sleep Disturbance

**Efficacy results:**

- Completers: 425 (81.9%) of 519 patients in Intent-to-Treat population
- The primary analysis (responder analysis) was not statistically significant (P=0.095). However, secondary analysis of average pain improvement after 12 weeks of treatment showed nominal significance (P<0.001, mixed model repeated measures)
- Significant improvements observed in sleep quality, patient global impression of change and fibromyalgia-specific measures (secondary analyses).

# TNX-102 SL 2.8 mg for Fibromyalgia:
## F301 Study Results and Program Updates



**Safety results:**

- Good tolerability and low rates of systemic AEs.
- The most common AEs were generally mild and transient events related to the sublingual administration of the study drug:
  - hypoaesthesia (tongue or oral numbness)
  - glossodynia (burning sensation or other tongue discomfort)
  - oral paraesthesias (tingling sensations)
  - abnormal product taste (bitter or noticeable taste)
- The severity and incidence of oral AEs are similar to those reported in our PTSD studies using TNX-102 SL 5.6 mg.

**Conclusion:**

- The results and efficacy findings support further investigation of TNX-102 SL at double the dose, 5.6 mg (2 x 2.8 mg tablets), as a chronic treatment for FM.

**Program updates:**

- Clear guidance received from FDA* to advance the FM program. The long-term safety exposure data from the PTSD program may support the fibromyalgia NDA*.
- TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) daily at bedtime will be studied in new Phase 3 study to support product registration

*March 2019 FDA meeting minutes

# TNX-102 SL 5.6 mg for Fibromyalgia:
## Planned New Phase 3 F304 Study



### General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia in approximately 40 U.S. sites (N=470)
- 2016 Revisions to the 2010/2011 Fibromyalgia Diagnostic Criteria for inclusion
- Adaptive Design: one planned unblinded interim analysis based on 50% of randomized participants[1]


### Primary endpoint (week 14):

- Daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from Baseline in the weekly average by numerical rating scale (NRS) analyzed by mixed model repeated measures analysis with multiple imputation

### Key Secondary endpoints (week 14) include:

- Patient Global Impression of Change (PGIC): Proportion of patients with a rating of "very much improved" or "much improved"
- Fibromyalgia Impact Questionnaire – Revised (FIQR): Symptoms Domain
- FIQR Function Domain
- PROMIS* Sleep Disturbance instrument T-score
- PROMIS Fatigue instrument T-score
- Daily diary sleep quality NRS (weekly average) score

**Interim analysis results expected 2H 2020 (budget dependent)**

**Potential pivotal efficacy study to support NDA approval**

[1]Pending agreement with FDA
[2]Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose *PROMIS = Patient Reported Outcome Measurement Information System

# TNX-102 SL: Potential Treatment for Agitation in Alzheimer's Disease (AAD)



**Agitation is one of the most distressing and debilitating of the behavioral complications of Alzheimer's disease**

- Includes emotional lability, restlessness, irritability and aggression[1]

**Link between disturbed sleep and agitation in Alzheimer's[1-3]**

- Agitation is commonly diurnal ("sundowning")

**Prevalence**

- Agitation is likely to affect more than half of the 5.3 million Americans who currently suffer from moderate to severe Alzheimer's disease; expected to nearly triple by 2050[4]

**Significant unmet need** with no FDA approved drugs for the treatment of AAD

**Proposed Phase 2 IND study can potentially serve as a pivotal efficacy study to support NDA approval[5]**

[1]Rose, K.et al. (2015). *American Journal of Alzheimer's Disease & Other Dementias*, *30*:78
[2]Shin, Y. H., et al. (2017). *Journal of the American Medical Directors Association*, *18*, 396.
[3]Canevelli, M., et al. (2016). *Frontiers in medicine*, *3*.
[4]The Alzheimer's Association, 2017 Alzheimer's Disease Facts and Figures: https://www.alz.org/facts/
[5]FDA comments on initial protocol received October 2018

# TNX-102 SL: Potential Treatment for Alcohol Use Disorder (AUD)



**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

**Sleep disturbance is extremely common in alcohol recovery**[1]

- Significantly impacts daytime cognition, mood, and ability to participate in alcohol treatment, and is associated with increased risk of relapse

**Prevalence**

- An estimated 16 million people (15.1 million adults) in the U.S. have AUD[2]

**Three FDA-approved medications**

- Remains an unmet need due to compliance and safety issues

**Pre-IND meeting with the FDA in October 2019**

- Discussed 505(b)(2) development plan for TNX-102 SL as a treatment for AUD
- Expect to file initial IND in 1Q2020 for Phase 2 Proof of Concept Study

[1]Arnedt et al, J Addict Dis. 2007 ; 26(4): 41–54
[2]National Institute on Alcohol Abuse and Alcoholism

# TNX-1300* for the Treatment of Cocaine Intoxication



**Recombinant protein that degrades cocaine in the bloodstream[1]**

- Double-mutant cocaine esterase (CocE)
- CocE was identified in bacteria (Rhodococcus) that use cocaine as its sole source of carbon and nitrogen and that grow in soil surrounding coca plants[2]
- CocE catalyzes the breakdown of cocaine into metabolites ecgonine methyl ester and benzoic acid

**Phase 2 study completed by Rickett Benckiser (TNX-1300 was formerly RBP-8000)[3]**

- Volunteer cocaine abusers received cocaine 50 mg *i.v.* infusion over 10 minutes
- TNX-1300 given one minute after completion of cocaine infusion
  - Rapidly reversed the physiologic effects of cocaine; cocaine plasma exposures dropped by 90% within two minutes
  - Well tolerated with the most frequently reported adverse events being gastrointestinal disorders (including dry mouth, nausea); nervous systems disorders (including headache, dizziness) and skin and subcutaneous tissue disorders (including hyperhidrosis, dermatitis)

**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.*

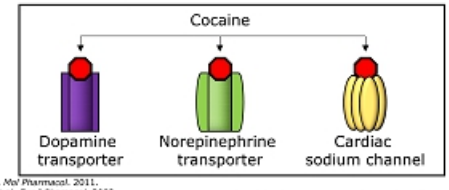
[1] Gao D et al, Mol Pharmacol. 2009. 75(2):318-23.
[2] Bresler MM et al, Appl Environ Microbiol. 2000. 66(3):904-8.
[3] Nasser AF et al, J Addict Dis, 2014;33(4):289-302.

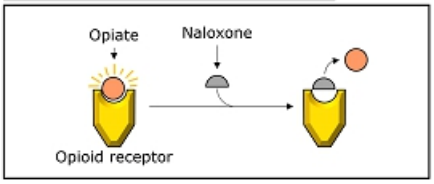
# Pharmacotherapies for Cocaine Intoxication Have Not Been Effective



**Treatments for opiates not effective for cocaine:**

| | Cocaine | Opiates |
|---|---|---|
| MOA of Toxicity | Complex; mediated by multiple targets with distinct biological functions[1] | Simple; mediated by opioid receptors[2] |
| Pharmacology | Antagonist[1] | Agonists[2] |
| Pharmacotherapy | **No FDA-approved medication exists[1]** | Naloxone[2] |

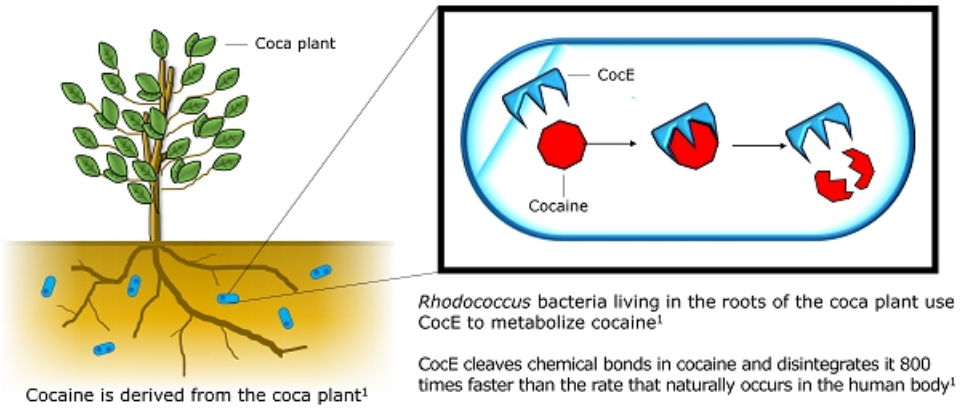



1. Brim et al. *Mol Pharmacol*. 2011.
2. Melichar et al. *Eur J Pharmacol*. 2003.
3. Narasimhan et al. *Future Medicinal Chemistry*. 2012.

# TNX-1300 (Cocaine Esterase or CocE) Is a Fast-acting Cocaine Antidote






Cocaine is derived from the coca plant[1]

*Rhodococcus* bacteria living in the roots of the coca plant use CocE to metabolize cocaine[1]

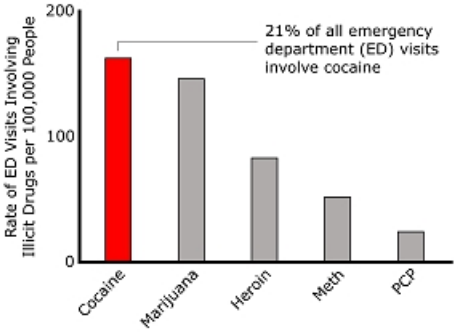
CocE cleaves chemical bonds in cocaine and disintegrates it 800 times faster than the rate that naturally occurs in the human body[1]

1. Narasimhan D et al. *Future Med Chem*. 2012.

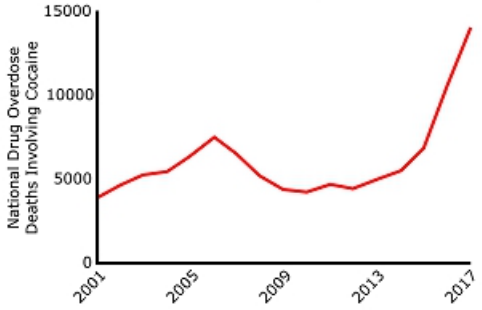
# Cocaine Intoxication Is a Growing Problem in the U.S.



**Cocaine is involved in more emergency department (ED) visits than any other illicit substance[1]**




**Drug overdose deaths involving cocaine have increased dramatically in recent years[2]**




1. CBHSQ. DAWN 2011. Rockville, MD: SAMHSA; 2013
2. NIDA. Overdose death rates. https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates.

Note: Figures are for illustrative purposes

# TNX-601* (Tianeptine Oxalate CR): A Potential Daytime Treatment for PTSD



**Pre-IND Candidate**

**Targeted as a 1st line monotherapy for PTSD: oral formulation for daytime dosing**

- Tianeptine sodium (amorphous), first marketed for depression in France in 1989, is approved as an antidepressant in the EU, Russia, Asia and Latin America; established post-marketing experience
- Identified new oxalate salt with improved pharmaceutical properties ideal for reformulation
- Preliminary human pharmacokinetic and safety data (non-IND study) from selected controlled release (CR) formulation expected in fourth quarter of 2019

**Issued patents directed to tianeptine and tianeptine oxalate**

- **Method of Use:** Issued US patent directed to methods of treating cognitive impairment associated with corticosteroid treatment [add numbers]
- **Composition of Matter:** Issued US patent directed to oxalate salt [add numbers]

**Targeting a Condition with Significant Unmet Need**

**PTSD is a heterogeneous condition, so not all patients are expected to respond to a single medicine**

- Distinct mechanism of action from TNX-102 SL – modulates the glutamatergic system
- Leverages Tonix expertise in PTSD (clinical and regulatory, market analysis, etc.)

**TNX-601 (tianeptine oxalate CR tablets) is an investigational new drug and has not been approved for any indication.*

# TNX-601* for PTSD



**Pharmacokinetic and safety study (ex-U.S.) of controlled release (CR) formulations underway**

- Targeting CR formulation for once-daily dosing

**Pre-IND meeting with FDA expected first half 2020**

- Discussion of clinical development plan for TNX-601 for PTSD
- IND expected to be based on ex-U.S. findings from pharmacokinetic and safety studies

**Clinical studies of tianeptine sodium immediate release (IR) in PTSD**

- Published studies show tianeptine is active in the treatment of PTSD[1-4]

[1] Frančišković T, et al. Psychiatr Danub. 2011 Sep;23(3):257-63. PMID: 21963693
[2] Rumyantseva GM and, Stepanov AL. Neurosci Behav Physiol. 2008 Jan;38(1):55-61. PMID: 18097761
[3] Aleksandrovskiĭ IA, et al. Zh Nevrol Psikhiatr Im S S Korsakova. 2005;105(11):24-9. PMID: 16329631 [Russian]
[4] Onder E, et al. Eur Psychiatry. 2006 (3):174-9. PMID: 15964747

**TNX-601 (tianeptine oxalate CR tablets) is an investigational new drug and has not been approved for any indication.*

# Milestones – Recently Completed and Upcoming



| | |
|---|---|
| ☑ March 2019 | P302/RECOVERY study initiated |
| ☑ April 2019 | Received FDA formal minutes with clear guidance and support for new Phase 3 FM study using TNX-102 SL 5.6 mg |
| ☑ May 2019 | In-licensed TNX-1300, product candidate in Phase 2 development for cocaine intoxication |
| ☑ August 2019 | In-licensed TNX-1600, product candidate in preclinical development for PTSD |
| ☑ August 2019 | Entered into research collaboration to study internally-developed TNX-1500 |
| ☑ September 2019 | In-licensed TNX-1700, product candidate in preclinical development for gastric and pancreatic cancers |
| ☑ October 2019 | Completed long-term exposure studies in participants with PTSD to evaluate tolerability of TNX-102 SL 5.6 mg |
| ☑ October 2019 | Meeting with FDA to discuss new program for TNX-102 SL to treat AUD |
| ☑ 4th Quarter 2019 | Preliminary human pharmacokinetic and safety data (non-IND study) from selected TNX-601 (tianeptine oxalate CR tablets) formulation expected |
| ☐ 2nd Quarter 2020 | Topline data from P302/RECOVERY study expected |
| ☐ 2nd Half 2020 | Interim analysis results for F304 Phase 3 fibromyalgia study expected (budget dependent) |

# Capitalization Table*



| As of 10/31/2019 | # of Shares | WAEP | $ Value | % of Fully Diluted |
|---|---|---|---|---|
| Common Shares Outstanding (D&O) | 6,853 | | | 0.3% |
| Common Shares Outstanding (Other) | 1,564,888 | | | 71.9% |
| Warrants | 496,486 | $42.14 | $20.9M | 22.8% |
| Stock Options | 109,036 | $199.57 | $21.8M | 5.0% |
| Fully Diluted Shares Outstanding | **2,177,263** | | | **100%** |

*All share and dollar amounts reflect a 1-for-10 reverse stock split which will be effective for trading purposes as of the commencement of trading on November 1, 2019. Any fractional share of common stock that would otherwise result from the reverse stock split will be rounded to a whole share.

# Pipeline Summary – by Select Therapeutic Areas



- **Psychiatry/PTSD:**
  - **TNX-102 SL – (sublingual cyclobenzaprine) for PTSD**
    - Phase 3
  - **TNX-601 – (tianeptine) for PTSD**
    - Phase 1 formulation development
  - **TNX-1600 – (triple reuptake inhibitor) for PTSD**
    - Pre-clinical
- **Pain:**
  - **TNX-102 SL for fibromyalgia**
    - Phase 3
- **Addiction Medicine:**
  - **TNX-1300 – (cocaine esterase) for cocaine intoxication**
    - Mid-Phase 2
  - **TNX-102 SL – (sublingual cyclobenzaprine) for alcohol use disorder (AUD)**
    - Pre-clinical; FDA meeting in October to approve IND and Phase 2
- **Biodefense:**
  - **TNX-801 – (live horsepox vaccine) – for preventing smallpox**
    - Pre-clinical
  - **TNX-701 – (oral radioprotective agent) – for radioprotection**
    - Pre-clinical

# Pipeline Summary – by Phase of Development



**Two Phase 3 Programs in indications affecting millions of Americans**

- TNX-102 SL for PTSD: affects an estimated 12 million adults in U.S.
- TNX-102 SL for Fibromyalgia: affects an estimated 6-12 million adults in U.S.

**Two Phase 2 Programs in indications for which there is no FDA-approved drug available**

- TNX-1300 for Cocaine Intoxication
- TNX-102 SL for Agitation in Alzheimer's Disease

**Robust pipeline of preclinical and Phase 1 products to improve biodefense, leverage PTSD and internal expertise**

TONIX PHARMACEUTICALS

NASDAQ: TNXP

*Thank you*!