

**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): April 17, 2017

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**TONIX PHARMACEUTICALS HOLDING CORP.**

(Exact name of registrant as specified in its charter)

Nevada  
(State or Other Jurisdiction  
of Incorporation)

001-36019  
(Commission  
File Number)

26-1434750  
(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

**Copy of correspondence to:**

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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))
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**Item 2.02 Results of Operations and Financial Condition.**

On April 17, 2017, Tonix Pharmaceuticals Holding Corp. (the "Company") announced its operating results for the fiscal year ended December 31, 2016. A copy of the press release that discusses this matter is filed as Exhibit 99.01 to, and incorporated by reference in, this report. The information in this Current Report is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934 or otherwise subject to the liabilities of that Section. The information in this Current Report shall not be incorporated by reference into any registration statement or other document pursuant to the Securities Act of 1933, except as shall be expressly set forth by specific reference in any such filing.

**Item 7.01 Regulation FD Disclosure.**

The Company intends to utilize an updated investor presentation 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 non-public information. A copy of the presentation is filed as Exhibit 99.02.

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.02, is furnished pursuant to, and shall not be deemed to be "filed" for the purposes of, Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section. The information contained in Item 7.01 of this Current Report shall not be incorporated by reference into any registration statement or any other document filed pursuant to the Securities Act of 1933, as amended, except as otherwise expressly stated in such filing. By filing this Current Report on Form 8-K and furnishing the information contained in this Item 7.01, including Exhibit 99.02, the Company makes no admission as to the materiality of any such information that it is furnishing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

99.01 [Press release, dated April 17, 2017, issued by Tonix Pharmaceuticals Holding Corp.\\*](#)

99.02 [Corporate Presentation by the Company for April 2017\\*](#)

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\* Furnished herewith.

**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: April 17, 2017

By: /s/ BRADLEY SAENGER

Bradley Saenger  
Chief Financial Officer



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## Tonix Pharmaceuticals Reports Fourth Quarter and Full Year 2016 Financial Results and Provides Programs Update

*First Participant Enrolled in Phase 3 HONOR Study of TNX-102 SL in Military-Related PTSD in 1Q2017*

*TNX-102 SL Designated a Breakthrough Therapy for PTSD by the U.S. FDA in 4Q2016*

NEW YORK, April 17, 2017 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (NASDAQ: TNXP) (Tonix), a company that is developing innovative pharmaceutical products to address public health challenges, announced financial results for the fourth quarter and full year ended December 31, 2016.

Seth Lederman, M.D., president and chief executive officer of Tonix, stated, “Tonix achieved significant momentum in the last quarter of 2016, which has carried over into 2017. Tonix is focused on pioneering a differentiated approach for the treatment of posttraumatic stress disorder (PTSD), through improving sleep quality. TNX-102 SL\*, having shown potential advantages over existing treatments for this disorder, received Breakthrough Therapy designation from the United States Food and Drug Administration (FDA) in December 2016.”

“In the first quarter of 2017, the FDA accepted the protocol design for our Phase 3 HONOR study to support the registration of TNX-102 SL for PTSD.” Dr. Lederman continued, “As we planned, the study was initiated in March and is on track to have an unblinded interim analysis (IA) by an independent data monitoring committee in the first half of 2018. If the IA results require continued enrollment, topline results from the full 550-participant trial are expected to be available in the second half of 2018. With successful capital raising activities completed in 2017, Tonix is fully funded through the completion of, and announcement of the topline results, from the HONOR study.”

At December 31, 2016, Tonix had cash, cash equivalents, and marketable securities of \$26.1 million. Since January 1, 2017, Tonix has raised approximately \$9.1 million in net proceeds through an at-the-market offering and approximately \$8.3 million of net proceeds from the sale of common stock in an underwritten public offering. Approximately 7.5 million shares were outstanding as of April 13, 2017.

### Recent Events:

- Enrolled the first participant in the 12-week, double-blinded, placebo-controlled Phase 3 HONOR study of TNX-102 SL 5.6 mg, in military-related PTSD.
  - Held the Initial Cross-Disciplinary Breakthrough meeting with the FDA. Minutes from the meeting indicated that registration of TNX-102 SL could be solely supported by the Phase 3 HONOR study if topline data are statistically persuasive.
  - Received Notice of Allowance for U.S. Patent Application 14/214,333, titled, “Eutectic Formulations of Cyclobenzaprine Hydrochloride and Amitriptyline Hydrochloride,” covering the proprietary sublingual formulation of TNX-102 SL. Patent expected to be issued in 2Q2017 with protection through 2034.
  - Synthesized a potential smallpox-preventing vaccine candidate, TNX-801, a live form of horsepox virus, which has demonstrated protective vaccine activity in mice. TNX-801 is the first-ever synthesized chimeric horsepox virus.
  - Developed a novel formulation of tianeptine oxalate, TNX-601, as a potential daytime treatment for PTSD.
  - Regained compliance with NASDAQ listing requirements by completing a 1-for-10 reverse stock split.
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## 2016 Highlights:

- Successfully transitioned Tonix's core development program of TNX-102 SL from fibromyalgia to PTSD, leveraging promising Phase 2 AtEase results, regulatory approval clarity, and the urgent public health issue in military-related PTSD.
- Cash used in operating activities for the fourth quarter of 2016 totaled \$5.4 million, representing a 35% decrease as compared to the third quarter of 2016, and a 54% decrease as compared to the fourth quarter of 2015.

## Programs Update

### *TNX-102 SL 5.6 mg, for PTSD*

- Completed a highly informative End-of-Phase 2 Chemistry, Manufacturing and Controls (CMC) meeting with the FDA and received FDA agreement on the proposed CMC data package to support the TNX-102 SL New Drug Application (NDA) submission.
- Completed a successful Pre-Phase 3/End-of-Phase 2 meeting with the FDA to thoroughly vet the Phase 3 clinical program to support the registration of TNX-102 SL for PTSD. Received FDA agreement on the proposed NDA clinical/nonclinical data package, and encouragement to submit a Breakthrough Therapy designation request.
- Awarded Breakthrough Therapy designation by the FDA for TNX-102 SL for the treatment of PTSD, providing eligibility for priority review of an NDA and increased guidance and organizational commitment from FDA senior managers.
- Presented encouraging topline data from the Phase 2 AtEase study.
- Presented clinical results from a retrospective analysis of the Phase 2 AtEase study demonstrating potential efficacy of TNX-102 SL 5.6 mg, in the reduction of reckless, self-destructive behavior and suicidal behaviors, with especially strong evidence of clinical improvement in combat-related PTSD patients.
- Hosted a PTSD Awareness Day with key opinion leaders in PTSD research, highlighting the challenges in treating this growing mental health concern, particularly among veterans.

### *TNX-801 (Live Virus Vaccine) for Smallpox Prevention*

- Successfully synthesized first-ever chimeric horsepox virus (HPXV), TNX-801, a live form of HPXV that has demonstrated protective vaccine activity in mice and is being developed as a smallpox preventing vaccine.
- If licensed by the FDA, TNX-801 is eligible for a highly-attractive priority review voucher. This voucher is fully transferrable and may be sold to other companies for priority review of any NDA or Biologics License Application (BLA).

### *TNX-601 (tianeptine oxalate) for PTSD*

- Developed a novel formulation of tianeptine that may provide improved stability, consistency, and manufacturability as compared to known forms of tianeptine. Currently there is no tianeptine-containing product approved in the U.S., although tianeptine sodium (amorphous) has been available in Europe, Asia, and Latin America for the treatment of depression since 1987. Clinical studies in Europe have shown activity of tianeptine sodium in treating PTSD.

## Fourth Quarter and Full Year Financial Results

Tonix reported a net loss of \$7.5 million, or \$2.08 per share, for the fourth quarter of 2016, compared to a net loss of \$13.4 million, or \$7.96 per share, for the fourth quarter of 2015. The net loss for the three months ended December 31, 2016, excluding non-cash expenditures of \$1.1 million, was \$6.4 million, as compared to a net loss of \$12.3 million, excluding non-cash expenditures of \$1.1 million, for the three months ended December 31, 2015. The reduced net loss was primarily due to decreased research and development expenses for clinical studies and related research, as well as lower general and administrative expenses needed to support these and other corporate development activities.

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Tonix reported a net loss of \$38.8 million, or \$15.41 per share, for the year ended December 31, 2016, compared to a net loss of \$48.1 million, or \$28.62 per share, for the year ended December 31, 2015. The net loss for the year ended December 31, 2016, excluding non-cash expenditures of \$3.6 million, was \$35.2 million, as compared to a net loss of \$43.5 million, excluding non-cash expenditures of \$4.6 million, for the year ended December 31, 2015. The reduced net loss was primarily due to decreased research and development expenses for clinical studies and related research, as well as lower general and administrative expenses needed to support these and other corporate development activities.

Cash used in operations was \$37.3 million for the year ended December 31, 2016, as compared to \$42.5 million for the year ended December 31, 2015. At December 31, 2016, Tonix's cash, cash equivalents and marketable securities totaled \$26.1 million, compared to \$43.0 million at December 31, 2015. Management believes that existing cash and marketable securities are sufficient to fund Tonix's operating expenses and planned clinical trial through at least the next 12 months.

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

#### **About Posttraumatic Stress Disorder**

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 8.6 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. It is estimated that more than 19 percent of the 1.9 million U.S. veterans who were deployed to the recent conflicts in Iraq and Afghanistan suffer from PTSD.

#### **About Tonix Pharmaceuticals Holding Corp.**

Tonix is developing innovative pharmaceutical products to address public health challenges. TNX-102 SL is in Phase 3 development and has been granted Breakthrough Therapy designation by the FDA for the treatment of PTSD. PTSD is a serious condition 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. The Protectic™ protective eutectic and Angstro-Technology™ formulation are essential elements of the proprietary TNX-102 SL composition for which a Notice of Allowance has been issued by the U.S. Patent and Trademark Office. Other development efforts include TNX-801, a potential smallpox-preventing vaccine based on a live synthetic version of horsepox virus and TNX-601 (tianeptine oxalate), a clinical candidate at Pre-IND (Investigational New Drug) application stage, designed for daytime use for the treatment of PTSD.

This press release and further information about Tonix can be found at [www.tonixpharma.com](http://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, 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 FDA clearances or approvals and noncompliance with FDA regulations. 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, 2016, as filed with the Securities and Exchange Commission (the "SEC") on April 13, 2017, and future periodic reports filed with the SEC on or after the date hereof. 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 hereof.*

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**TONIX PHARMACEUTICALS HOLDING CORP.**  
**CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS**  
(in thousands, except per share amounts) (1)

|   | Three Months ended December 31, |          | Twelve Months ended December 31, |          |
|---|---------------------------------|----------|----------------------------------|----------|
|   | 2016                            | 2015     | 2016                             | 2015     |
|   | <b>(unaudited)</b>              |          |                                  |          |
| <b>Costs and expenses</b>                                     |                                 |          |                                  |          |
| Research and development                                      | \$ 4,879                        | 9,490    | \$ 28,533                        | 35,504   |
| General and administrative                                    | 2,631                           | 3,912    | 10,436                           | 12,658   |
| Total costs and expenses                                      | 7,510                           | 13,402   | 38,969                           | 48,162   |
| Operating loss  | (7,510)                         | (13,402) | (38,969)                         | (48,162) |
| <b>Interest income, net</b>                                   | 28                              | 43       | 127                              | 108      |
| Net loss  | \$ (7,482)                      | (13,359) | \$ (38,842)                      | (48,054) |
| Net loss per common share, basic and diluted                  | \$ (2.08)                       | (7.96)   | \$ (15.41)                       | (28.62)  |
| Weighted average common shares outstanding, basic and diluted | 3,596                           | 1,883    | 2,521                            | 1,679    |

(1) The condensed consolidated statements of operations for the years ended December 31, 2016 and 2015 have been derived from the audited financial statements, but do not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements.

**TONIX PHARMACEUTICALS HOLDING CORP.**  
**CONDENSED CONSOLIDATED BALANCE SHEETS**  
(in thousands) (1)

|  | December 31, 2016 |           | December 31, 2015 |  |
|--|-------------------|-----------|-------------------|--|
| <b>Assets</b>                                    |                   |           |                   |  |
| Cash, cash equivalents and marketable securities | \$ 26,121         | \$ 43,016 |                   |  |
| Prepaid expenses and other current assets        | 1,019             | 3,343     |                   |  |
| Total current assets                             | 27,140            | 46,359    |                   |  |
| Non-current assets                               | 370               | 659       |                   |  |
| Total assets                                     | \$ 27,510         | \$ 47,018 |                   |  |
| <b>Liabilities and stockholders' equity</b>      |                   |           |                   |  |
| Total liabilities                                | \$ 2,149          | \$ 6,756  |                   |  |
| Stockholders' equity                             | 25,361            | 40,262    |                   |  |
| Total liabilities and stockholders' equity       | \$ 27,510         | \$ 47,018 |                   |  |

(1) The condensed consolidated balance sheets for the years ended December 31, 2016 and 2015 have been derived from the audited financial statements, but do not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements.

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**Investor Presentation**

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April 2017

**Version P0060 4-17-17**

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## Cautionary Note on Forward-Looking Statements

2

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, 2016, as filed with the Securities and Exchange Commission (the “SEC”) on April 13, 2017, and future periodic reports filed with the SEC on or after the date hereof. All of Tonix’s forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.



# Tonix (TNXP): Developing Innovative Pharmaceutical Products to Address Public Health Challenges

3

## Targeting central nervous system conditions

- In Phase 3 development, TNX-102 SL\* for posttraumatic stress disorder (PTSD) with **Breakthrough Therapy designation** from the U.S. Food and Drug Administration (FDA)
  - Encouraging evidence of safety and efficacy was demonstrated in Phase 2 AtEase trial of **military-related PTSD** formed the basis of the Breakthrough Therapy designation
  - Regulatory clarity for PTSD based on FDA acceptance of PTSD Phase 3 clinical program at End-of-Phase 2 meeting
  - Expedited development and accelerated review are expected
- Second clinical candidate for PTSD with a different mechanism of action in pre-Investigational New Drug (IND) stage development

## Other development efforts include a smallpox preventing vaccine program, which leverages our government affairs efforts and capabilities

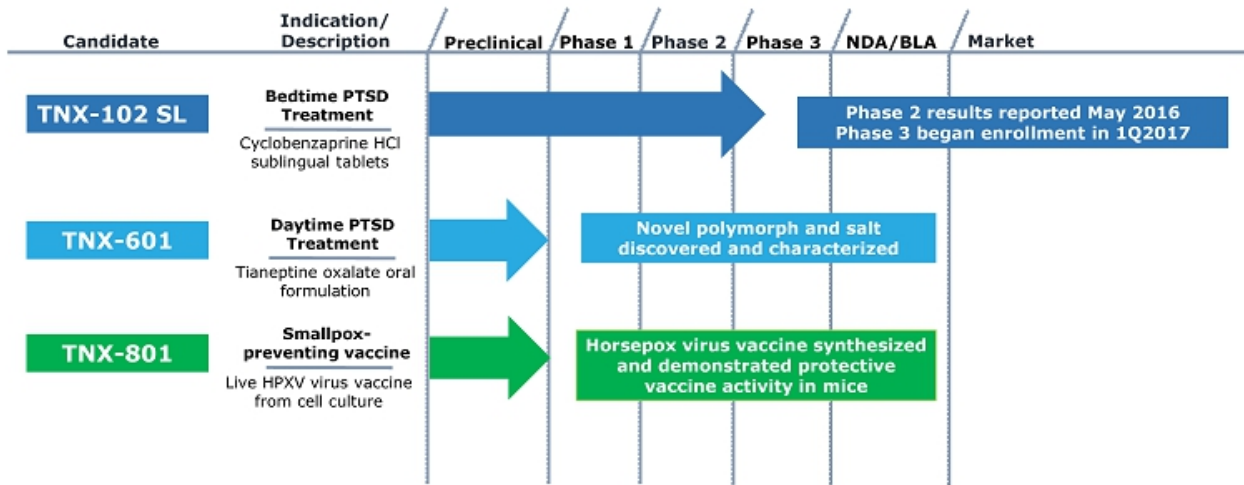
- Development of medical countermeasure drugs and biologics is incentivized with Priority Review Voucher by the recently enacted "21<sup>st</sup> Century Cures Act"

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

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# Product Pipeline







## Phase 3 Program

### TNX-102 SL (cyclobenzaprine HCl sublingual tablets)

- A unique, innovative product designed for bedtime administration
- Targeting a chronic and serious psychiatric disorder: **PTSD**
  - ✓ Therapeutic dose identified in Phase 2 study
  - ✓ Phase 3 clinical and product registration plan accepted by the FDA<sup>1</sup>
  - ✓ Designated Breakthrough Therapy for expedited development and review
  - ✓ Initial Breakthrough Therapy Multidisciplinary meeting held with FDA in March 2017
  - ✓ Phase 3 study in military-related PTSD began enrollment in March 2017

## Targeting a Current and Emerging Public Health Challenge

### PTSD

- High prevalence worldwide and receiving greater attention
- Not well served - high off-label usage<sup>2</sup> with unproven or contraindicated treatments<sup>3</sup>
- Potential opportunity to displace current standard-of-care and expand market

1. August 2016 FDA End-of-Phase 2 Meeting Minutes

2. Bernardy et al., J Clin Psychiatry, 2012; 73: 297

3. VA/DoD Clinical Practice Guideline for the Management of Post-Traumatic Stress, Version 2, 2010



## PTSD Characteristics

6

- **Unmet medical need**
  - PTSD is a serious condition and the prevalence is increasing, especially combat PTSD
  - Military-related PTSD is not satisfactorily treated by existing FDA-approved therapies
  - Two selective serotonin reuptake inhibitors (SSRIs) are approved for PTSD, but have not shown efficacy in military-related PTSD
- **Endpoint**
  - TNX-102 SL 5.6 mg had significant effects on the FDA-recognized primary endpoint, the Clinician-Administered PTSD Scale for DSM-5, "CAPS-5"
- **Potential development and partners**
  - Several companies have U.S. psychiatry-focused specialty sales forces
  - Department of Defense (DoD) is interested in military-related PTSD and has the capacity to support basic science and clinical development
- **Important target population**
  - U.S. veterans are in great need of a medicine that works for this serious condition



# Breakthrough Therapy Designation

7

- **FDA granted TNX-102 SL Breakthrough Therapy designation – reported December 19, 2016**
  - PTSD is a serious condition
  - TNX-102 SL has potential advantages over existing therapies in military-related PTSD
- **Benefits of Breakthrough Therapy designation**
  - Eligibility for priority review of the New Drug Application (NDA) within 6 months instead of 10 months
  - Option to submit completed portions of the NDA for rolling review
  - An organizational commitment involving FDA's senior managers to accelerate the development and approval process, an opportunity to compress development time



# What is PTSD?

8

## A chronic response to traumatic event(s)

- A majority of people will experience a traumatic event at some point in their lifetime<sup>1</sup>
  - 20% of women and 8% of men in the U.S. who experience significant trauma develop PTSD<sup>1</sup>
- Lifetime prevalence: 6.8%<sup>2</sup> (~ 17 million adults in the U.S.)
  - Persistent - >1/3 fail to recover, even after several years following the trauma<sup>2</sup>
- Twelve month prevalence: U.S. 3.5%<sup>3</sup> (~ 8.6 million adults)  
EU 2.3%<sup>4</sup> (~10 million adults)

## Most common forms of trauma<sup>1</sup>

- Witnessing someone being badly injured or killed
- Natural disaster
- Life-threatening accident
- Sexual or physical assault

1. Kessler et al., Arch Gen Psychiatry, 1995;52: 1048

2. Kessler et al., Arch Gen Psychiatry, 2005;62: 593

3. Kessler et al., Arch Gen Psychiatry, 2005;62: 617; Prevalence rate of 3.5% applied to U.S. Census estimate of 247 million U.S. adult (≥18) population in 2015 ([www.census.gov/quickfacts/table/PST045215/00](http://www.census.gov/quickfacts/table/PST045215/00))

4. The European Union Market Potential for a New PTSD Drug. Prepared for Tonix Pharmaceuticals by Proceta Consultants Ltd September 2016  
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# What Are the Symptoms of PTSD?

## Symptoms of PTSD fall into four clusters:

1. Intrusion (aversive memories, nightmares, flashbacks)
2. Avoidance (avoiding persons, places or situations)
3. Mood/cognitions (memory block, emotional numbing, detachment from others)
4. Hyperarousal (anxiety, agitation & sleep disturbance)

## Symptoms assessed for diagnosis, severity and treatment effect

- **Clinician Administered PTSD Scale (CAPS-5)**
  - Recognized as the standard for rating PTSD severity in clinical trials
  - Takes into account all four symptom clusters



## What Are the Consequences of PTSD?

10

### Consequences:

- Impaired daily function and substantial interference with work and social interactions
- Reckless or destructive behavior
- Increased health care utilization and greater medical morbidity

### PTSD as a risk factor for:

- Depression
- Alcohol or substance abuse
- Absenteeism/unemployment
- Homelessness
- Violent acts
- Suicidal thoughts and suicide

### Unmet needs:

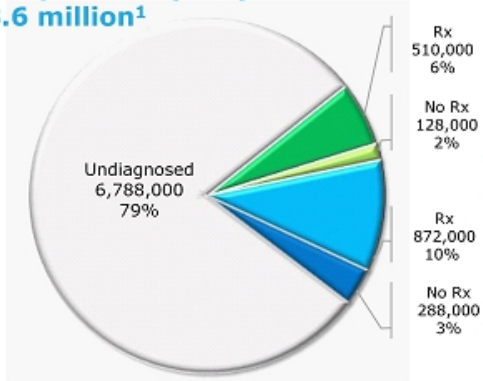
- Effective therapy for populations not well served by current treatment (males, military trauma)
- Alternative therapy for the majority of patients unresponsive or intolerant to current treatments
- Drug therapy compatible and complementary with behavioral therapy

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# PTSD Prevalence and Market Characteristics

## Prevalent Population (U.S.) ~8.6 million<sup>1</sup>



## Diagnosed population

Large population (~1.8 million)  
Majority receive drug treatment  
Civilians: ~75%<sup>2</sup>  
Veterans: ~80%<sup>4</sup>

Veterans  
Treated  
in Veterans  
Administration  
(VA)<sup>3,4</sup>

Civilian  
Population<sup>2</sup>

1. Kessler, et al., 2005; Prevalence rate of 3.5% applied to U.S. Census estimate of 247 million U.S. adult (≥18) population in 2015 ([www.census.gov/quickfacts/table/PST045215/00](http://www.census.gov/quickfacts/table/PST045215/00))

2. IMS Consulting, *Market Sizing & Treatment Dynamics: "Post-Traumatic Stress Disorder (PTSD) Patients"*, 2016

3. Bove and Rosenheck, 2015 (638,451 veterans diagnosed with PTSD in the VA in fiscal year 2012 across all medical centers)

4. Bernardy et al., 2012 (80% of veterans diagnosed with PTSD had at least one medication from the Clinical Practice Guidelines)



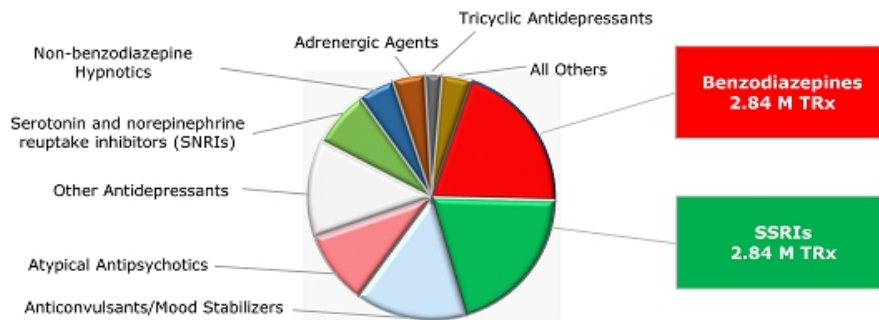
## What Drug Classes are Used to Treat PTSD?

12

### Market highly fragmented, with benzodiazepines being widely prescribed (but not indicated)<sup>1</sup>

- Multiple medications per patient (or "Polypharmacy") is the norm
  - Approximately 55% of patients receive a benzodiazepine, and 53% receive an SSRI
- SSRIs are the only FDA-approved drug class

### Estimated PTSD Market Volume (Civilian Population Only) ~14.1 million TRx\*<sup>2</sup>



\* TRx = Total prescriptions

1. VA/DoD Clinical Practice Guideline for the Management of Post-Traumatic Stress, Version 2, 2010

2. IMS Consulting, *Market Sizing & Treatment Dynamics: "Post-Traumatic Stress Disorder (PTSD) Patients"*, 2016

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## Sleep Disturbances Are a Core Feature Of PTSD<sup>1</sup>

Sleep disturbances are a core feature of PTSD and a component of three of the four major symptom clusters:

| Diagnostic Criteria for PTSD (DSM-5) <sup>2</sup>                  |
|--|
| B. Presence of one (or more) intrusion symptoms                    |
| C. Persistent avoidance of stimuli associated with traumatic event |
| D. Negative alterations in cognitions and mood                     |
| E. Marked alterations in arousal and reactivity                    |



<sup>1</sup>Germain A. *Am J Psychiatry*. 2013; <sup>2</sup>American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

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## What Is Restorative Sleep?

14

**Restorative Sleep Hypothesis<sup>1</sup>:** Sleep is an **active**, necessary state for **processing emotionally charged memories**, replenishing energy, and resetting homeostasis to circuitry in the brain



**ENERGY**

**Homeostasis**

**Sleep Deprivation  
Sleep Disturbances**



**Depression, Chronic  
Pain, Anxiety, and  
PTSD**

<sup>1</sup>Germain A. *Am J Psychiatry*. 2013.



## Relevance of Sleep Disturbances for PTSD

### Sleep disturbances:

- Core symptom of PTSD (component of intrusion and hyperarousal symptom clusters)
- Believed to play roles in the pathophysiology of PTSD

|      | Sleep As a Core Symptom   | Pathophysiology  | Pharmacological Action<br>2° Clinical Endpoint | Therapeutic Benefit<br>1° Clinical Endpoint |
|------|---|--|--|---|
| PTSD | <ul style="list-style-type: none"><li>• Nightmares</li><li>• Hyperarousal</li></ul> | <b>Stress ≈ Hyperarousal ≈ Sleep Disturbances</b><br>Hyperarousal and hypervigilance interfere with sleep and emotional memory processing during sleep | Reduced hyperarousal                           | Reduced PTSD symptoms and disability        |



## TNX-102 SL: Proprietary Patented<sup>1</sup> Formulation

16

**Active Pharmaceutical Ingredient (API) is cyclobenzaprine (CBP), is structurally related to tricyclic antidepressants (TCAs)**

- TCAs and their metabolites differ widely in their receptor binding and pharmacokinetic profiles<sup>2</sup>

Different from other tricyclics

- **CBP is more selective for high affinity sites believed to have a role in sleep quality<sup>3</sup>**
  - 5-HT<sub>2A</sub>
  - $\alpha_1$ -adrenergic
  - histamine H<sub>1</sub>
- **CBP undergoes extensive first-pass hepatic metabolism when administered orally**
  - Major metabolite, norcyclobenzaprine (nCBP)
  - Long half-life (~72 hours)
  - Less selective for target receptors (5-HT<sub>2A</sub>,  $\alpha_1$ -adrenergic, histamine H<sub>1</sub>)
  - More selective for norepinephrine transporter

Different from oral CBP formulation

**TNX-102 SL: Proprietary sublingual formulation of CBP**

- Innovation by design
- Rapid systemic exposure
- Increased bioavailability
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, nCBP

<sup>1</sup> Notice of Allowance for Eutectic Proprietary Protectic™ Formulation Patent issued by the U.S. Patent and Trademark Office

<sup>2</sup> Rudorfer and Potter, *Cellular and Molecular Neurobiology*, 1999 19:373

<sup>3</sup> Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada



# High Prevalence of PTSD Among Combat Veterans



**3-9%**  
General population<sup>1</sup>



**19-31%**  
Vietnam veterans<sup>2</sup>



**>19%**  
Operation Enduring Freedom  
(OEF; Afghanistan) /  
Operation Iraqi Freedom  
(OIF) veterans / Operation  
New Dawn (OND)<sup>3</sup>



**8.6 million** American adults affected<sup>1</sup>



**Women** more likely to develop than men<sup>1</sup>



Susceptibility may **run in families**<sup>1</sup>

<sup>1</sup>Kessler et al., *Arch Gen Psych* 2005; Prevalence rate of 3.5% applied to U.S. Census estimate of 247M U.S. adult ( $\geq 18$ ) population in 2015 ([www.census.gov/quickfacts/table/PST045215/00](http://www.census.gov/quickfacts/table/PST045215/00)); <sup>2</sup>Norris, *PTSD Res Quar.* 2013; <sup>3</sup>*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.



## Growing Economic and Social Burden to Care for Veterans with PTSD

18

**Health care costs associated with PTSD for OEF/OIF/OND veterans:**

### Direct costs

**\$3,000-5,000**  
per patient per year for  
OEF/OIF Veterans<sup>1</sup>

**~ 1.9M Veterans  
out of 2.7M**  
servicemembers deployed  
between 10/1/2001 and  
3/31/2015<sup>3</sup>



### Indirect costs

**\$2-3 billion**  
estimated yearly cost  
to society<sup>2</sup>

Families, social care  
agencies, schools,  
employers, welfare system<sup>2</sup>

<sup>1</sup>CBO Report 2012; <sup>2</sup>Tanielian, *Invisible Wounds of War*, 2005;  
<sup>3</sup>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; OEF/OIF/OND, Operations Enduring Freedom,  
Iraqi Freedom and New Dawn.



## Why Initially Target Military-Related PTSD?

19

### Military-related PTSD not well-served by existing FDA-approved therapies

- **No clear treatment response observed in U.S. military population**

Sertraline: failed to show efficacy in a large multicenter trial in U.S. military (placebo numerically better)<sup>1</sup>  
Paroxetine: no large trials conducted with predominantly military trauma

- **Inconsistent treatment response observed in males**

Sertraline: FDA-conducted post-hoc analysis concluded no effect for male civilian subgroup<sup>2</sup>  
Paroxetine: no sex-related difference in treatment outcomes<sup>3</sup>

- **Important tolerability issues with SSRIs in this population**

Sexual dysfunction<sup>2,3</sup>  
Insomnia<sup>2,3</sup>  
SSRI withdrawal syndrome<sup>4</sup>

<sup>1</sup> Friedman et al., J Clin Psychiatry 2007; 68:711

<sup>2</sup> Zoloft Package Insert, August, 2014

<sup>3</sup> Paxil Package Insert, June, 2014

<sup>4</sup> Fava et al., Psychother Psychosom 84:72-81, 2015



## Phase 2 AtEase Study in Military-Related PTSD

20

- Randomized, double-blind, placebo-controlled trial in military-related PTSD

TNX-102 SL at bedtime once-daily  
2.8 mg *N* = 90

TNX-102 SL at bedtime once-daily  
5.6 mg (2 x 2.8 mg) *N* = 49

Placebo at bedtime once-daily  
*N* = 92

- Enrolled patients with baseline CAPS-5  $\geq 29$
- Analysis from 231 patients; 24 U.S. clinical sites
- TNX-102 SL was active at 5.6 mg dose

- **Primary efficacy analysis:**

- Difference in CAPS-5 score between TNX-102 SL 2.8 mg and placebo at week 12

————— 12 weeks —————>..... *open-label extension*

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## AtEase Study Demographics and Characteristics

- ◊ **93% of the randomized patients were male**
- ◊ **98% had trauma during military service**
- ◊ **Deployed an average of 2.3 times**
- ◊ **Mean time since index trauma was 7 years**
- ◊ **Race and ethnicity generally consistent with U.S. military distribution**
- ◊ **Current Major Depressive Disorder 14% by MINI 7.0**
- ◊ **Similar baseline CAPS-5 scores and MADRS scores across treatment arms**

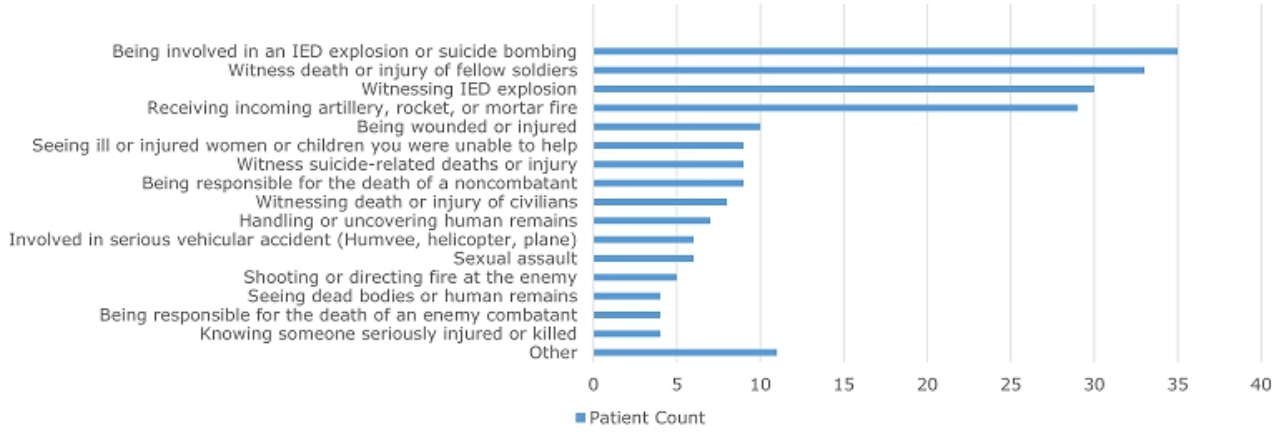
| Variable                    | Placebo<br>N=92 | TNX-102 SL 2.8 mg<br>N=90 | TNX-102 SL 5.6 mg<br>N=49 | Overall<br>N=231 |
|-----------------------------|-----------------|---------------------------|---------------------------|------------------|
| Baseline CAPS-5 Scores (SD) | 39.5 (7.7)      | 39.5 (8.0)                | 39.3 (8.1)                | 39.5 (7.85)      |
| Baseline MADRS Scores (SD)  | 17.3 (6.5)      | 17.6 (5.2)                | 16.1 (5.5)                | 17.1 (5.83)      |

CAPS-5, Clinician Administered PTSD Scale for DSM-5  
MADRS, Montgomery-Åsberg Depression Rating Scale  
MINI 7.0, Mini-International Neuropsychiatric Interview, Version 7  
SD, standard deviation



# AtEase Study: Traumas Associated with PTSD

Index Trauma During Military Service\*



\*Some patients experienced more than one trauma



## AtEase Study – Summary of Primary and Secondary Analyses (week 12)

| Assessment               | Domain                           | Analysis                      | p-Values           |               |
|--------------------------|----------------------------------|-------------------------------|--------------------|---------------|
|                          |                                  |                               | 2.8 mg (N=90)      | 5.6 mg (N=49) |
| CAPS-5                   | Total                            | MMRM                          | 0.259 <sup>^</sup> | 0.053         |
|                          | Total                            | MMRM with Multiple Imputation | 0.211              | 0.031*        |
|                          | Total                            | MMRM w/ Hybrid LOCF/BOCF      | 0.172              | 0.037*        |
|                          | Total                            | ANCOVA                        | 0.090              | 0.038*        |
| CAPS-5 clusters/items    | Arousal & Reactivity cluster (E) | MMRM                          | 0.141              | 0.048*        |
|                          | Sleep item (E6)                  | MMRM                          | 0.185              | 0.010*        |
|                          | Exaggerated Startle item (E4)    | MMRM                          | 0.336              | 0.015*        |
| CGI-I                    | Responders                       | Logistic Regression           | 0.240              | 0.041*        |
| PGIC                     | Mean score                       | MMRM                          | 0.075              | 0.035*        |
| Sheehan Disability Scale | Work/school item                 | MMRM                          | 0.123              | 0.050*        |
|                          | Social/leisure item              | MMRM                          | 0.198              | 0.031*        |

BOCF, baseline observation carried forward; CGI-I, Clinical Global Impression - Improvement scale; LOCF, last observation carried forward; MMRM, mixed model repeated measures; PGIC, Patient Global Impression of Change

<sup>^</sup>Primary analysis p-value not significant comparing TNX-102 SL 2.8 mg versus placebo

\*p<0.05



## AtEase Study: Safety and Tolerability Profile

### No serious adverse events reported with TNX-102 SL deemed related to treatment

| <b>Systemic Adverse Events*</b>       | <b>Placebo<br/>(N=94)</b> | <b>TNX-102 SL 2.8 mg<br/>(N=93)</b> | <b>TNX-102 SL 5.6 mg<br/>(N=50)</b> |
|---------------------------------------|---------------------------|-------------------------------------|-------------------------------------|
| 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%                               |
| <b>Administration Site Reactions*</b> |                           |                                     |                                     |
| Hypoesthesia oral                     | 2.1%                      | 38.7%                               | 36.0%                               |
| Paraesthesia                          | 3.2%                      | 16.1%                               | 4.0%                                |
| Glossodynia                           | 1.1%                      | 3.2%                                | 6.0%                                |

**Trial completion rates: 73% placebo; 79% TNX-102 SL 2.8 mg; 84% TNX-102 SL 5.6 mg**

\*at rates of >5% in either drug-treated arm, Safety population N=237

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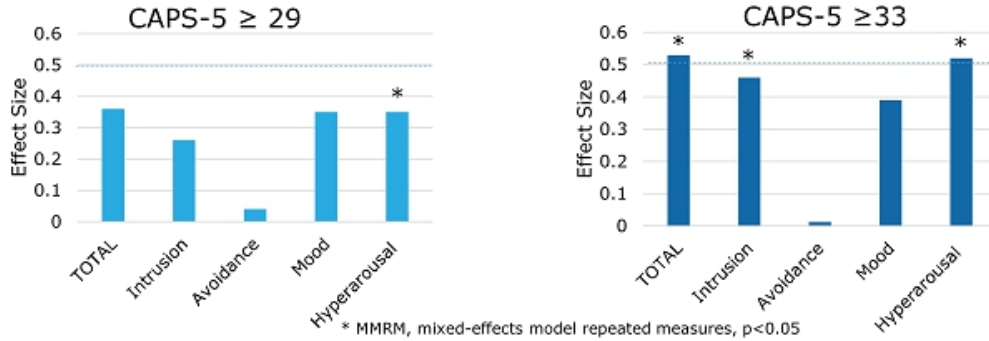
# AtEase: Retrospective Analysis for TNX-102 SL 5.6 mg

### Prior pharmacotherapy trials in PTSD used earlier versions of CAPS (e.g. CAPS-2)

- Different scoring range from CAPS-5
- Most frequently used a score of  $\geq 50$  for entry (similar to CAPS-5  $\geq 33$ <sup>1</sup>)
- FDA has accepted this higher entry criteria (CAPS-5  $\geq 33$ ) for Phase 3 program

### Compared CAPS-5 Severity Entry Criteria $\geq 29$ versus $\geq 33$ on Effect Size for AtEase

- Retrospective analysis showed more robust effect with high entry criteria

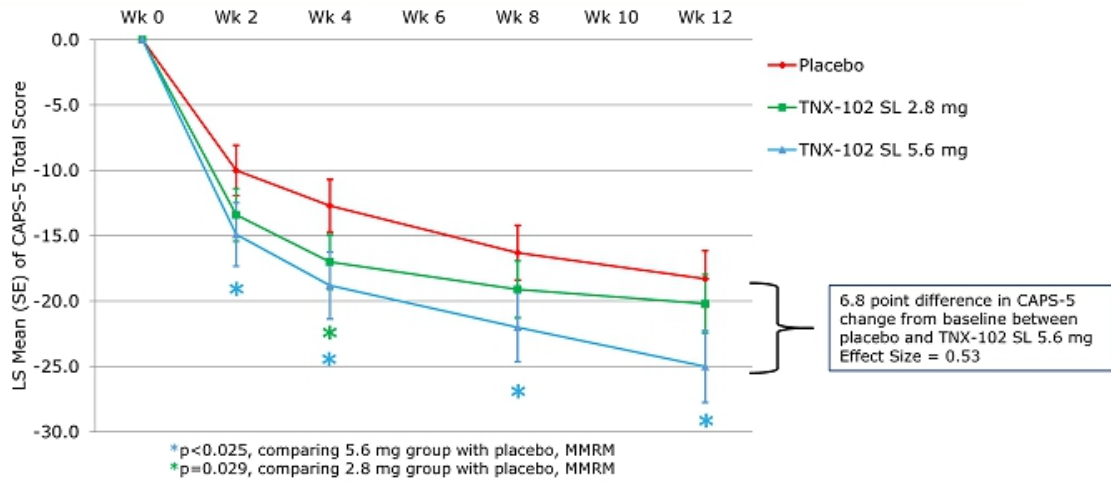


\* MMRM, mixed-effects model repeated measures,  $p < 0.05$

<sup>1</sup>Sullivan, Gregory, et al. Poster session presented at: Military Health System Research Symposium (MHSRS) 2016 Annual Meeting; 2016 Aug 15-18; Kissimmee, FL. URL: <http://bit.ly/2bF04mx>



# Retrospective Analysis of CAPS-5 in Patients with Entry CAPS-5 $\geq 33$ <sup>1</sup>



<sup>1</sup>Primary analysis was TNX-102 SL 2.8 mg with entry CAPS-5  $\geq 29$



## Retrospective Analyses of Week 12 Outcome Measures for TNX-102 SL 5.6 mg vs. Placebo in Military-related or Combat PTSD Subset and for CAPS-5 $\geq 29$ and CAPS-5 $\geq 33$ at Baseline

27

| CAPS-5 at Baseline                     | Military-related PTSD |                      | Combat PTSD          |                      |
|--|-----------------------|----------------------|----------------------|----------------------|
|  | $\geq 29$             | $\geq 33$            | $\geq 29$            | $\geq 33$            |
| N: PBO/TNX-102 SL 5.6 mg               | 92/49                 | 77/38                | 74/46                | 64/35                |
| Outcome Measure                        | p-value <sup>1</sup>  | p-value <sup>1</sup> | p-value <sup>1</sup> | p-value <sup>1</sup> |
| <b>CAPS-5</b>                          |                       |                      |                      |                      |
| Total score                            | 0.053                 | <b>*0.013</b>        | <b>*0.037</b>        | <b>*0.013</b>        |
| Cluster B (intrusion)                  | 0.161                 | <b>*0.026</b>        | 0.183                | <b>*0.031</b>        |
| Cluster C (avoidance)                  | 0.963                 | 0.522                | 0.824                | 0.570                |
| Cluster D (mood/cognition)             | 0.062                 | 0.065                | <b>*0.035</b>        | 0.061                |
| Cluster E (arousal and reactivity)     | <b>*0.048</b>         | <b>*0.012</b>        | <b>*0.036</b>        | <b>*0.012</b>        |
| E6 (Sleep item)                        | <b>*0.010</b>         | <b>*0.013</b>        | <b>*0.003</b>        | <b>*0.010</b>        |
| E2 (Reckless/Self Destruct)            | 0.140                 | <b>*0.012</b>        | 0.178                | <b>*0.019</b>        |
| CGI-I (responders)                     | <b>*0.041</b>         | <b>*0.042</b>        | <b>*0.049</b>        | 0.082                |
| <b>SDS</b>                             |                       |                      |                      |                      |
| Total Score                            | 0.079                 | 0.093                | <b>*0.039</b>        | <b>*0.032</b>        |
| Work/School item                       | 0.050                 | <b>*0.040</b>        | <b>*0.026</b>        | <b>*0.015</b>        |
| Social/Leisure item                    | <b>*0.031</b>         | 0.116                | <b>*0.013</b>        | <b>*0.028</b>        |
| Family Life/Home Responsibilities item | 0.524                 | 0.455                | 0.328                | 0.274                |

<sup>1</sup>CAPS-5 and Sheehan Disability Scale outcome measures: p-values from mixed-effects model repeated measures statistical test on the mean change from baseline difference between TNX-102 SL 5.6 mg and placebo; CGI-I: p-values from a repeated measure logistic regression (Responder defined as a patient who was rated as "1" very much improved, or "2" much improved at week 12). \*denotes statistical significance difference with  $p < 0.05$ , not adjusted for multiple comparisons; Abbreviations: 5.6 mg=TNX-102 SL 5.6 mg; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; N=number of patients; PBO=Placebo; SDS=Sheehan Disability Scale.

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## Phase 2 AtEase Study Conclusions

28

### **First large multi-center trial demonstrating efficacy of an investigational new drug in military-related PTSD**

- ✓ TNX-102 SL therapeutic dose (5.6 mg) identified
- ✓ Symptom reduction (CAPS-5)
- ✓ Functional improvement (Sheehan Disability Scale domains)
- ✓ Clinical global impression of improvement (CGI-I)
- ✓ Evidence of meaningful clinical improvement supports the Breakthrough Therapy designation

### **Effects on sleep and hyperarousal**

- ✓ Consistent with mechanistic hypothesis

### **Well-tolerated; side effects include:**

- ✓ Systemic: somnolence, dry mouth, headache and sedation
- ✓ Local administration site reactions: transient tongue numbness

**Comprehensive AtEase study results from scientific presentations available at:**

<http://www.tonixpharma.com/research-development/scientific-presentations>





## Phase 3 HONOR Study in PTSD Enrolling

29

### To confirm AtEase findings in military-related PTSD:

- Larger adaptive design study
- Enrollment started in 1Q 2017

**TNX-102 SL once-daily at bedtime**  
5.6 mg N ~ 275 (140\*)

**Placebo once-daily at bedtime**  
N ~ 275 (140\*)

————— **12 weeks** —————>..... **open-label extension**

\* Interim analysis

**1H 2018 - IA outcome anticipated**  
**2H 2018 - topline data anticipated, if 550 patients are studied**

### General study characteristics:

- Randomized, double-blind, placebo-controlled, entrance CAPS-5  $\geq 33$
- One unblinded interim analysis (IA) by an independent data monitoring committee at 50% recruitment
- IA (N ~275) for efficacy stop, continuation as planned or sample size adjustment
- Potential to enroll 550 patients
- Approximately 35 U.S. clinical sites

### Primary efficacy endpoint:

- Mean change from baseline in total CAPS-5 at Week 12 compared between TNX-102 SL 5.6 mg and placebo



## Commercialization Options

30

Tonix is exploring a variety of options to commercialize TNX-102 SL, including commercializing on our own or partnering all or some indications in specific regions of the world.

### Commercial considerations:

- Primary physician audience is well defined: psychiatrists (~30,000 in U.S.)
  - Small specialty sales force sufficient for coverage
- Primary market research with psychiatrists indicate strong interest in new therapeutic options



### TNX-102 SL

#### Portfolio of international patents filed under the Patent Cooperation Treaty (PCT)

##### Composition-of-matter (eutectic)

- Notice of Allowance issued by U.S. Patent and Trademark Office
- Additional claims and jurisdictions pending
- Protection expected to 2034

##### Pharmacokinetics (PK)

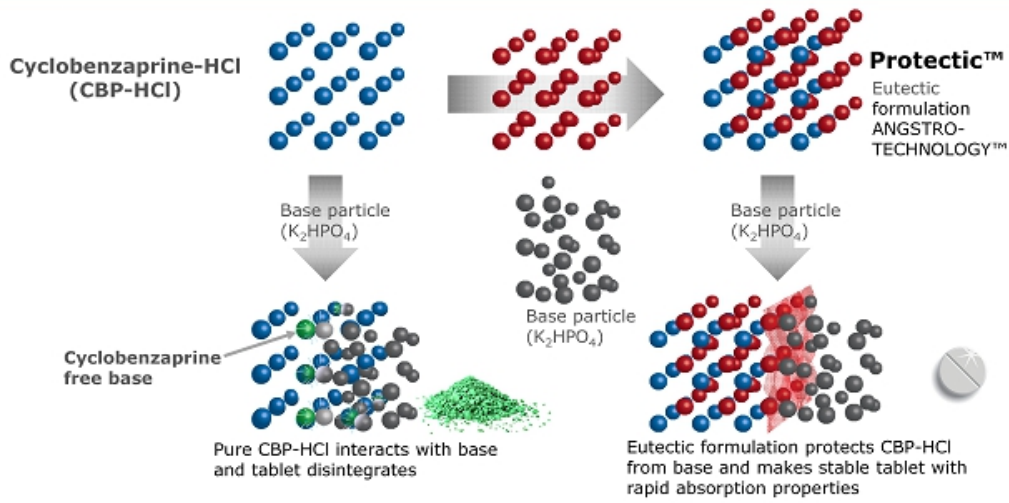
- Patents filed
- Protection expected to 2033

##### Method-of-use

- PTSD: patents filed

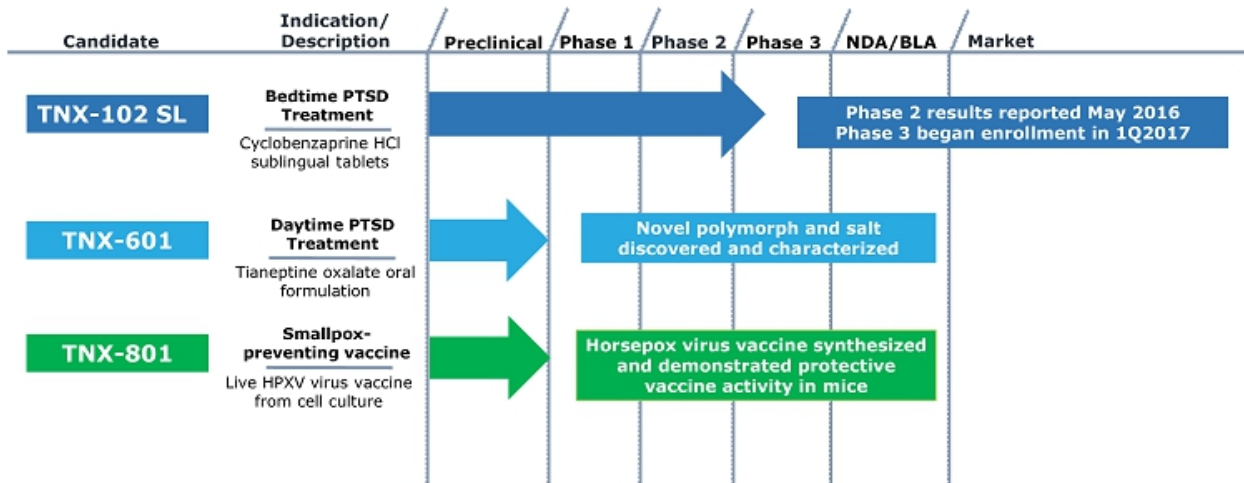


# Proprietary Cyclobenzaprine Hydrochloride Eutectic Mixture Stabilizes Tablet Formulation





# Product Pipeline





# TNX-601 - A Potential Clinical Candidate for PTSD

## TNX-601 (tianeptine oxalate oral formulation)

34

Pre-IND  
Candidate

Targeting a  
Public Health  
Challenge

- Targeted as a 1<sup>st</sup> line monotherapy for **PTSD**: daytime dosing
  - ✓ **Leverages expertise in PTSD (clinical and regulatory experience, market analysis, etc.)**
  - ✓ **Mechanism of Action (MOA) is different from TNX-102 SL**
- Tianeptine sodium (amorphous) has been approved in EU, Russia, Asia and Latin America for depression since 1987 with established post-marketing experience
- Identified new oxalate salt polymorph with improved pharmaceutical properties ideal for reformulation
- **Filed patent application on novel salt polymorph**
- Issued patent on steroid-induced cognitive impairment and memory loss issues
- GMP synthesis developed
- IND-enabling nonclinical studies and formulation development can proceed simultaneously
- **Clinical evidence for PTSD**
- Several studies have shown tianeptine to be active in the treatment of PTSD<sup>1-4</sup>
- US clinical development benefited from the dose identified and dosing regimen developed ex-U.S.

<sup>1</sup> Frančičković T, et al. Psychiatr Danub. 2011 Sep;23(3):257-63. PMID: 21963693

<sup>2</sup> Rumyantseva GM and, Stepanov AL. Neurosci Behav Physiol. 2008 Jan;38(1):55-61. PMID: 18097761

<sup>3</sup> Aleksandrovskii IA, et al. Zh Nevrol Psikhiatr Im S S Korsakova. 2005;105(11):24-9. PMID: 16329631 [Russian]

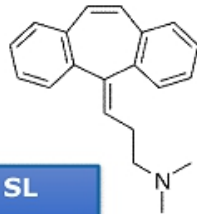
<sup>4</sup> Onder E, et al. Eur Psychiatry. 2006 (3):174-9. PMID: 15964747



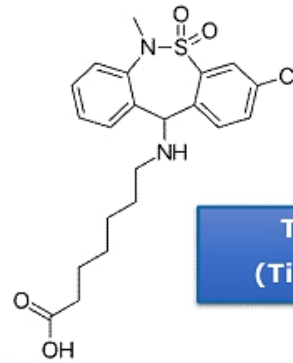
## Structural Comparison: TNX-102 SL and TNX-601

35

- Cyclobenzaprine and tianeptine share structural similarities with classic tricyclic antidepressants (TCAs) and to each other, but each has unique pharmacological properties
  - Tianeptine has a 3-chlorodibenzothiazepine nucleus with an aminoheptanoic side chain
- Tianeptine leverages Tonix's expertise in the pharmacology and development of tricyclics



**TNX-102 SL**  
**(Cyclobenzaprine)**



**TNX-601**  
**(Tianeptine)**

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# TNX-601: A Potential Clinical Candidate for PTSD

36

- **API is a novel oxalate salt of tianeptine**

- Shares structural features with tricyclic antidepressants, but has unique pharmacological and neurochemical properties<sup>1</sup>

## Mechanism of Action

- **Tianeptine modulates the glutamatergic system indirectly**
  - Does not have significant affinity ( $K_i > 10\mu\text{M}$ ) for NMDA<sup>2</sup> or AMPA<sup>3</sup> receptors
- **Tianeptine is a weak  $\mu$ -opioid receptor (MOR) agonist**
  - Controlled substance in France, Bahrain and Singapore
- **Tianeptine has been shown to oppose deleterious effects of chronic stress on brain structure and plasticity**

## Important Characteristics of TNX-601

- **TNX-601: Novel oxalate salt and polymorph of tianeptine**
  - Improved stability, consistency and manufacturability
  - Benefited from human experience established in ex-U.S. approved countries
  - Potential safety and efficacy evidence in published PTSD studies<sup>4-7</sup>
- **5 year Hatch-Waxman exclusivity for first time approval in the U.S.**
- **Patent filed on novel oxalate salt and polymorph**

<sup>1</sup> McEwen, Bruce S., et al. The neurobiological properties of tianeptine (Stablon): from monoamine hypothesis to glutamatergic modulation. *Molecular psychiatry* 2010; 15.3: 237-249

<sup>2</sup> N-methyl-D-aspartate

<sup>3</sup> D-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

<sup>4</sup> Frančičković T, et al. *Psychiatr Danub*. 2011 Sep;23(3):257-63. PMID: 21963693

<sup>5</sup> Rumyantseva GM and, Stepanov AL. *Neurosci Behav Physiol*. 2008 Jan;38(1):55-61. PMID: 18097761

<sup>6</sup> Aleksandrovskii IA, et al. *Zh Nevrol Psikiatr Im S S Korsakova*. 2005;105(11):24-9. PMID: 16329631 [Russian]

<sup>7</sup> Onder E, et al. *Eur Psychiatry*. 2006 (3):174-9. PMID: 15964747





# TNX-801: A Potential Smallpox-Preventing Vaccine

Pre-IND  
Candidate

### TNX-801 (live virus vaccine - synthetic horsepox (HPXV) vaccine)

- Potential improvement over current methods for biodefense against **smallpox**
  - ✓ **Leverages government affairs effort**
- Tonix is developing a new vaccine (TNX-801) with improved properties
  - ✓ **Collaboration with Professor David Evans and Dr. Ryan Noyce at University of Alberta**
  - ✓ **Protective vaccine activity in mice has been demonstrated**
  - ✓ **Patent application on novel vaccine submitted**

### Regulatory strategy

- FDA's "Animal Rule" can be applied to establish human efficacy
- Good Manufacturing Practice (GMP) virus in development for human safety study

Targeting a  
Public Health  
Issue

### Material threat medical countermeasure under 21<sup>st</sup> Century Cures Act

- Qualifies for receiving **Priority Review Voucher** on approval
  - ✓ **Priority Review Vouchers are transferrable and have sold for ~\$125 M**
- ACAM2000 vaccine developed by Acambis was acquired by Sanofi in 2008 for \$513 M
  - ✓ **ACAM2000 was sold to U.S. Strategic National Stockpile<sup>1</sup>**

<sup>1</sup> Nalca, A et al. Drug design, development and Therapy: 4:71-79 (2010)



## TNX-801: Synthetic Live Horsepox Virus

38

**Synthesis from sequence of a 1976 Mongolian isolate<sup>1</sup>**  
**In mice, TNX-801 behaved like attenuated vaccinia virus**  
**(vaccinia virus is foundation of current smallpox vaccines)**

### **How is horsepox related to modern vaccines?**

- Multiple sources<sup>2-4</sup> indicate that the smallpox vaccine discovered by Dr. Edward Jenner in the early 19<sup>th</sup> century was likely a horsepox virus
- Evidence indicates that modern smallpox vaccines descend from a HPXV-like ancestral strain
- Horsepox is now believed to be extinct<sup>4</sup>

<sup>1</sup> Tulman et al., *Journal of Virology*, 2006; 80(18): 9244-9258.

<sup>2</sup> Qin et al., *Journal of Virology*, 2011; 85(24):13049-13060.

<sup>3</sup> Medaglia et al., *Journal of Virology*, 2015; 89(23):11909-11925.

<sup>4</sup> Esparza J. *Veterinary Record*. 2013; 173: 272-273.



## **Horsepox - Better Tolerability as a Vaccine?**

39

- **Horsepox is caused by HPXV and is characterized by mouth and skin eruptions**
- **HXPV isolate from the 1976 outbreak later sequenced**
- **Modern vaccinia virus smallpox vaccines are associated with cardiotoxicity; may have acquired undesirable properties not present in an ancestral virus (likely HPXV)**
- **Horsepox has potential for slower proliferation or decreased toxicity**



## **A Better Smallpox-Preventing Vaccine is Important and Necessary Today**

40

- **Smallpox was eradicated as a result of global public health campaigns**
- **No cases of naturally-occurring smallpox have been reported since 1977**
- **Accidental or intentional transmission of smallpox does not require a natural disease reservoir**
- **Stockpiles of smallpox-preventing vaccines are currently maintained and refreshed in case of need**



## TNX-801: A Potential Medical Countermeasure

41

- **21st Century Cures Act (2016), Section 3086**
  - Encouraging treatments for agents that present a national security threat
- **Medical countermeasures are drugs or vaccines intended to treat:**
  - Biological, chemical, radiological, or nuclear agents that present a national security threat
  - Harm from a condition that may be caused by administering a drug or biological product against such an agent
- **New Priority Review Voucher program for “material threat medical countermeasures”**
- **Priority Review Voucher may be transferred or sold**



# TNX-801: A Potential Smallpox-Preventing Vaccine

42

## Synthetic live virus HPXV TNX-801

- Shares structural characteristics with vaccinia-based vaccines
- Unique properties that suggest lower toxicity
- Smallpox has a ~30% mortality rate in vaccine-naïve populations

### Mechanism of Action

#### **Live virus vaccines stimulate cross-reactive immunity**

- Protects from consequences of infection with smallpox agent
- Renders recipient "immune"
- Provides additional protection of non-immunized population

### Important Characteristics of TNX-801

#### **Potential safety advantage over existing vaccines**

- Cardiotoxicity limits use of existing vaccines

#### **Exclusivity**

- Patent filed on novel virus composition
- Anticipate 12 years exclusivity



## Financial overview

43

### NASDAQ: TNXP

|   |                |
|---|----------------|
| Cash, cash equivalents, and marketable securities reported at December 31, 2016 | \$26.1 million |
| Approximate net proceeds from at-the-market offering since January 1, 2017      | \$9.1 million  |
| Approximate net proceeds from underwritten offering closed in April 2017        | \$8.3 million  |
| Shares outstanding as of April 13, 2017   | 7.5 million    |



# Management Team



**Seth Lederman, MD**  
President & CEO



**Gregory Sullivan, MD**  
Chief Medical Officer



**Bradley Saenger, CPA**  
Chief Financial Officer



**Jessica Morris**  
EVP, Operations







## Board of Directors

45

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**Seth Lederman, MD**

Chairman

**Ernest Mario, PhD**

ALZA, Glaxo, Reliant Pharma

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**Stuart Davidson**

Labrador Ventures, Alkermes, Combion

**Charles Mather**

BTIG, Janney, Jefferies, Cowen, Smith Barney

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**Patrick Grace**

Apollo Philanthropy, WR Grace, Chemed

**John Rhodes**

NYSERDA, NRDC, Booz Allen Hamilton

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**Donald Landry, MD, PhD**

Chair of Medicine, Columbia University

**Samuel Saks, MD**

Jazz Pharma, ALZA, Johnson & Johnson

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## Milestones – recent and upcoming

46

### TNX-102 SL – Posttraumatic Stress Disorder

- |                                     |               |   |
|-------------------------------------|---------------|---|
| <input checked="" type="checkbox"/> | May 2016      | Reported results from AtEase study  |
| <input checked="" type="checkbox"/> | August 2016   | End-of-Phase 2 meeting with FDA<br>- Proposed Phase 3 clinical and NDA plan accepted  |
| <input checked="" type="checkbox"/> | December 2016 | Breakthrough Therapy designation granted by FDA                                       |
| <input checked="" type="checkbox"/> | January 2017  | FDA concurrence with protocol design for Phase 3 HONOR study in military-related PTSD |
| <input checked="" type="checkbox"/> | 1Q 2017       | Initial Multidisciplinary Breakthrough Therapy Meeting with FDA                       |
| <input checked="" type="checkbox"/> | 1Q 2017       | Notice of Allowance for Eutectic Proprietary Protectic™ Formulation Patent            |
| <input checked="" type="checkbox"/> | 1Q 2017       | Commenced enrollment of Phase 3 HONOR study   |
| <input type="checkbox"/>            | 1H 2018       | Anticipated interim analysis of Phase 3 HONOR study in ~275 participants              |
| <input type="checkbox"/>            | 2H 2018       | Anticipated topline results of Phase 3 HONOR study in 550 participants (if needed)    |



## Summary

47

### **Strong position for value growth with Phase 3 development in a major medical indication: PTSD including military-related PTSD**

- Phase 3 asset not previously well-known to the investor marketplace

### **TNX-102 SL for PTSD is designated as a Breakthrough Therapy by FDA**

- Accelerated development and approval process is expected

### **Phase 3 HONOR study in military-PTSD began enrollment in 1Q 2017**

- Outcome of the interim analysis on ~275 participants expected to be available 1H 2018
- Topline results from 550 participants, if needed, expected to be available 2H 2018
- Fully funded through the completion of the 550-participant trial and announcement of topline results in 2H 2018



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**TONIX**  
PHARMACEUTICALS  
NASDAQ: TNXP

*Thank you!*

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