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

FORM 8-K

CURRENT REPORT

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

Date of report (date of earliest event reported): March 18, 2019

TONIX PHARMACEUTICALS HOLDING CORP.
(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

509 Madison Avenue, Suite 306, New York, New York 10022
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (212) 980-9155

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition

On March 18, 2019, Tonix Pharmaceuticals Holding Corp. (the "Company") announced its operating results for the quarter and year ended December 31, 2018. A copy of the press release that discusses this matter is filed as Exhibit 99.01 to, and incorporated by reference in, this report.

Item 7.01 Regulation FD Disclosure

The Company 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 99.02, 99.03 and 99.04 hereto and incorporated herein by reference

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press Release dated March 18, 2019, issued by the Company
99.02	Corporate Presentation by the Company for March 2019 (Long Form)
99.03	Corporate Presentation by the Company for March 2019 (Short Form)
99.04	Corporate Presentation by the Company for March 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: March 18, 2019

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

Exhibit 99.01

Tonix Pharmaceuticals Reports Fourth Quarter and Full Year 2018 Financial Results and Operational Highlights

Phase 3 RECOVERY Trial of Tonmya® for the Treatment of PTSD Initiated and Enrolling

Topline Data Expected First Half 2020

NEW YORK, March 18, 2019 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix, or the Company), a clinical-stage biopharmaceutical company focused on developing pharmaceutical products to treat serious neuropsychiatric conditions and biological products to improve biodefense, today announced financial results for the fourth quarter and full year ended December 31, 2018, and an overview of recent operational highlights.

“Looking forward into 2019, we are excited about the recent initiation of our new Phase 3 study of Tonmya for PTSD. The RECOVERY study incorporates learnings and analyses from our Phase 2 and Phase 3 studies in over 500 military-related PTSD participants and is intended to support the registration of Tonmya for PTSD. We look forward to topline data in the first half of 2020,” said Seth Lederman, M.D., President and Chief Executive Officer. “In addition to Tonmya for PTSD, we maintain a strong and growing pipeline of product candidates, including TNX-102 SL as a bedtime treatment of fibromyalgia and agitation in Alzheimer’s disease, and TNX-601 as a daytime treatment for PTSD and neurocognitive dysfunction associated with corticosteroid use, a potential indication.”

Recent Clinical and Regulatory Highlights

- Enrolled first participant in the Phase 3 RECOVERY study of Tonmya for the treatment of PTSD in March. This pivotal efficacy study incorporates several innovative design features, based on analyses of data from our prior PTSD trials. In November 2018, we received Food and Drug Administration (FDA) acceptance of the study design, which includes participants who have experienced civilian traumas in addition to those with military-related traumas and restricts enrollment to participants who experienced an index trauma within nine years of screening.

- Completed a Clinical Guidance meeting with the FDA in March to discuss the fibromyalgia registration plan for TNX-102 SL and a new Phase 3 study to support this indication.

- Received European use patent issuance for TNX-601 (tianeptine oxalate) for the treatment of neurocognitive dysfunction associated with corticosteroids use, a potential indication. TNX-601 is also being developed as a daytime treatment for PTSD. A Phase 1 pharmacokinetic study of proprietary tianeptine oxalate formulations will be conducted outside of the U.S. and the result is expected in the second half of 2019.

- Successfully completed a Phase 1 pivotal bridging pharmacokinetic study of TNX-102 SL in 2018, the data for which was deemed sufficient by the FDA to support the 505(b)(2) NDA submission for Tonmya and TNX-102 SL.

Recent Corporate Highlights

- Strengthened our balance sheet in December 2018 by completing a public equity offering. The transaction resulted in gross proceeds of $15.9 million, including the over-allotment proceeds, which will be used, in part, to fund the new Phase 3 RECOVERY trial of Tonmya for PTSD.

- Announced a Share Repurchase Program to buy up to $2 million in value of the Company's outstanding stock from time to time.

Fourth Quarter 2018 Financial Results

Research and development expenses for the fourth quarter of 2018 totaled $5.1 million, compared to $3.6 million for the same period in 2017. This increase is due primarily to costs related to the close-out of the Phase 3 HONOR study as well as other activities related to the PTSD program.

General and administrative expenses for the fourth quarter of 2018 were $2.6 million, compared to $1.9 million for the same period in 2017. This increase is due primarily to an increase in legal fees related to patent prosecution, as well as an increase in investor and public relations expenses due to increased investor meetings.

Net loss available to common stockholders was $10.9 million, or $6.10 per share, for the fourth quarter of 2018, compared to net loss of $5.5 million, or $7.07 per share, for the fourth quarter of 2017. In addition to the factors above, fourth quarter 2018 net loss available to common stockholders was impacted by a one-time, non-cash preferred stock deemed dividend in the fourth quarter of 2018. The weighted average common shares outstanding, basic and diluted for the fourth quarter of 2018 was 1,778,524 shares. The weighted average common shares outstanding, basic and diluted for the fourth quarter of 2017 was 750,804 shares.

As of March 13, 2019, all Series A convertible preferred stock had been converted into common stock. Total common stock outstanding as of March 13, 2019 was 6,089,728.

Full Year 2018 Financial Results

Research and development expenses for full year 2018 totaled $17.6 million, compared to $13.3 million for full year 2017. This increase is due primarily to the continued development work related to the PTSD program, including the completion of the NDA-required pivotal bridging pharmacokinetic study of TNX-102 SL in 2018.

General and administrative expenses for full year 2018 were $8.8 million, compared to $8.0 million for full year 2017. This increase is due primarily to increased patent prosecution costs and an increase in investor and public relations expenses due to increased investor meetings.

Net loss available to common stockholders was $29.4 million, or $26.81 per share, for full year 2018, compared to net loss of $21.1 million, or $31.69 per share, for full year 2017. The weighted average common shares outstanding, basic and diluted for 2018 was 1,094,867 shares. The weighted average common shares outstanding, basic and diluted for 2017 was 666,509 shares.

At December 31, 2018, Tonix had $25.0 million of cash and cash equivalents, compared to $25.5 million as of December 31, 2017. Cash and cash equivalents at December 31, 2018 includes net proceeds of $14.4 million from the Company's public offering of common stock in December 2018. Cash used in operations was $24.0 million for full year 2018, compared to $19.1 million for full year 2017.

About Tonix Pharmaceuticals Holding Corp.
Tonix is a clinical-stage biopharmaceutical company focused on discovering and developing pharmaceutical products to treat serious neuropsychiatric conditions and biological products to improve biodefense through potential medical counter-measures. Tonix's lead program is for the development of Tonmya, which is in Phase 3 development as a bedtime treatment for PTSD. Tonix is also developing TNX-102 SL as a bedtime treatment for fibromyalgia and agitation in Alzheimer's disease under separate INDs to support potential pivotal efficacy studies. The agitation in Alzheimer's disease IND has been designated a Fast Track development program by the FDA. TNX-601 (tianeptine oxalate) is in the pre-IND application stage, also for the treatment of PTSD but using a different mechanism from TNX-102 SL and designed for daytime dosing. TNX-601 is also in development for a potential indication -neurocognitive dysfunction associated with corticosteroid use. A Phase 1 pharmacokinetic study of proprietary tianeptine oxalate formulations will be conducted outside of the U.S. in 2019. Tonix's lead biologic candidate, TNX-801, is a potential smallpox-preventing vaccine based on a live synthetic version of horsepox virus, currently in the pre-IND application stage.

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

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

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2018, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2019, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

Tonix Pharmaceuticals Reports Fourth Quarter 2018 Financial Results

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

	Three Months Ended December 31,		Year Ended December 31,	
	2018	2017	2018	2017
	(Unaudited)			
Costs and expenses				
Research and development	$ 5,057	$ 3,634	$ 17,558	$ 13,342
General and administrative	2,593	1,909	8,764	7,949
Total costs and expenses	7,650	5,543	26,322	21,291
Operating loss	(7,650)	(5,543)	(26,322)	(21,291)
Interest income, net	62	50	233	168
Net loss	$ (7,588)	$ (5,493)	$ (26,089)	$ (21,123)
Preferred stock deemed dividend	3,266	—	3,266	—
Net loss available to common shareholders	$ (10,854)	$ (5,493)	$ (29,355)	$ (21,123)
Net loss per common share, basic and diluted	$ (6.10)	$ (7.07)	$ (26.81)	$ (31.69)
Weighted average common shares outstanding, basic and diluted	1,778,524	750,804	1,094,867	666,509

[1] The condensed consolidated statements of operations for the years ended December 31, 2018 and 2017 have been derived from the audited financial statements, but do not include all 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, 2018	December 31, 2017
Assets		
Cash and cash equivalents	$ 25,034	$ 25,496
Prepaid expenses and other current assets	1,022	947
Total current assets	26,056	26,443
Other non-current assets	263	311
Total assets	$ 26,319	$ 26,754
Liabilities and stockholders' equity		
Total liabilities	$ 2,655	$ 2,138
Stockholders' equity	23,664	24,616
Total liabilities and stockholders' equity	$ 26,319	$ 26,754

(1) *The condensed consolidated balance sheets for the years ended December 31, 2018 and 2017 have been derived from the audited financial statements, but do not include all the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements.*

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Exhibit 99.02

Investor Presentation

TONIX PHARMACEUTICALS

March 2019

Version P0167 3-18-19 (Doc 0451)

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.

Tonix Pharmaceuticals

Who we are:

- A clinical stage pharmaceutical company dedicated to developing innovative treatments for patients and making meaningful contributions to society

What we do:

- Target therapeutics with high need for improvement
  - Conditions with no or ineffective treatments
  - Significant patient segments not well served by existing therapies
- Develop innovative treatment options with possibility to be a "game changer"
  - Scientifically unique and innovative
  - Supported by strong scientific rationale
  - Confirmed by clinical evidence and published literature
  - Utilize proven regulatory pathway and established clinical endpoint
  - Built on a foundation of proprietary intellectual property

Tonix Development Highlights

TNX-102 SL Cyclobenzaprine Sublingual Tablets

Posttraumatic Stress Disorder (PTSD) – Lead program; new bedtime treatment - Tonmya®[1]

- P302/RECOVERY Phase 3 clinical study initiated in March 2019
- Results from 2 efficacy studies improve the new Phase 3 study design New Phase
- P302/RECOVERY study design features accepted by the FDA[2]

Fibromyalgia Syndrome (FM)

- IND[3] ready to support Phase 3 potential pivotal efficacy study

Agitation in Alzheimer's disease (AAD)

- IND[3] ready to support Phase 2 potential pivotal efficacy study

Pipeline

TNX-601[4] – Daytime PTSD treatment and treatment of neurocognitive dysfunction from corticosteroids

- Pre-IND candidate; nonclinical development ongoing

TNX-801[5] - Smallpox-preventing vaccine candidate

- Efficacy demonstrated in mouse model

[1] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the treatment of PTSD. TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2] FDA Meeting Minutes (November 26, 2018)
[3] IND- Investigational New Drug Application
[4] Tianeptine oxalate
[5] Synthesized live horsepox virus

Lead Program: TNX-102 SL – Product Concept

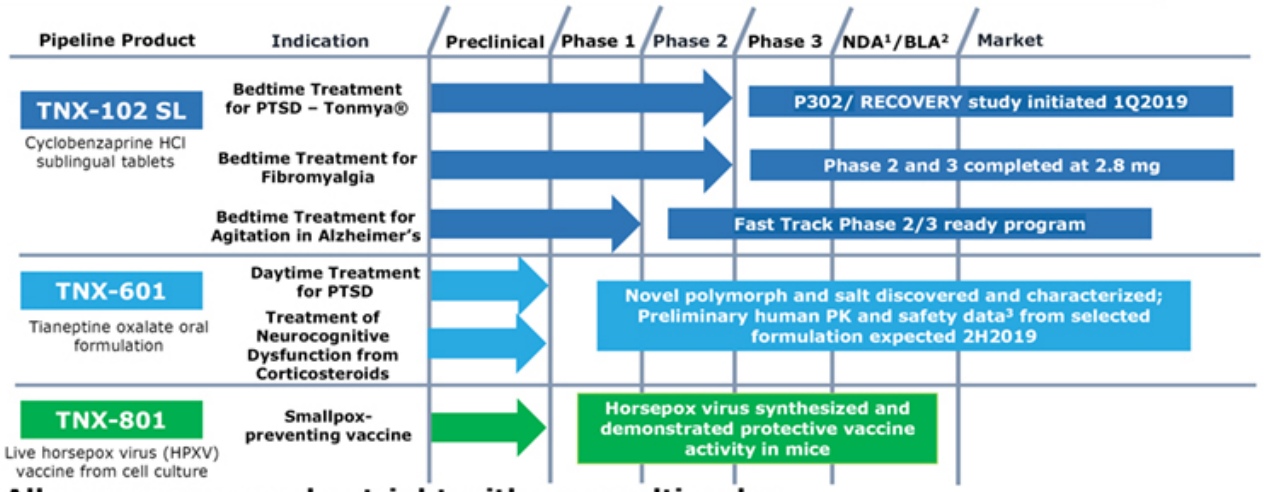
Sleep disturbances are associated with a constellation of disorders

- Considered co-morbid or a key symptom in these disorders
- Believed to have a role in the onset, progression and severity of these disorders

The focus of TNX-102 SL development is both unique and innovative

- Testing the therapeutic benefit of sleep ('sleep quality')
  - Restorative sleep…in contrast to time spent sleeping ('sleep quantity')
- Targeting clinical conditions for which improved sleep quality may have a therapeutic benefit
  - Reduction in disease-specific symptoms, with sleep improvement as a secondary endpoint

Candidates in Development



All programs owned outright with no royalties due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³non-IND study

Tonmya: a Potential Bedtime Treatment for PTSD

First investigational new drug to show treatment effect in military-related PTSD in two potential pivotal efficacy studies

- Phase 2 study (P201/AtEase) showed Tonmya 5.6 mg had a strong signal of treatment effect at Week 12 as measured by CAPS-5[1]
- Phase 3 study (P301/HONOR) provided evidence of effectiveness as early as 4 weeks after treatment but diminished over time due to high placebo response
  - Retrospective analysis showed persistent effectiveness at Week 12 in subgroup with trauma ≤9 years from screening
- Both studies can be used as supportive evidence of efficacy and safety for Tonmya NDA submission
- No serious or unexpected adverse events related to Tonmya were reported

FDA feedback and acceptance on new Phase 3 study (P302/RECOVERY) received in November[2]

Patent protection through 2034 in U.S.[3]

- Composition of matter patent for transmucosal delivery of cyclobenzaprine

Novel mechanism targets sleep quality

- Memory processing during sleep is important to recovery from PTSD

[1] CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
[2] FDA Meeting Minutes, November 26, 2018; [3]U.S. Patent No. 9,636,408 for eutectic proprietary Protectic™ formulation

No Recognized Abuse Potential in Clinical Studies

Active ingredient is cyclobenzaprine, which is structurally related to tricyclic antidepressants

- Cyclobenzaprine interacts with receptors that regulate sleep quality: 5-$HT_{2A,}$ α_1-adrenergic and histamine H_1 receptors
- Cyclobenzaprine does **NOT** interact with the same receptors as traditional hypnotic sleep drugs, benzodiazepines or non-benzodiazepines that are associated with retrograde amnesia
- Cyclobenzaprine-containing product was approved 40 years ago and current labeling (May 2016) indicates no abuse or dependence concern

Tonmya NDA can be filed without drug abuse and dependency assessment studies

- Discussed at March 9, 2017 meeting with the FDA

TNX-102 SL Intellectual Property – U.S. Protection until 2034

Composition of matter (eutectic) : Protection expected to 2034

- United States Patent and Trademark Office (USPTO) issued U.S. Patent No. 9,636,408 in May 201 7U.S. Patent No. 9,956,188 in May 2018 and U.S. Patent No. 10,117,936 in November 2018
- Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018
- New Zealand Intellectual Property Office (NZIPO) issued New Zealand Patent No. 631152 in May 2017
- 37 patent applications pending (2 allowed (US and South Africa))

Pharmacokinetics (PK) : Protection expected to 2033

- JPO issued Japanese Patent No. 6259452 in December 2017
- NZIPO issued New Zealand Patent No. 631144 in March 2017
- Taiwanese Intellectual Property Office issued Taiwanese Patent No. I590820 in July 2017
- 21 patent applications pending (1 allowed (Australia))

Method of use for active ingredient cyclobenzaprine : Protection expected to 2030

- European Patent Office issued European Patent No. 2 501 234B1 in September 2017 (validated in 38 countries). Opposition filed in June 2018
- USPTO issued U.S. Patent 9,918,948 in March 2018
- 2 patent applications pending

TNX-102 SL: Sublingual Formulation is Designed for Bedtime Administration

TNX-102 SL: Proprietary sublingual formulation of cyclobenzaprine (CBP) with transmucosal absorption

- Innovation by design with patent protected CBP/mannitol eutectic
- Rapid systemic exposure
- Increases bioavailability during sleep
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, norcyclobenzaprine (norCBP)

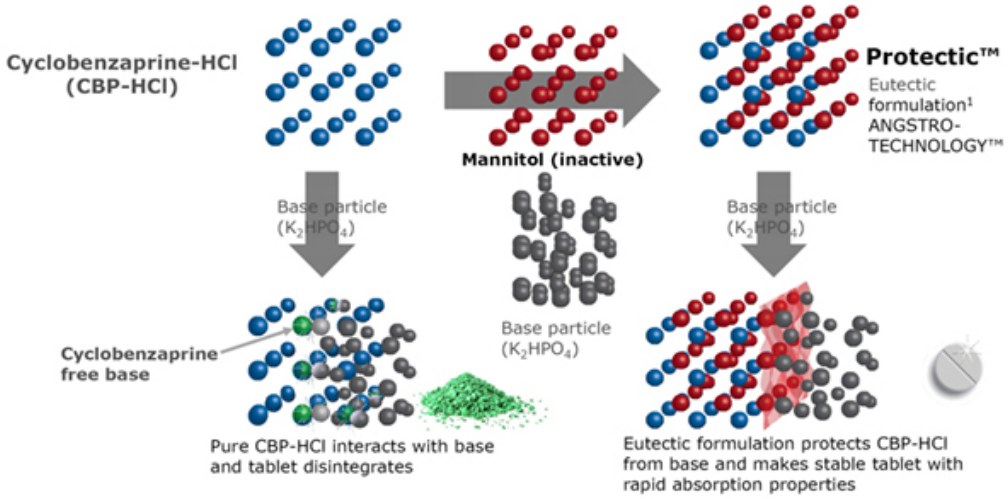
CBP undergoes extensive first-pass hepatic metabolism when orally ingested

- Active major metabolite, norCBP[1]
  - Long half-life (~72 hours)
  - Less selective for target receptors (5-$HT_{2A,}$ α_1-adrenergic, histamine H_1)
  - More selective for norepinephrine transporter and muscarinic M_1

TNX-102 SL 505(b)(2) NDA approval can rely on the safety of the reference listed drug (AMRIX®)[2]

[1] Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada
[2] FDA Minutes (November 26, 2018)

Proprietary Cyclobenzaprine Hydrochloride Eutectic Mixture Stabilizes Sublingual Tablet Formulation



[1] U.S. Patent issued May 2, 2017

Tonmya: Hypothesized Novel Mechanism Targets Sleep Quality for Recovery from PTSD

PTSD is a disorder of recovery

- Most people exposed to extreme trauma recover over a few weeks
- In PTSD, recovery process impeded due to insufficient sleep-dependent memory processing[1,2]

Memory processing is essential to recovery

- Vulnerability to memory intrusions and trauma triggers remains if no consolidation of new learning (extinction)

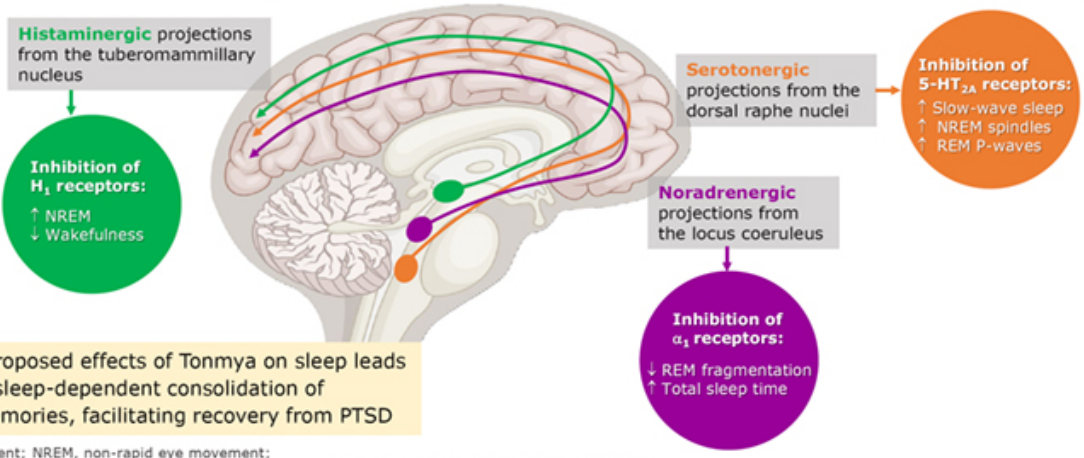
Tonmya targets sleep quality[3]

- The active ingredient in Tonmya, cyclobenzaprine, interacts with receptors that regulate sleep quality: strongly binds and potently blocks 5-HT_{2A}, α_1-adrenergic and histamine H_1 receptors, permissive to sleep-dependent recovery processes

[1]Straus LD, Acheson DT, Risbrough VB, Drummond SPA. Sleep Deprivation Disrupts Recall of Conditioned Fear Extinction. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017; 2(2):123-129. [2]Murkar ALA, De Koninck J. Consolidative mechanisms of emotional processing in REM sleep and PTSD. Sleep Med Rev. 2018; 41:173-184.
[3]Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada

Proposed Mechanism of Action of Tonmya in the Treatment of PTSD:
The Effects of Nocturnal Neuroreceptor Blockade on Sleep

Cyclobenzaprine is a functional antagonist at serotonergic 5-HT_{2A} receptors, noradrenergic α_1 receptors, and histaminergic H_1 receptors



The overall proposed effects of Tonmya on sleep leads to increased sleep-dependent consolidation of extinction memories, facilitating recovery from PTSD

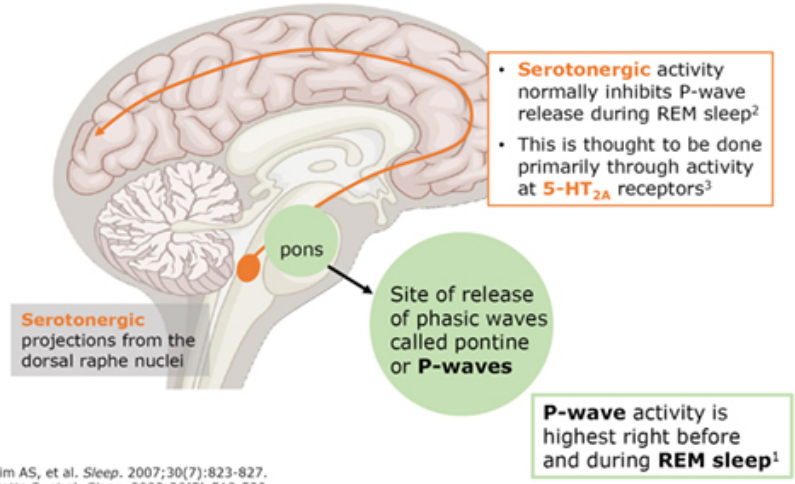
REM, rapid eye movement; NREM, non-rapid eye movement; P-waves, ponto-geniculo-occipital waves

Proposed Mechanism of Action of Tonmya in the Treatment of PTSD:
Focus on Nocturnal 5-HT_{2A} Receptor Blockade in REM

- Generally, serotonin (5-HT) activity promotes the awake state and inhibits REM sleep; whereas once in REM sleep, the 5-HT system is normally quiescent
- Extinction learning is critical to recovery from trauma, and such new learning is consolidated (moving from labile short term to established long term memory) during particular stages of sleep[1,2]
- Recent rodent research shows how particular brain wave patterns during REM sleep, known as "P-waves" are critical to extinction consolidation[3]
- 5-HT activation of pontine brainstem region richly expressing 5-HT_{2A} receptors inhibits P-wave generation during REM[4]
- Nocturnal blockage of 5-HT_{2A} receptors may restore extinction consolidation by inhibition of errant 5-HT stimulation during REM (see model in next 2 slides)

1. Pace-Schott, et al. *Biology of Mood & Anxiety Disorders*. 2015;5(3):1-19.
2. Straus et al. Biol Psych: CNNI. 2017;2(2):123-129.
3. Datta S, et al. *J Neurosci*. 2013;33(10):4561-4569.
4. Datta S, et al. *Sleep*. 2003;26(5):513-520.

Fear Extinction Memory Consolidation: The Proposed Role of P-Waves, REM Sleep, and Serotonergic Neuroreceptor Activity



- Increased P-wave activity during REM sleep is critical for fear extinction memory consolidation in rats[4]
- By blocking 5-HT_{2A} receptors, cyclobenzaprine may sustain P-wave activity during REM sleep
- This blockade may lead to better quality of REM sleep with increased fear extinction consolidation in individuals with PTSD, facilitating recovery

P-waves, ponto-geniculo-occipital waves; REM, rapid eye movement

1. Lim AS, et al. *Sleep*. 2007;30(7):823-827.
2. Datta S, et al. *Sleep*. 2003;26(5):513-520.
3. Tamas K, Gyorgy B. Effect of 5-HT2A/2B/2C receptor agonists and antagonists on sleep and waking in laboratory animals and humans. In: Monti JM, Pandi-Perumal SR, Jacobs BL, Nutt DJ, eds. Serotonin and sleep: Molecular, functional, and clinical aspects. Basel, Switzerland: Birkhäuser Basel; 2008.
4. Datta S, et al. *J Neurosci*. 2013;33(10):4561-4569.

Overview of Posttraumatic Stress Disorder (PTSD)

PSTD is a chronic disabling disorder in response to experiencing traumatic event(s)

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)

Diagnosis, symptom severity, as well as treatment effect, is determined by CAPS-5*

- Recognized as the standard for rating PTSD severity in clinical trials
- Takes into account all four symptom clusters
- Higher Total CAPS-5 score reflects more severe PTSD symptoms

* Clinician-administered PTSD scale for Diagnostic Statistical Manual version 5 (DSM-5)

Impact of PTSD on People

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

PTSD: U.S. Prevalence and Index Traumas

PTSD is a chronic response to traumatic event(s)

- A majority of people will experience a traumatic event at some point in their lifetime[1]
  - 20% of women and 8% of men in the U.S. who experience significant trauma develop PTSD[1]

Adult Civilians:

- *Lifetime prevalence:* 6.1% (14.4 million adults in the U.S.)[2]
  - Persistent - >1/3 fail to recover, even after several years following the trauma[2]

- *Twelve month prevalence:* *U.S.* *4.7%* (12 million adults)[2]
  EU 2.3% (~10.0 million adults)[3]

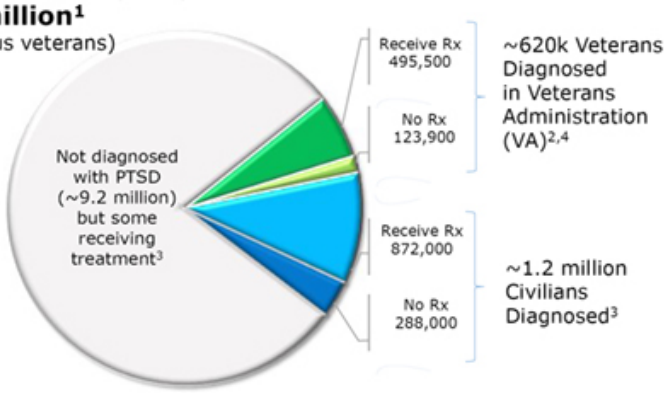
Most common forms of trauma[1]

- 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] Goldstein et al., 2016 (adjusted for 2019)
[3] The European Union Market Potential for a New PTSD Drug. Prepared for Tonix Pharmaceuticals by Procela Consultants Ltd, September 2016

PTSD Prevalence and Market Characteristics

Prevalent Population (U.S.)
~12 million[1]
(civilians plus veterans)



Diagnosed population
Large population (~1.8 million)
Majority receive drug treatment
Civilians: ~75%[3]
Veterans: ~80%[4]

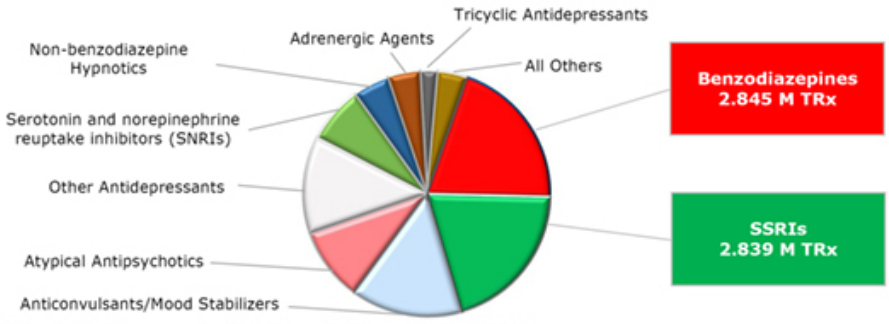
[1] Goldstein et al., 2016 (adjusted for 2019)
[2] Veterans: VA/DOD Clinical Practice Guidelines for the Managements of PTSD and Acute Stress Disorder, 2017, page 15 (619,493 vets diagnosed with PTSD in VA for 2016)
[3] IMS Consulting, *Market Sizing & Treatment Dynamics: Post-Traumatic Stress Disorder (PTSD) Patients"*, 2016
[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?

Market highly fragmented, with benzodiazepines widely prescribed (but not indicated)[1]

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

Estimated PTSD Market Volume (Civilian Population Only) ~14.1 million TRx*[2]



* 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

PTSD: Not Well-Served by Approved Treatments

FDA-approved SSRIs, paroxetine and sertraline, are indicated as a treatment for PTSD

- Neither drug has shown efficacy in military-related PTSD
- Majority of male PTSD patients unresponsive or intolerant to current treatments
- Side effects relating to sexual dysfunction, sleep disturbance and weight gain are commonly reported

Characteristics of an ideal drug therapy that would be compatible and complementary with behavioral therapy

- Lack of retrograde amnesia (e.g., unlike off-label use of benzodiazepines and non-benzodiazepines)
- Lack of interference on sleep (e.g., unlike approved SSRIs)

Tonmya is being investigated in both military and civilian PTSD and is expected to be indicated as a "treatment for PTSD"

Why Initially Targeted Military-Related PTSD?

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)[1]
  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[2]
  Paroxetine: no sex-related difference in treatment outcomes[3]

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

  Sexual dysfunction[2,3]
  Insomnia[2,3]
  SSRI withdrawal syndrome[4]

[1] Friedman et al., J Clin Psychiatry 2007; 68:711
[2] Zoloft Package Insert, August, 2014
[3] Paxil Package Insert, June, 2014
[4] Fava et al., Psychother Psychosom 84:72-81, 2015

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.

Growing Economic and Social Burden to Care for Veterans with PTSD

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[1]

~ 1.9M Veterans out of 2.7M
Service members deployed between 10/1/2001 and 3/31/2015[3]

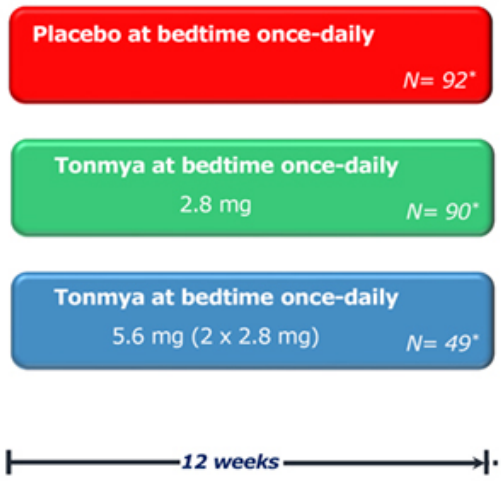
Indirect costs

$2-3 billion
estimated yearly cost to society[2]

Families, social care agencies, schools, employers, welfare system[2]

[1] CBO Report 2012; [2] Tanielan, *Invisible Wounds of War*. 2005; [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; OEF/OIF/OND, Operations Enduring Freedom, Iraqi Freedom and New Dawn.

Phase 2 P201/AtEase[1] Study in Military-Related PTSD



- Randomized, double-blind, placebo-controlled trial in military-related PTSD
- Efficacy analysis from 231* patients; 24 U.S. clinical sites
- Enrolled patients with baseline CAPS-5[2] ≥ 29
- Primary Efficacy Analysis:
  - Difference in CAPS-5 score change from baseline between Tonmya 2.8 mg and placebo at Week 12
- Key Secondary Measures:
  - PROMIS Sleep Disturbance, CGI-I, SDS

[1]ClinicalTrials.gov Identifier: NCT02277704
[2]CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
*Modified intent-to-treat

P201/AtEase Study

P201 was a large adequate well-controlled Phase 2 study in military-related PTSD

- Primary endpoint (Week 12 CAPS-5) did not separate from placebo for TNX-102 SL 2.8 mg
- No safety or tolerability issue discovered
- Retrospective analyses showed TNX-102 SL 5.6 mg had a strong signal of treatment effect at Week 12 CAPS-5 (P=0.053) and CGI-I (P=0.041) scores
- Retrospective analyses suggested CAPS-5 ≥ 33 enrollment criteria for Phase 3

P201/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 (Primary Analysis)	0.259^	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
^Primary analysis p-value not significant comparing Tonmya 2.8 mg versus placebo
*p<0.05

P301/HONOR[1] Study –Evidence of Efficacy at Week 4
Discontinued Due to High Placebo Response at Week 12

General study characteristics:

Randomized, double-blind, placebo-controlled, adaptive design, planned 550 military-related PTSD participants with baseline CAPS-5[2] ≥ 33 in approximately 40 U.S. sites

Tonmya once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets) *N= 125**

Placebo once-daily at bedtime
*N= 127**

12 weeks ⟶ ····· ***12-week and/or 40-week open-label extension studies***

Primary endpoint CAPS-5[2]:

- Mean change from baseline at Week 12 (Tonmya 5.6 mg vs. placebo)

Unblinded interim analysis at 274 randomized participants (mITT* N= 252)

- Study stopped due to not meeting a pre-specified study continuation threshold at Week 12
- Participants discontinued in HONOR or 12-week open-label extension (OLE) studies can enroll in the 40-week OLE study

[1]ClinicalTrials.gov Identifier: NCT03062540
[2]CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
*Modified intent-to-treat

P301/HONOR Study- Primary Analysis in mITT Population

Visit	Placebo N=127		TNX-102 SL 5.6 mg N=125		
Statistic	CAPS-5 Value	MCFB	CAPS-5 Value	MCFB	Difference
Week 4					
LS Mean (SE)	31.0 (1.62)	-11.2 (1.62)	27.5 (1.73)	-14.7 (1.73)	-3.6 (1.51)
95% CI	(27.8,34.2)	(-14.4,-8.0)	(24.1,30.9)	(-18.1,-11.4)	(-6.5,-0.6)
p-value					0.019
Week 8					
LS Mean (SE)	29.4 (1.76)	-12.8 (1.76)	27.6 (1.86)	-14.6 (1.86)	-1.8 (1.77)
95% CI	(25.9,32.8)	(-16.3,-9.4)	(24.0,31.3)	(-18.2,-10.9)	(-5.2,1.7)
p-value					0.321
Week 12					
LS Mean (SE)	28.0 (1.80)	-14.2 (1.80)	27.0 (1.90)	-15.2 (1.90)	-1.0 (1.88)
95% CI	(24.5,31.5)	(-17.7,-10.7)	(23.3,30.8)	(-18.9,-11.4)	(-4.7,2.7)
p-value					0.602

MMRM with Multiple Imputation

In P301 study both TNX-102 SL and placebo-treated groups improved but the greater improvement on TNX-102 SL compared with placebo diminished over time

- TNX-102 SL did not separate from placebo at primary endpoint

LS Mean (SE) = Least Squares Mean (Standard Error)

CI = Confidence Interval

MCFB = Mean Change From Baseline

TNX-102 SL: Sublingual Formulation is Designed for Bedtime Administration

TNX-102 SL: Proprietary sublingual formulation of cyclobenzaprine (CBP) with transmucosal absorption

- Innovation by design with patent protected CBP/mannitol eutectic
- Rapid systemic exposure
- Increases bioavailability during sleep
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, norcyclobenzaprine (norCBP)

CBP undergoes extensive first-pass hepatic metabolism when orally ingested

- Active major metabolite, norCBP[1]
  - Long half-life (~72 hours)
  - Less selective for target receptors (5-$HT_{2A,}$ α_1-adrenergic, histamine H_1)
  - More selective for norepinephrine transporter

TNX-102 SL 505(b)(2) NDA approval can rely on the safety of the reference listed drug (AMRIX®)[2]

[1] Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada
[2] FDA Meeting Minutes (November 26, 2018)

Differences Between P201/AtEase and P301/HONOR Studies Design

Categories	P201	P301
No. of US Sites Randomizing ≥ 1	24	43
No. of Treatment Arms	3	2
Baseline Entry CAPS-5 Threshold	≥ 29	≥33
Range of Includable Ages, years	18-65	18-75
Depression Rating Scale Employed	MADRS	BDI-II
Minimum Time Since No TFT	1 month	3 months
Primary Endpoint Analytic Method	MMRM	MMRM with MI
No. of In-Clinic Study Visits	9	5
No. of CAPS-5 Administrations	6	5
Key Secondary Endpoints	CGI-I, SDS, PROMIS SD	CGI-I, SDS

Phase 2 and 3 studies were very similar – both studied military related PTSD at multiple sites in the US

- CAPS-5 ≥ 33 entry criteria used in Phase 3

BDI-II= Beck Depression Inventory-II; CGI-I=Clinical Global Impression – Improvement; MI= multiple imputation; MMRM=mixed model repeated measures; MADRS=Montgomery-Åsberg Depression Rating Scale; PROMIS SD=Patient-Reported Outcomes Measurement Information System – Sleep Disturbance; SDS=Sheehan Disability Scale; TFT=trauma-focused therapy

P201/AtEase and P301/HONOR Demographics and Characteristics

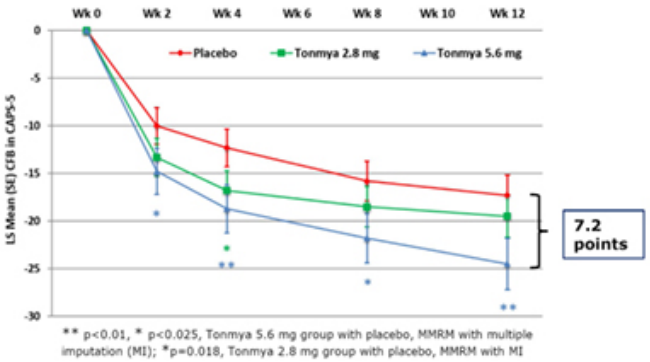
Variable	P201			P301	
	Placebo N=92	TNX 2.8 mg N=90	TNX 5.6 mg N=49	Placebo N=127	TNX 5.6 mg N=125
Females, %	6.50%	6.70%	8.20%	13.40%	8.00%
Age, yrs. (SD)	32.0	34.5	34.8	35.5	35.9
Body Mass Index, kg/m^2	28.9	29.0	29.0	29.3	29.9
Employment (current), %	58.7%	62.2%	67.3%	63.0%	55.2%
Unable to work due to PTSD, %	9.8%	11.1%	14.3%	12.6%	16.8%
Active Duty/Reservists/Veterans, No.	8/4/79	9/5/71	5/7/37	17/0/110	9/0/116
Time since trauma, mean years	7.1	7.3	6.2	9.2	9.2
Time since trauma, median years	7.0	7.2	6.0	9.3	9.5
Combat index trauma, %	80.4%	85.6%	93.8%	77.2%	83.2%
Number of deployments	2.2	2.3	2.6	3.0	2.6
Baseline CAPS-5 Scores	39.5	39.5	39.3	42.4	42.0
Baseline BDI-II Scores	NA	NA	NA	23.0	25.6
Baseline MADRS Scores	17.3	17.6	16.1	NA	NA

The striking difference between P201 and P301 was time since trauma

- Phase 2 P201 study recruited many participants from the surge in Iraq who were mostly <9 years since trauma

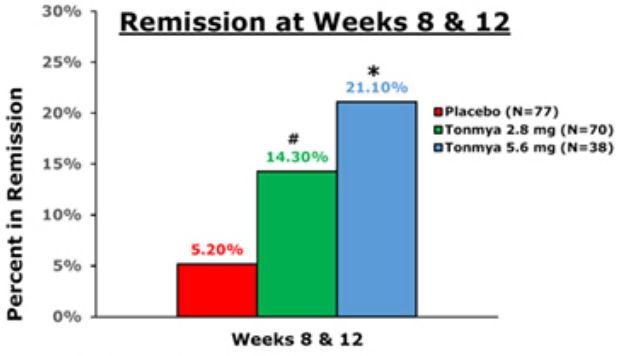
Tonmya Phase 2 Dose-Effect in Military-Related PTSD[1]

PTSD Symptoms (CAPS-5[2] Score)



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

Remission at Weeks 8 & 12



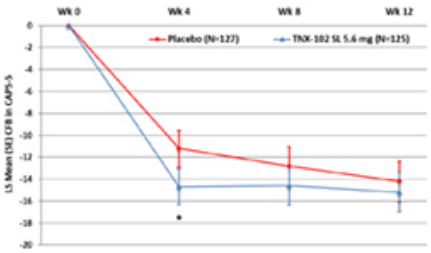
Remission = Loss of Diagnosis and CAPS-5 < 11
Asterisk and hashmark represent pairwise comparisons between Tonmya and Placebo; #p=0.08, Odds Ratio 3.01 (0.89, 10.18)
*p=0.02, Odds Ratio 4.60 (1.27, 16.66); logistic regression

[1]Completed Phase 2 P201/AtEase study: Retrospective analysis of Tonmya 5.6 mg on CAPS-5 ≥33 (high-moderate) subgroup. Primary analysis of P201/AtEase was on Tonmya 2.8 mg in participants with entry CAPS-5 ≥29, moderate PTSD severity.
[2]Clinician administered PTSD Scale for DSM-5

Primary Outcome (CAPS-5) in Phase 3 (mITT) and ≤9 Years Time Since Trauma (TST) Subgroups

Phase 3 P301/HONOR Study[1]

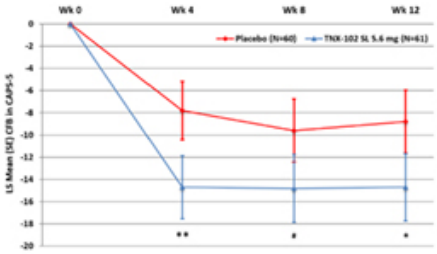
Modified intent to treat (mITT) population



*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

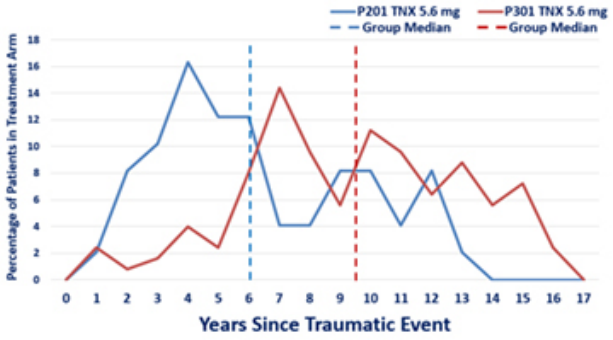
Time Since Trauma ≤9 yrs



**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.

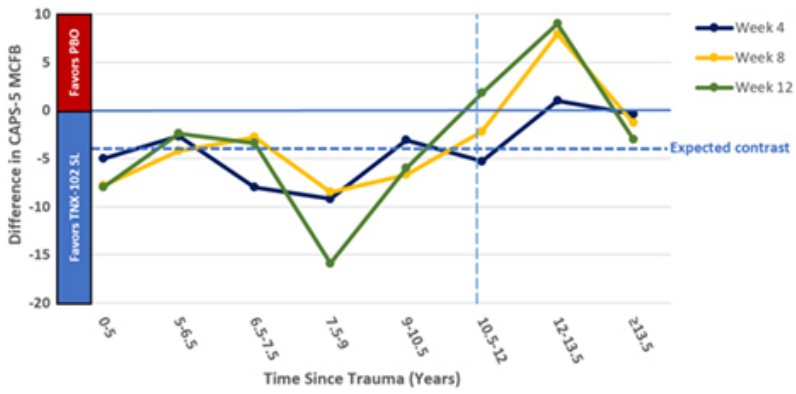
Retrospective Comparison of Time Since Trauma in P201/AtEase versus P301/HONOR (Tonmya 5.6 mg Groups)



P301 study was initiated approximately two years later than Phase 2 P201

- The median time since trauma in Phase 3 was 9.5 years compared to the median time since trauma in Phase 2 of 6.0 years for TNX-102 SL 5.6 mg treated groups

CAPS-5 Mean Change from Baseline Difference from Placebo of Tonmya 5.6 mg in TST Subgroups in P301[1]



Group TST (yrs)	0-5	5-6.5	6.5-7.5	7.5-9	9-10.5	10.5-12	12-13.5	≥ 13.5
Placebo 'N'	12	23	11	13	21	18	13	18
TNX-5.6 mg 'N'	14	17	16	12	22	10	17	18

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

- The mITT population was divided into subgroups based on TST (1.5-2 years each as well as 0-5 years and ≥13.5 years subgroups)
- Graph shows the CAPS-5 differences in MCFB between TNX 5.6 mg and PBO for Weeks 4, 8, and 12 post-baseline timepoints
- "Expected contrast" horizontal dashed line indicates observed effect from Phase 2 P201 study
- For TST <10.5 years groups, TNX 5.6 mg showed good separation from PBO (left side of vertical dashed 10.5 year line)
- For TST >10.5 years groups, separation of TNX 5.6 mg from PBO was either small or worked in the favor of PBO (right side of vertical dashed 10.5 year line)

[1]Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November 1-4, 2018 and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10. https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

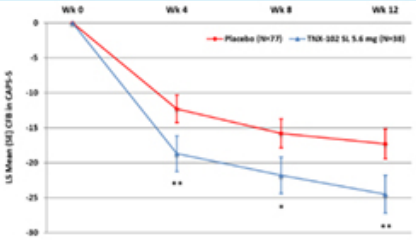
PTSD Treatment Response to Tonmya in Phase 2 and Phase 3 Studies: Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

Change in CAPS-5 over course of treatment with Tonmya

CAPS-5 is a structured interview assessing PTSD severity

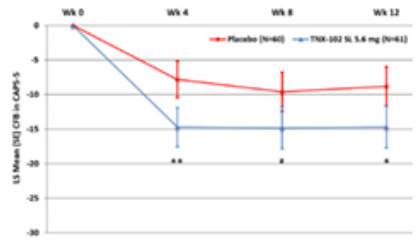
- Required primary endpoint for PTSD drug approval

Decrease in PTSD severity in Phase 3 subgroup ≤9 years since TST is similar to Phase 2 subgroup with baseline CAPS-5 ≥ 33



P201 Baseline CAPS-5 ≥33 *(majority TST[1] ≤9 yr)*

**p<0.01, *p=0.017, TNX-102 SL 5.6 mg group v. placebo, using mixed model repeated measures (MMRM) with multiple imputation (MI)



P301 *TST* ≤9 yr

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

[1]Time since trauma; [2]Majority of P201 participants were ≤9 years since trauma and ~80% of P201 participants and all of P301 participants were ≥33 CAPS-5 at baseline

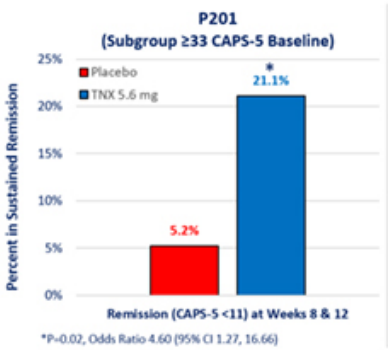
Sustained Remission in Phase 2 and Phase 3 Studies:
Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

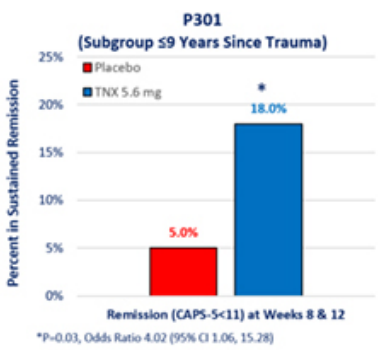
Remission is a clinical state that is essentially asymptomatic

In order to confirm remission:

- Determined rates of participants who met remission status at *both* Week 8 and Week 12

Rate of remission in ≤9 years since trauma group in P301 is similar to baseline CAPS-5 ≥ 33 group in P201[1]





[1]Majority of P201 participants were ≤ 9 years since trauma and ~80% of P201 participants and all of P301 participants were ≥ 33 CAPS-5 at baseline

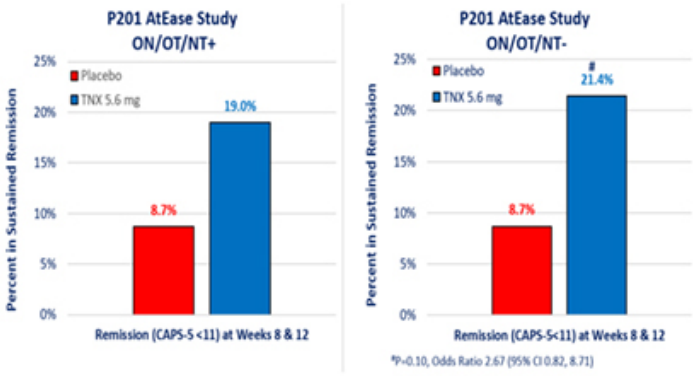
Sustained Remission in P201/AtEase Study Retrospective Analyses of Phase 2 Subgroups with and without Oral AE's (ON/OT/NT)

Oral numbness (ON), oral tingling (OT) and noticeable taste (NT) are local administration site reactions that are potentially unblinding

- Subgroups with and without ON/OT/NT were studied in participants who met remission status at *both* Week 8 and Week 12

Similar rates of remission were observed in participants in P201 with and without oral AE's

- Unblinding was unlikely to account for treatment effect



Retrospective Analyses of ≤9 Years Since Trauma Subgroup on Primary and Secondary Endpoints in P301/HONOR Study

			P301 mITT PBO (N=127) v. TNX-5.6 (N=125)				P301 ≤9 Year Subgroup PBO (N=60) v. TNX-5.6 (N=61)			
			Week 4		Week 12		Week 4		Week 12	
	Measure	Analysis	LSMD	p-value	LSMD	p-value	LSMD	p-value	LSMD	p-value
1°	CAPS-5	MMRM/MI	-3.6	**0.019**	-1.0	0.602	-6.9	**0.004**	-5.9	**0.039**
2°s	CGI-I	MMRM	-0.3	**0.015**	-0.1	0.403	-0.6	**0.002**	-0.5	**0.021**
	SDS	MMRM	-0.2	0.785	-1.6	0.101	-1.8	0.167	-4.3	**0.007**
	PGIC	MMRM	-0.2	0.238	-0.3	**0.020**	-0.4	**0.045**	-0.6	**0.007**
	PROMIS SD	MMRM	-3.1	**0.015**	-2.7	0.082	-4.5	**0.029**	-5.0	**0.042**
	BDI-II	MMRM	-1.1	0.330	-1.4	0.255	-5.2	**0.008**	-6.6	**0.001**

BOLDED p-values are all p<0.05; BDI-II=Beck Depression CAPS-5=Clinician-Administered PTSD Scale for DSM-5; CGI-I=Clinical Global Impression – Improvement scale; mITT=modified Intent-to-Treat sample; MMRM=mixed model repeated measures analysis; MI=multiple imputation; PGIC=Patient Global Impression of Change scale; PROMIS SD=Patient-Reported Outcome Measurement Information System Sleep Disturbance instrument (short form 8a); PBO=placebo; SDS=Sheehan Disability Scale; TNX-5.6=TNX-102 SL 5.6 mg; yrs=years; 1°=primary; 2°s=secondaries

Secondary endpoints also showed strong treatment effects in ≤9 yrs TST

- Support CAPS-5 results and similar to Phase 2 P201 Study results

Retrospective Analyses of ≤9 Years Since Trauma Subgroup on Key Secondary Endpoints in P301/HONOR Study

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

Key secondary endpoints showed strong treatment effects

- CGI-I, PGIC and PROMIS SD were pre-specified secondary analyses
- Supports CAPS-5 results and similar to Phase 2 P201 Study results

CGI-I=Clinical Global Impressions – Improvement scale
PGIC, Patient Global Impression of Change scale
PROMIS SD=Patient-Reported Outcome Measures Information System Sleep Disturbance
SDS=Sheehan Disability Scale
LSMD = Least Squares Mean Difference

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

	P201			P301	
Category of Adverse Reaction Preferred Term	Placebo (N=94)	TNX 2.8 mg (N=93)	TNX 5.6 mg (N=50)	Placebo (N=134)	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 Tonmya

- 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

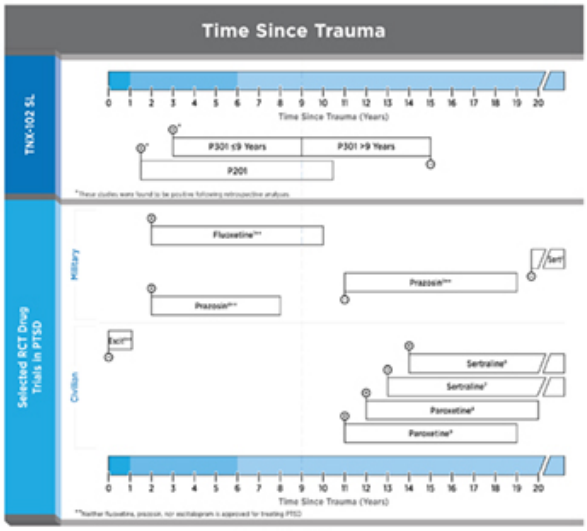
Time Since Trauma – Review of Published Studies

Published studies of prazosin suggested effects in military-PTSD prior to 9 years

- Loss of treatment effect >9 years

Paroxetine and sertraline studies supporting FDA approval were conducted on PTSD > 9 years

- SSRIs have a benefit long after trauma



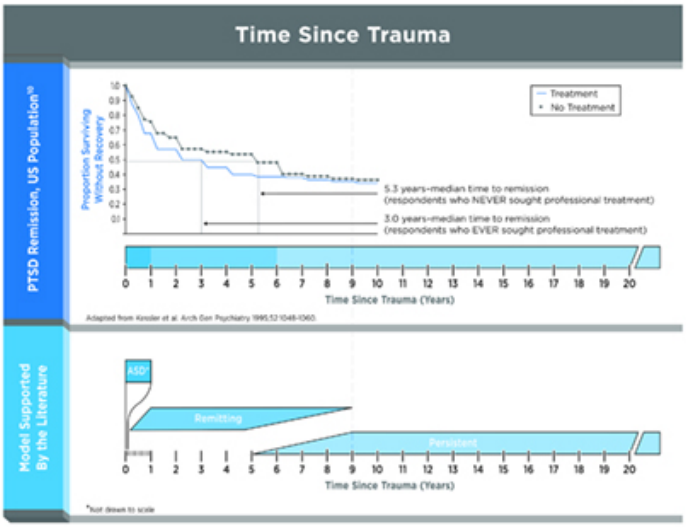
Escit=escitalopram

[1]Martenyi et al. *J Clin Psychiatry* 2002;63:199-206.
[2]Friedman et al. *J Clin Psychiatry* 2007;68:711-720.
[3]Raskind et al. *NEJM* 2018;378:507-517.
[4]Raskind et al. *Am J Psychiatry* 2013;170:1003-1010.
[5]Shalev et al. *Arch Gen Psychiatry* 2012;69:166-176.
[6]Davidson et al. *Arch Gen Psychiatry* 2001;58:485-492.
[7]Brady et al. *JAMA* 2000;283:1837-1844.
[8]Marshall et al. *Am J Psychiatry* 2001;158:1982-1988.
[9]Tucker et al. *J Clin Psychiatry* 2001;62:860-868.

Time Since Trauma – Remitting and Persistent Phases of PTSD

Kessler et al[1] studied remission in PTSD with and without therapy

- Identified remitting and persistent phase of PTSD – with transition at approximately 6 years post trauma
- Supported by other studies[2-6]



[1]Kessler et al. *Arch Gen Psychiatry* 1995;52:1048-1060.
[2]Armenta et al. *BMC Psychiatry* 2018;18:48.
[3]Galatzer-Levy et al. *PLOS ONE* 2013;8:e70084.
[4]Perkonigg et al. *Am J Psychiatry* 2005;162:1320-1327.
[5]Santiago et al. *PLOS ONE* 2013;8:e59236.
[6]Davidson & Connor. *Eur Neuropsychopharmacol* 2001;11(Supp3):S148-S149.

Response to Tonmya for Female Participants in P301/HONOR Study[1]

Females made up only 11% of the P301/HONOR study mITT population

Difference in mean change from baseline in CAPS-5 in females between placebo (N=17) and Tonmya 5.6 mg (N=10) was:

- At 4 weeks -11.5 points
- At 12 weeks -9.1 points

Indicates substantial separation from placebo in the small number of female participants

Predicts therapeutic response to Tonmya 5.6 mg likely in mixed civilian and military PTSD population to be studied in upcoming P302/RECOVERY trial

- Civilian PTSD population tends to be about 2/3 female

[1]*Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November 1-4, 2018 and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.* https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

Response to Tonmya for Non-Combat Traumas in P301/HONOR Study in ≤9 Years Time Since Trauma Subgroup[1]

Non-combat traumas studied are similar to traumas experienced in civilian populations with PTSD

To determine the therapeutic effects of Tonmya 5.6 mg in a mixed civilian and military population, difference in MCFB in CAPS-5 was assessed in non-combat traumas in ≤9 years TST subgroup (placebo N=14, Tonmya 5.6 mg N=10):

- At 4 weeks -4.8 points
- At 12 weeks -4.4 points

Non-combat traumas treated with Tonmya 5.6 mg showed clinically meaningful separation from placebo at Weeks 4 and 12, suggesting a mixed civilian and military sample within 9 years of index trauma may show a therapeutic response to Tonmya

[1]*Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November, 2018; and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.*https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

CAPS-5=Clinician-Administered PTSD Scale for DSM-5; MCFB=mean change from baseline; mITT=modified Intent-to-Treat sample; TST=time since trauma

Summary of Clinical Experience with Tonmya/ TNX-102 SL in PTSD

Median time since trauma (TST) in TNX-102 SL 5.6 mg group in the P301/HONOR study (9.5 years) was longer than P201/AtEase study (6 years)

- Both studied military-related PTSD
- Time has passed since the surge in Iraq

In retrospective analysis, the ≤ 9 year subgroup of P301 study had similar results as the P201 study (primary and secondary)

- TST is important in placebo-controlled clinical study
- Potential enrichment in ≤ 9 years TST subgroup for treatment responders

The ≤ 9 year subgroup of P301 may be enriched for "Remitting Phase" of PTSD[1-4]

- Expect remitting phase of PTSD is more amenable to drug studies

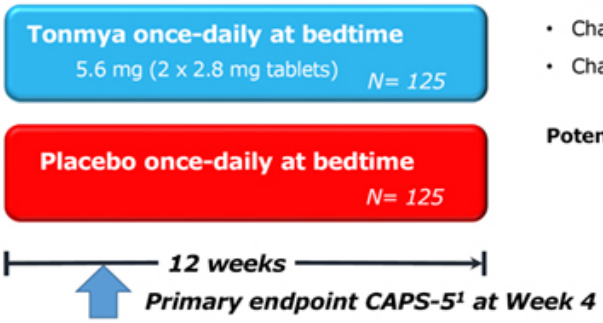
Results from retrospective analyses lead to improved Phase 3 study design

[1]Kessler et al. *Arch Gen Psychiatry* 1995;52:1048-1060.
[2]Armenta et al. *BMC Psychiatry* 2018;18:48.
[3]Galatzer-Levy et al. *PLOS ONE* 2013;8:e70084.
[4]Perkonigg et al. *Am J Psychiatry* 2005;162:1320-1327.

New Phase 3 P302/RECOVERY Study – Initiated 1Q 2019

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 (Tonmya 5.6 mg vs. placebo)

Key Secondary endpoints include:

- CAPS-5 mean change from baseline at Week 12 (Tonmya 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

Late-Stage PTSD Drug Candidates

Tonmya

- Phase 3 development focused on military-related and civilian PTSD; showed activity in treatment of military-related PTSD in large multi-center trials

MDMA-assisted psychotherapy

- Breakthrough therapy that is Phase 3-ready; showed activity in a Phase 2 study of PTSD; enrolling in Phase 3

Other drugs currently (or recently) in Phase 2 development

- Rexulti® (brexpiprazole) - Otsuka/Lundbeck; atypical antipsychotic; positive clinical results from Phase 2 study reported in November 2018 for brexpiprazole, when used in combination with an approved PTSD medication, sertraline, but not as monotherapy
- NYX-783 - Aptinyx; NMDA receptor modulator (enrolling for 8-week Phase 2 study of 144 patients using 50 mg either once daily or once weekly)
- BNC-201 – Bionomics; nicotinic receptor modulator (program planned to resume after reformulation)

Commercialization Options

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

Tonix has participated in numerous partnering meetings

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 – Multi-Functional Mechanism Involves Antagonism at 3 Neuronal Receptors

Active ingredient, cyclobenzaprine, interacts with 3 receptors

- Antagonist at 5-HT_{2A} receptors
  - Similar activity to trazodone and Nuplazid® (pimivanserin)
- Antagonist at α_1-adrenergic receptor
  - Similar activity to prazosin
- Antagonist at histamine H_1 receptors
  - Similar activity to Benadryl® (diphenhydramine) and hydroxyzine

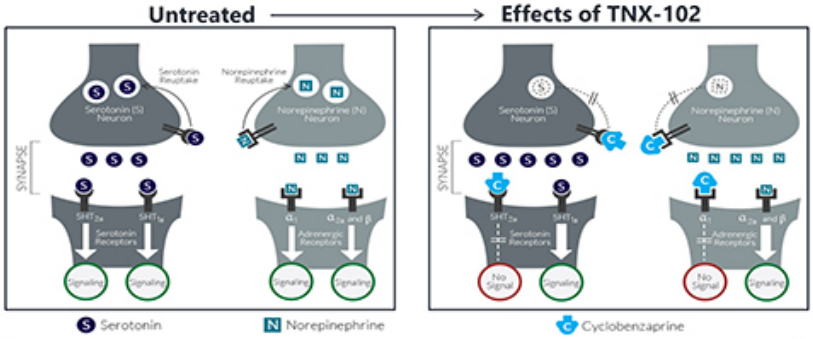
Multi-functional activity suggests potential for other indications

- TNX-102 SL was developed for the management of fibromyalgia (Phase 3)
- Sleep quality is a problem in other conditions

Cyclobenzaprine Effects on Nerve Cell Signaling

Cyclobenzaprine is a multi-functional drug - SNARI

- inhibits serotonin and norepinephrine reuptake
- blocks serotonin 5-HT_{2A} and norepinephrine α_1 receptors

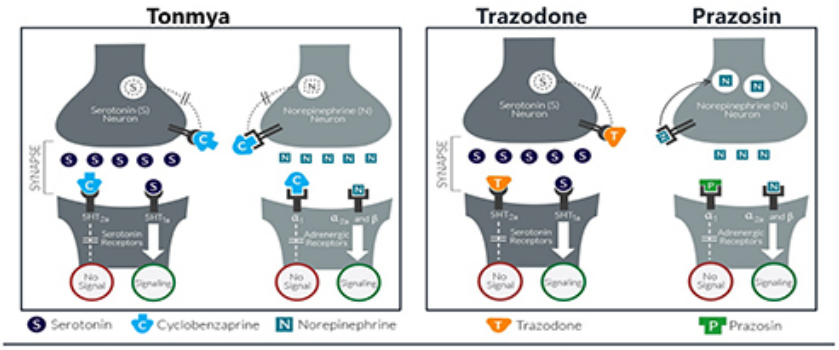


SNARI = Serotonin and Norepinephrine receptor Antagonist and Reuptake Inhibitor

Comparison of Tonmya with Drugs Used Off-Label in PTSD

Trazodone (disordered sleep), prazosin (night terrors)

- Trazodone inhibits serotonin $5HT_{2A}$ receptors and serotonin reuptake (SARI)
- Prazosin blocks norepinephrine α_1 receptors



SARI – Serotonin Receptor Antagonist & Reuptake Inhibitor (Stahl SM, CNS Spectrums, 2009;14:536).

Opportunities to Expand to Other 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

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

Growing recognition that there are many disorders where sleep disturbances may have a role in the pathophysiology (cardiovascular, metabolic, neurologic)

- Homeostatic role of sleep quality *in several disorders*

TNX-102 SL – Bedtime Treatment for Multiple Potential Indications

Management of Fibromyalgia (FM) – chronic pain condition

- TNX-102 SL studied at low dose (2.8 mg) – half the dose being developed for PTSD – did not separate from placebo on primary endpoint, average pain improvement (responder analysis)
- Retrospective analysis showed average pain improvement (secondary endpoint) after 12 weeks of treatment showed statistical significance (P< 0.05, MMRM)
- Low dose TNX-102 SL (2.8 mg) showed an improvement in sleep quality in Phase 2 and Phase 3 FM trials
- Efficacy of TNX-102 SL 5.6 mg in FM can be studied in a potential pivotal study to support product registration

Agitation in Alzheimer's Disease

- Fast Track designation granted July 2018
- Phase 2/ potential pivotal efficacy study protocol received FDA comments in October 2018

What is Agitation in Alzheimer's Disease?

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, and this number is expected to nearly triple by 2050[4]

[1]Rose, K.et al. (2015). *American Journal of Alzheimer's Disease & Other Dementias*, *30*:78
[2]Shih, 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/

Consequences of Agitation in Alzheimer's Disease

Outcomes

- Agitation is associated with significant poor outcomes for Alzheimer's patients and challenges for their caregivers

Common reason for institutionalization

- Development of agitation, or its worsening, is one of the most common reasons for patients having to transition from lower- to higher levels of care (nursing homes and other long-term care settings)[1]

Cost

- The presence of agitation nearly doubles the cost of caring for patients with Alzheimer's disease, and agitation is estimated to account for more than 12% of the healthcare and societal cost of Alzheimer's disease, which is currently estimated to be $256 Billion for the year 2017 in the United States[1]

[1]The Alzheimer's Association, 2017 Alzheimer's Disease Facts and Figures: https://www.alz.org/facts/

Agitation in Alzheimer's Disease – Additional Indication Being Developed for TNX-102 SL

FDA designated Fast Track development program

Significant unmet need

- No FDA approved drugs for the treatment of agitation in Alzheimer's

Mechanism of improving sleep quality

- Sleep disturbance is a significant and common symptoms in Alzheimer's

Pharmacological advantages outweigh potential concerns of using TNX-102 SL in treating agitation in Alzheimer's disease

- Blocks 3 receptors, not just one (e.g., 5-HT_{2A})

TNX-102 SL for Agitation in Alzheimer's – Regulatory Status and Registration Strategy

FDA confirmed no additional study was needed prior to IND submission

- Pre-IND meeting established open dialogue with the FDA on pivotal clinical study design and efficacy endpoints to support product registration

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

- FDA comments on final protocol received October 2018

Registration Strategy of TNX-102 SL for agitation in Alzheimer's disease

- Efficacy Supplement (sNDA[1]) may be leveraged from the PTSD/FM development program and supported by Initial NDA approval for PTSD/FM

[1]Supplemental New Drug Application

TNX-102 SL Potentially Addresses Some of the Challenges in Treating Agitation in Alzheimer's

Sublingual route of administration (no swallowing)

- Swallowing can be an issue for a significant number of Alzheimer's patients

Low dose taken daily at bedtime

- Potentially minimize daytime anticholinergic side effects → improved tolerability and patient compliance

Role of sleep in clearing debris from the brain

- Animal studies have shown debris clearance from the brain during sleep including toxic proteins associated with Alzheimer's progression[1]

[1]T Xie L, et al. Science. (2013);342(6156):373

Scientific Rationale for Developing TNX-102 SL for Agitation in Alzheimer's Disease

Connection between Sleep Disturbance and Agitation

- Agitation in Alzheimer's Disease is associated with sleep disturbance[1,2]
- Evidence that improving sleep could improve agitation[3]

Supported by Potential Mechanism of Action

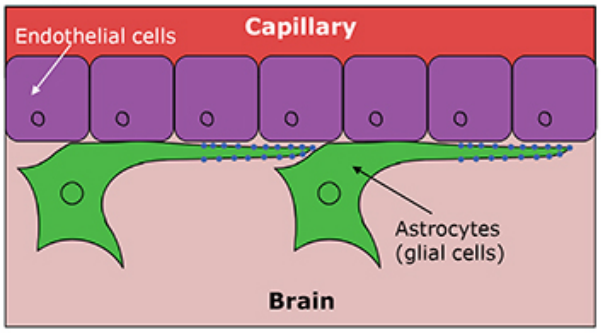
- TNX-102 is a multifunctional agent including antagonism of 5-HT_{2A}, α_1-adrenergic and histamine H_1 receptors
- Certain 5-HT_{2A} antagonists have shown clinical efficacy against agitation in dementia including trazodone[4,5], and mirtazapine[6]
- The α_1-adrenergic antagonist prazosin has shown efficacy in the treatment of agitation in dementia[7]
- The histamine H_1 antagonist hydroxyzine had historical use in treating agitation in dementia[8]

[1]Bachmen, D. and Rabins, P. Annu Rev Med. 2006;57:499.
[2]Rose, K et al. Am J Alzheimers Dis Other Demen. 2015 30(1):78.
[3]Figueiro MG Sleep Med. 2014 15(12):1554-64.
[4]Lebert F. et al. Dement Geriatr Cogn Disord. 2004:17(4):355.
[5]Sulzer DL et al.Am J Geriatr Psychiatry. 1997 5(1):60.
[6]Cakir S. et el., Neuropsychiatr Dis Treat. 2008 4(5):963.
[7]Wang, LY et al., Am J Geriatr Psychiatry. 2009 17(9):744
[8]Settel E. Am Pract Dig Treat. 1957 8(10):1584.

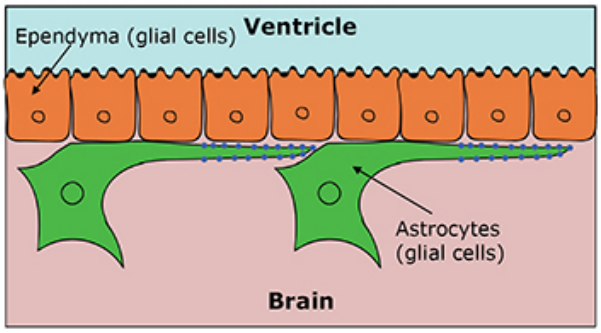
Protective Barriers in the Central and Peripheral Nervous Systems

Glial cells are cells that reside in the central nervous system and can provide protective barriers between the central and peripheral nervous systems[1,2]

Blood–Brain Barrier:
supplies nutrients to the brain and filters toxins[1]



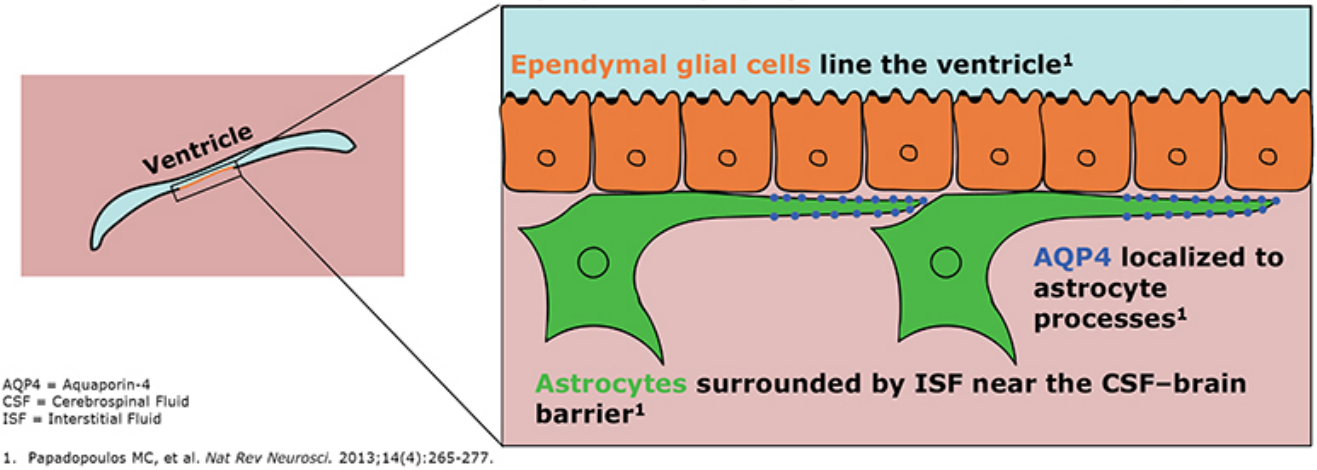
Cerebrospinal Fluid (CSF)–Brain Barrier/Glymphatic System:
extracts toxins from the brain[2]



1. Ballabh P, et al. *Neurobiol Dis.* 2004;16(1):1-13.
2. Jessen NA, et al. *Neurochem Res.* 2015;40(12):2583-2599.

During Wakefulness, Proteins Linked to Neuronal Death and Neurodegeneration Accumulate in the Brain's Extracellular Space

The pathways of interchanging CSF and ISF depend on aquaporin-4 (AQP4) water channels on astrocytes[1]

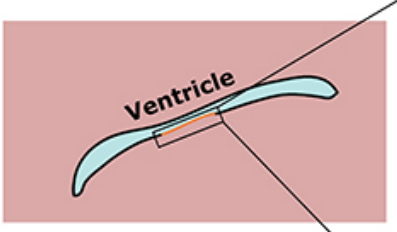


AQP4 = Aquaporin-4
CSF = Cerebrospinal Fluid
ISF = Interstitial Fluid

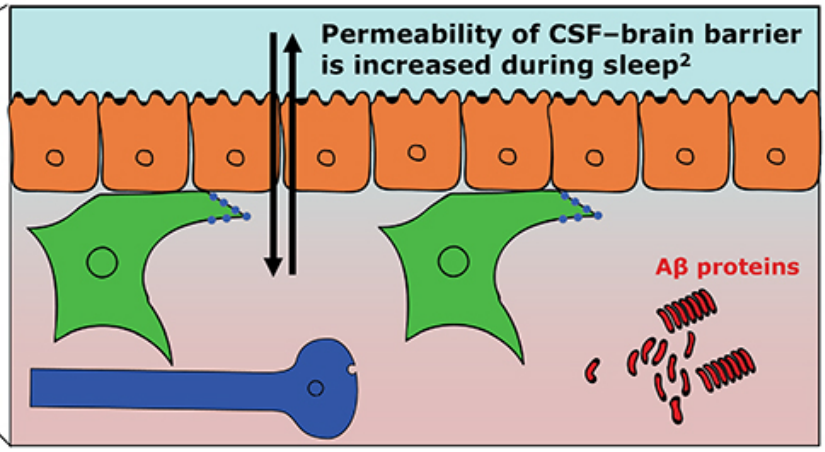
1. Papadopoulos MC, et al. *Nat Rev Neurosci.* 2013;14(4):265-277.

During Sleep, the CSF–Brain Barrier Is More Permeable, Allowing Debris to Clear

Extracellular volume increases during sleep[2]



Astrocytes change shape, promoting fluid exchange[1]



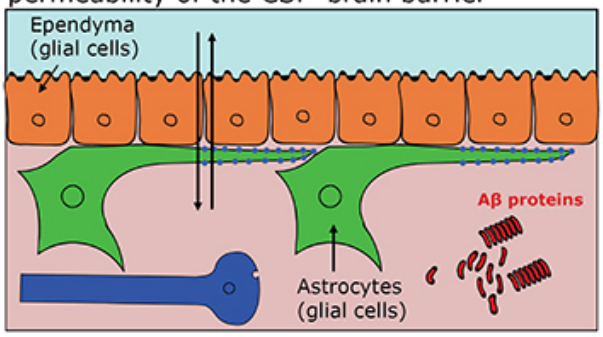
Aβ = β-amyloid
CSF = Cerebrospinal Fluid

1. Bellesi M, et al. *BMC Biol.* 2015;13:66.
2. Xie L, et al. *Science.* 2013;342(6156):373-377.

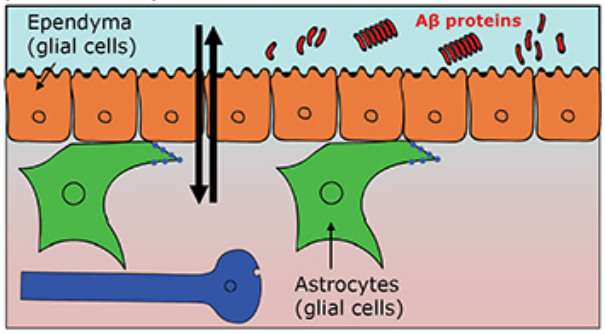
Sleep–Wake Cycles Alter Permeability of the CSF–Brain Barrier

Fluid exchange at the CSF–brain barrier allows for clearance of toxic proteins called β–amyloids (Aβ).[1] Glial cells in the brain work to facilitate this fluid exchange.[2] Sleep–wake cycles alter glial cell morphology, which may affect fluid exchange at the CSF–brain barrier.[3]

Wakefulness:
Fluid exchange is reduced due to limited permeability of the CSF–brain barrier[1]



Sleep:
Fluid exchange is increased due to greater permeability of the CSF–brain barrier[1]



1. Xie L, et al. *Science.* 2013;342(6156):373-377. 2. Papadopoulos MC, et al. *Nat Rev Neurosci.* 2013;14(4):265-277.
3. Bellesi M, et al. *BMC Biol.* 2015;13:66.

Agitation in Alzheimer's – Competitive Landscape of Select Drugs in Development

Competitive landscape

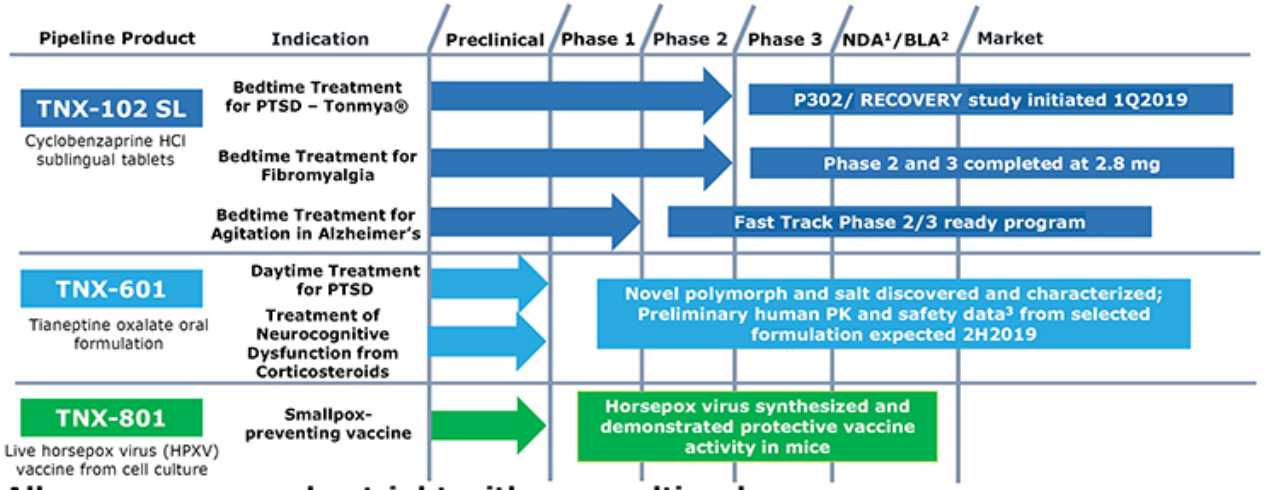
- $5HT_{2A}$ Antagonists/inverse agonists
  - Nelotanserin (Axovant)
- Atypical Antipsychotics (also have $5HT_{2A}$ antagonism)
  - Rexulti® brexpiprazole (Otsuka/Lundbeck)
  - Lumateperone (Intra-Cellular)
- Dextromethorphans – believed to act as SSRI, glutamate/NMDA and sigma-1 receptor modulators
  - Deudextromethorphan (Avanir/Otsuka) - deuterated version of Nuedexta®
  - Dextromethorphan/bupropion (Axsome Therapeutics)

TNX-102 SL uniquely designed for bedtime dosing and transmucosal absorption

- Maximize drug exposure during sleep → improving sleep quality
- Other 5-HT_{2A} antagonists not designed for bedtime sublingual dosing

NDA approval can rely on reference listed drug (AMRIX) safety information

Candidates in Development



All programs owned outright with no royalties due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³non-IND study

TNX-601 (Tianeptine Oxalate): A Potential Clinical Candidate for PTSD

Pre-IND Candidate

Targeting a Condition with Significant Unmet Need

Targeted as a 1st line monotherapy for PTSD: oral formulation for 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
- Preliminary human pharmacokinetic and safety data (non-IND study) from selected formulation expected in second half 2019

Filed patent application on novel salt polymorph

- Issued patent on steroid-induced cognitive impairment and memory loss issues

Clinical evidence for PTSD

- Several studies have shown tianeptine to be active in the treatment of PTSD[1-4]

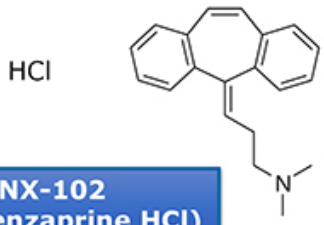
[1] Frančišković T, et al. Psychiatr Danub. 2011 Sep;23(3):257-63. PMID: 21963693
[2] Rumyantseva GM and, Stepanov AL. Neurosci Behav Physiol. 2008 Jan;38(1):55-61. PMID: 18097761
[3] Aleksandrovskii IA, et al. Zh Nevrol Psikhiatr Im S S Korsakova. 2005;105(11):24-9. PMID: 16329631 [Russian]
[4] Onder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

Structural Comparison: TNX-102 and TNX-601

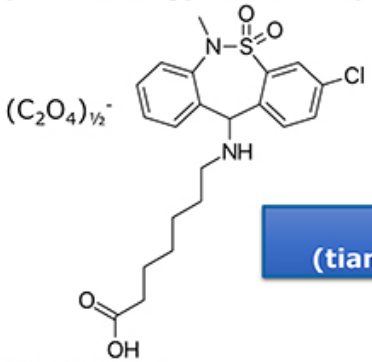
Cyclobenzaprine and tianeptine share structural similarities with classic tricyclic antidepressants (TCAs) and to each other, but each has unique pharmacological properties

- 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 (cyclobenzaprine HCl)



TNX-601 (tianeptine oxalate)

TNX-801 (Synthesized Live Horsepox Virus): A Smallpox-Preventing Vaccine Candidate

Pre-IND Stage

Potential improvement over current biodefense tools against smallpox

- ✓ Leverages Tonix's government affairs effort
- ✓ Collaboration with Professor David Evans and Dr. Ryan Noyce at University of Alberta
- ✓ Demonstrated protective vaccine activity in mice
- ✓ Patent application on novel vaccine submitted

Regulatory strategy

- We intend to meet with FDA to discuss the most efficient and appropriate investigational plan to support the licensure, either:
  - ✓ Application of the "Animal Rule", or
  - ✓ Conducting an active comparator study using ACAM2000
- Good Manufacturing Practice (GMP) viral production process in development

Targeting a Potential Public Health Issue

Material threat medical countermeasure under 21st Century Cures Act

- Qualifies for **Priority Review Voucher (PRV)** upon licensure*
  - ✓ **PRVs have no expiration date, are transferrable and have sold for ~$125 M**

*BLA/NDA priority 6-month review is expected.

TNX-801 (Synthesized Live Horsepox Virus): A Smallpox-Preventing Vaccine Candidate

Synthesis[1] from sequence of a 1976 Mongolian isolate[2]

In mice, TNX-801 behaved like attenuated vaccinia virus

- Vaccinia is the term used to classify the live poxviruses that are used as smallpox vaccines, including ACAM2000, which is the latest smallpox vaccine licensed in the U.S.

How is HPXV related to modern vaccines?

- Multiple sources[3-5] indicate that the smallpox vaccine discovered by Dr. Edward Jenner in the early 19th century was either HPXV or a very similar virus and that vaccinia vaccines are derived from this ancestral strain
- A 1902 U.S. smallpox vaccine was found to be highly similar (99.7% similarity in core genome[6]) to HPXV sequence from the 1976 Mongolian isolate
- Horsepox is now believed to be extinct[5]

[1] Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453 https://doi.org/10.1371/journal.pone.0188453
[2] Tulman et al., Journal of Virology, 2006; 80(18): 9244-9258
[3] Qin et al., Journal of Virology, 2011; 85(24):13049-13060
[4] Medaglia et al., Journal of Virology, 2015; 89(23):11909-11925
[5] Esparza J. Veterinary Record. 2013; 173: 272-273
[6] Schrick, L. et al. , N Engl J Med 2017; 377:1491-1492, http://www.nejm.org/doi/full/10.1056/NEJMc1707600

The Currently Licensed Smallpox Vaccine ACAM2000 is a Live Vaccinia Virus (VACV) Vaccine

ACAM2000 is sold to the U.S. Strategic National Stockpiles[1]

- Sold by Emergent BioSolutions
- Sanofi divested ACAM2000 to Emergent BioSolutions in 2017 for $97.5 M upfront plus milestones
- ACAM2000 was developed by Acambis which was acquired by Sanofi in 2008 for $513 M

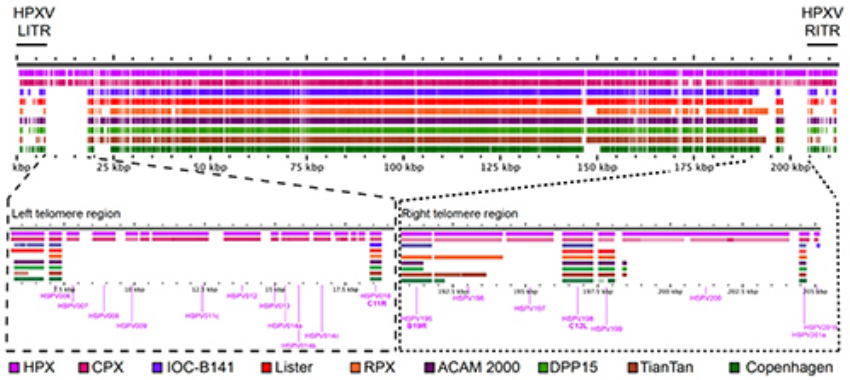
Vaccinia (VACV) strains have demonstrated potential for zoonotic infections and re-infection of humans[2-5]

- No known evidence for zoonosis of ACAM2000, but it has not been widely administered

Modern VACV smallpox vaccines are associated with cardiotoxicity[6]

[1]Nalca, A et al. Drug design, development and Therapy. (2010) 4:71-79
[2]Medaglia MLG, et al. J Virol. (2015) 89:11909 –11925. doi:10.1128/JVI.01833-15.
[3]Trindade,GS. et al. Clinical Infectious Diseases. (2009) 48:e37–40
[4]Leite,JA, et al. Emerging Infectious Diseases. (2005) www.cdc.gov/eid • Vol. 11, No. 12
[5]Medaglia MLG, et al. Emerging Infectious Diseases (2009) www.cdc.gov/eid • Vol. 15, No. 7
[6]Engler RJM et al., PloS ONE (2015) 10(3): e0118283. doi:10.1371/journal.pone.0118283

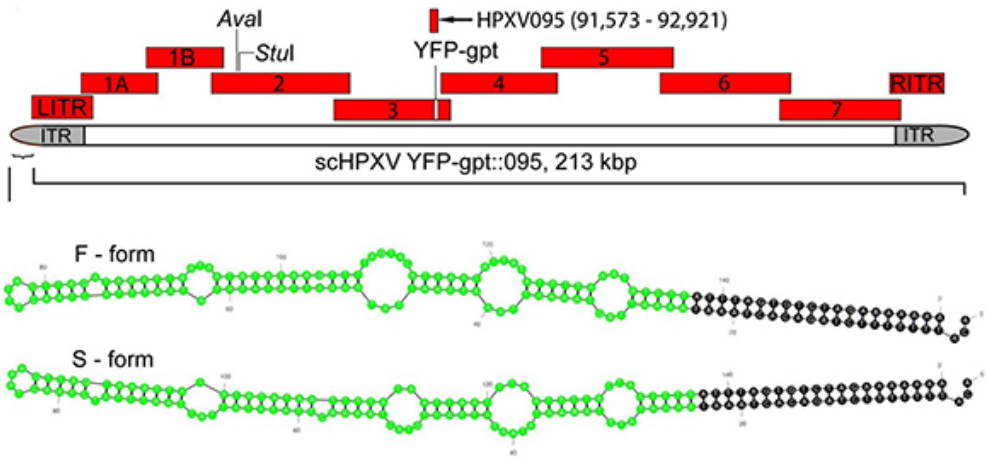
HPXV and its Relationship to Other Orthopoxviruses



HSPV074 – fragmented homolog of VACV I4L (ribonucleotide reductase)
HSPV200 – 216 kDa protein probably regulates T-cell activation with homologs still present in variola, cowpox, and monkeypox viruses

Evans, D. U. of Alberta (2018) with permission

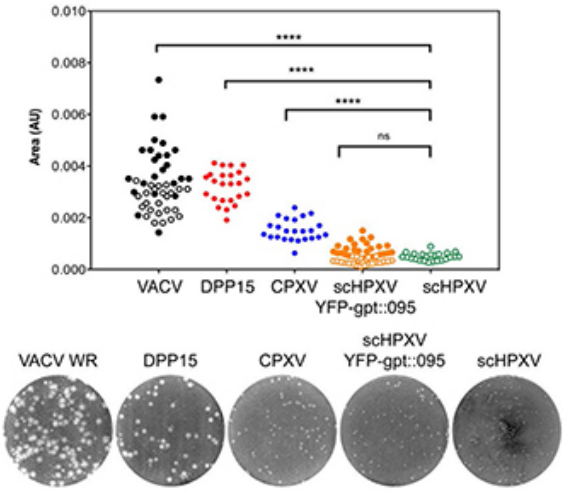
Genome Assembly (212 kbp) by Synthesis of Fragments and Construction of Telomeres



Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Sequence: GenBank entry DQ792504; DNA: GeneArt

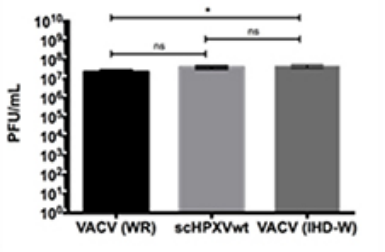
HPXV Produces Small Plaques that are More Like Cowpox Than Vaccinia (VACV)



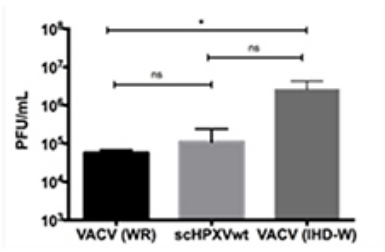
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Production of Cell-Associated and Extracellular Virus

Cell-associated virus

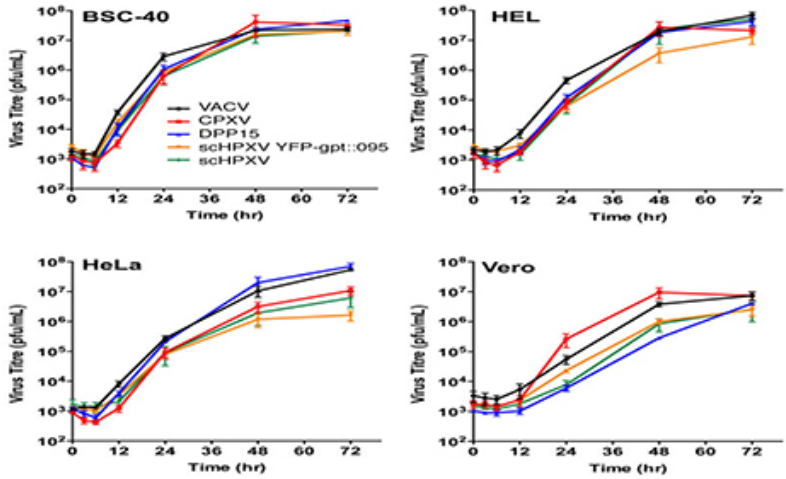


Virus in the media



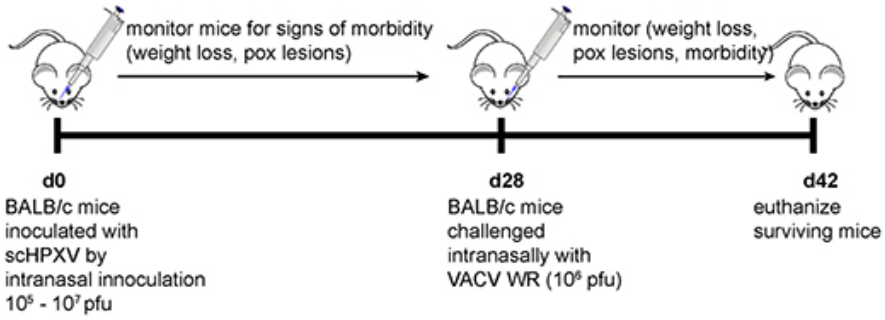
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

HPXV Growth Characteristics



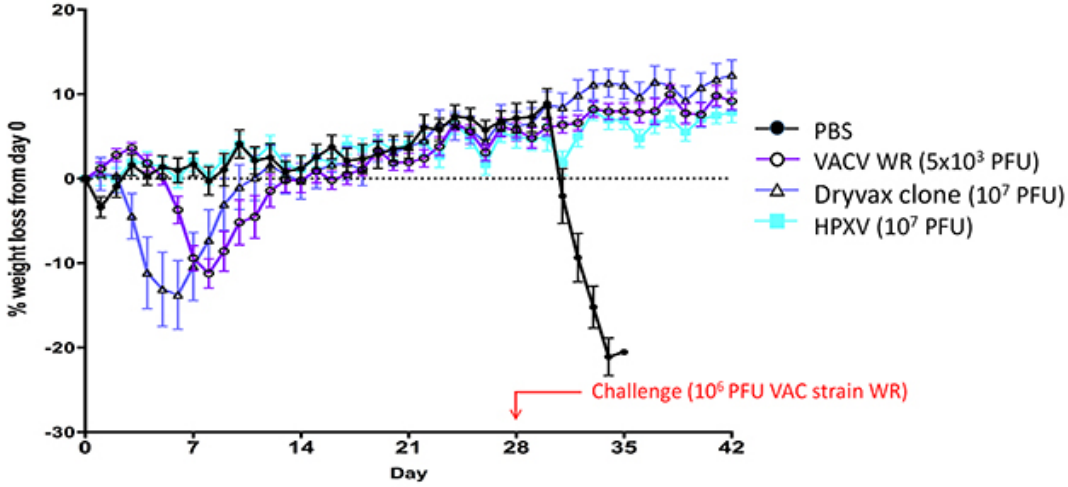
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Testing Vaccine Protective Activity of HPXV in Mice Model



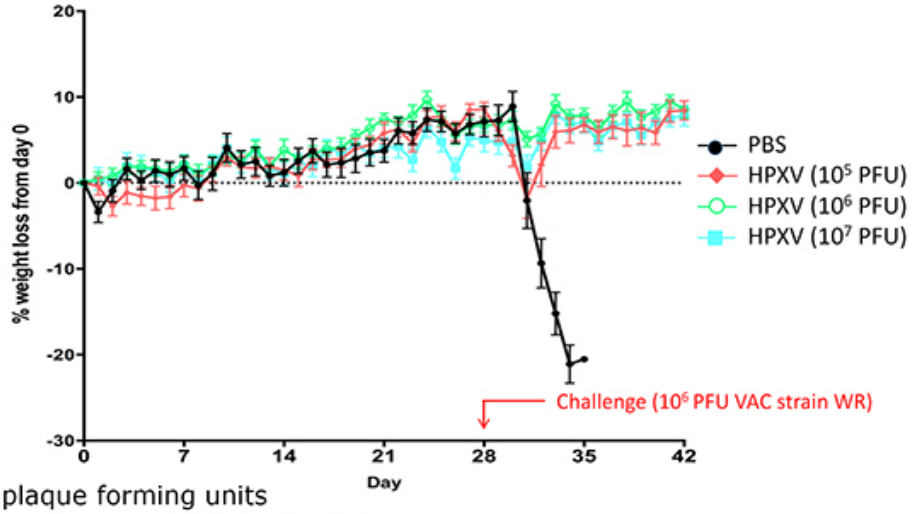
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Biological Properties of HPXV: Less Virulent than a Dryvax Clone, but Produces Protective Immunity



Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

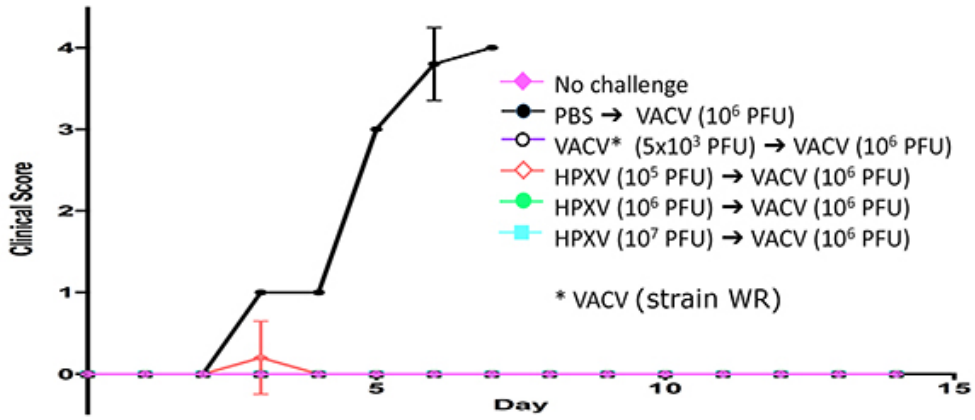
HPXV Vaccine Protection Activity Observed As Low As 10^5 PFU*



*PFU = plaque forming units

Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

No Overt Clinical Sign Observed in HPXV Vaccinated Mice After VACV Challenge



Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

HPXV or TNX-801– May Have an Improved Safety Profile as a Smallpox Preventing Vaccine

Horsepox is caused by HPXV and is characterized by mouth and skin eruptions

HXPV isolate from the 1976 outbreak later sequenced

Modern smallpox vaccines are associated with cardiotoxicity[1]

HPXV has potential for slower proliferation leading to possibly decreased toxicity[2]

[1] Engler RJM et al., PloS ONE 10(3): e0118283. doi:10.1371/journal.pone.0118283 (2015)
[2] Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453 https://doi.org/10.1371/journal.pone.0188453

An Improved Smallpox-Preventing Vaccine is Important and Necessary for a Potential Public Health Issue

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 reservoir

Stockpiles of smallpox-preventing vaccines are currently maintained and refreshed in case of need

Current Needs to Vaccinate Against Smallpox

Ongoing vaccination of U.S. troops

- Troops in the Global Response Force

Threat of smallpox re-introduction

- Strategic National Stockpile & public health policy

Re-emergence of monkey pox[1]

- Believed to resurgent because of vaccinia-naïve populations in Africa
- Multiple U.S. military operations ongoing in Africa

[1]Nda- Isaiah, J. Nigeria: Monkey Pox Scourge Spreads to Seven States. All Africa. 12 OCTOBER 2017, HTTP://ALLAFRICA.COM/STORIES/201710120177.HTML

TNX-801: A Potential Medical Countermeasure

21st Century Cures Act (2016), Section 3086

- Encouraging treatments for agents that present a national security threat

Medical countermeasures are drugs, biologics (vaccines) or devices intended to treat:

- Biological, chemical, radiological, or nuclear agents that present a national security threat
- Public health issues stemming from a naturally occurring emerging disease or a natural disaster

New Priority Review Voucher program for "Material Threat Medical Countermeasures"

- Priority Review Voucher may be transferred or sold

TNX-801 (Synthesized Live Horsepox Virus): A Smallpox-Preventing Vaccine Candidate

TNX-801 (HPVX)

- Synthesized live horsepox virus
- Shares structural characteristics with vaccinia-based smallpox vaccines
- Unique properties that suggest lower toxicity

Mechanism of Action

Live virus vaccines stimulate cross-reactive immunity

- Protects from possible infection with smallpox virus
- Renders recipient "immune"
- Provides indirect protection to non-immunized population "herd immunity"

Possible advantages of TNX-801

Potential safety improvement over existing vaccines

- Cardiotoxicity limits widespread smallpox vaccination in at-risk population

Exclusivity

- Patent application filed on novel virus composition
- 12 years exclusivity can be anticipated

Eligibility for Priority Review Voucher upon licensure if accepted as medical counter-measure

Evidence of Effectiveness for Smallpox Vaccine

Given that smallpox is eradicated the only evidence of effectiveness for modern vaccines is from historical use when smallpox was endemic

- Stimulates interest in the evolution of vaccinia

Vaccinia stocks around the world diverged from Jenner's 1798 vaccine

- Evolutionary argument that common progenitor was horsepox or a similar virus

U.S. vaccine from 1902 was found to be 99.7% similar to horsepox in core viral sequence[1]

- Strong evidence linking a horsepox-like virus as progenitor to modern vaccinia
- Effectiveness of older vaccines support belief that HPXV will be protective against smallpox

[1]Schrick, L. et al (2017) An Early American Smallpox Vaccine Based on Horsepox N Engl J Med 2017; 377:1491

ACAM2000[1] – Best Technology of its Time

Single clone picked from "swarm" of Dryvax®[1]

- Some rationale for selection[2]

Growth in serum free Vero cells

- Eliminates risk of Bovine Spongiform Encephalopathy (BSE)/prion contamination – safety concerns in Wyeth's Dryvax (grown in calf lymph)

In 2000, the evolutionary connection between vaccinia and horsepox was not understood

- Tulman's sequence of horsepox was published in 2006[3]

[1]US licensed smallpox preventing vaccine – ACAM2000 is currently marketed, Dryvax has been withdrawn from marketing
[2]Monath, TP et al. Int. J. of Inf. Dis. (2004) 8S2:S31
[3]Tulman, ER. Genome of Horsepox Virus J. Virol. (2006) 80(18) 9244

Rationale for Developing a Potentially Improved New Smallpox Vaccine

Toxicity concern of modern vaccinia (VACV) vaccines limit wildly administration

- Not recommended for use, even in first responders
- U.S. soldiers in the Global Response Force are immunized

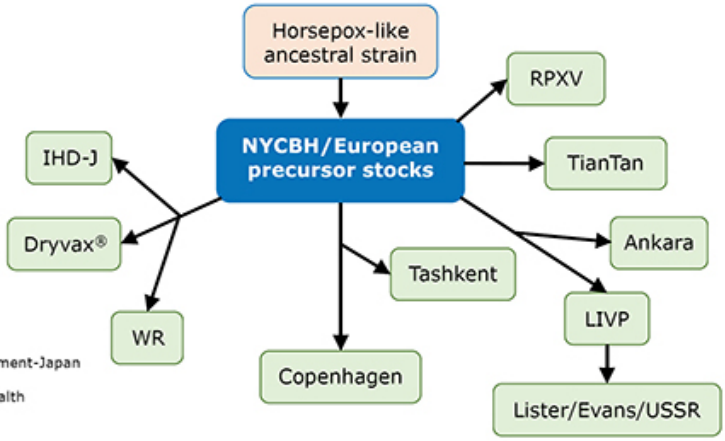
Modern VACV vaccination safety studied in 1081 VACV (Dryvax [62.5%] and ACAM2000 [37.5%]) vaccinees[1]

- New onset chest pain, dyspnea and/or palpitations 10.6% of VACV-vaccinees and 2.6% of control immunized (TIV)[2]
- Clinical: 4 probable myo- and 1 suspected peri-carditis (5 cases out of 1081 VACV vaccinees – 0.5%)
- Cardiac specific troponin T (cTnT) elevation in 31 VACV vaccinees (3%)

[1]Engler RJM,, et al. (2015) A Prospective Study of the Incidence of Myocarditis/Pericarditis and New Onset Cardiac Symptoms following Smallpox and Influenza Vaccination. PLoS ONE 10(3)
[2]TIV = trivalent influenza vaccine - control vaccinees

Proposed Evolution of Vaccinia Vaccines

Postulated Divergence of Historical Strains of Vaccinia

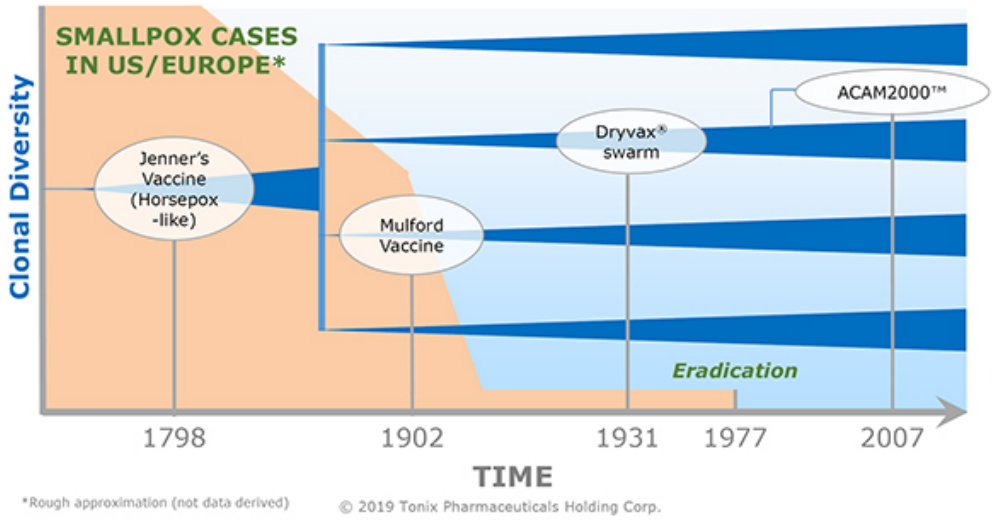


IHD-J=International Health Department-Japan
LIVP=Lister Vaccine Strain
NYCBH=New York City Board of Health
RPXV=Rabbitpox Virus
WR=Western Reserve

Figure Adapted from Qin et al. *Journal of Virology.* 2015;89(3):1809-1824.

Proposed Evolution of Vaccinia Vaccines

Relationship to Smallpox Incidence and Eradication



*Rough approximation (not data derived)

What's the Evidence of Effectiveness of Smallpox Vaccines for Preventing Smallpox?

Theoretical effectiveness of modern vaccinia vaccines are based on extrapolation from older vaccines

- Newer/modern vaccines were not widely used when smallpox was endemic

MVA (Modified Virus Ankara) which has large deletions also produces different T cell responses

- In non-human primates, MVA is less effective than ACAM2000 in protecting against monkeypox[1]
- MVA has fewer epitopes, and elicits different responses to existing epitopes[2]
  - MVA effectiveness argument is based on the immune response to intracellular mature virus (IMV)
  - Immunity to the other form of virus, extracellular enveloped virus (EEV), is weak because the immunodominant B5 gene is heavily mutated and deleted in MVA

[1]Golden JW, et al. (2012). PLoS ONE 7(7): e42353. doi:10.1371/journal.pone.0042353
[2]Tscharke, DC et al., J. Exp. Med. 2005 201(1):95

Possible Smallpox Prevention and Treatment Strategies

Preventing Vaccine

- Jenner's vaccine, HPXV (upon licensure), Vaccinia

Post-exposure vaccination[1]

- Jenner's vaccine

Priming of the immune system

- Imvamune® (MVA) and DNA vaccines[2]

Pharmacotherapy for infected or exposed individuals

- Arestvyr®/TPOXX® (tecovirimat, formerly ST-246)

Treatment of disseminated viremia in immunocompromised[3]

- Arestvyr®/TPOXX®, Brincidofovir and vaccinia immune globulin

[1]Described by Jenner as one of his major discoveries
[2]Hooper, JW et al. Smallpox DNA Vaccine Protects Nonhuman Primates Against Lethal Monkeypox. J. Virol. 2004. 78 (9) 4433
[3]Lederman, ER et al, Progressive Vaccinia: Case Description and Laboratory-Guided Therapy With Vaccinia Immune Globulin, ST-246, and CMX001 JID 2012. 206:1372

Viral Replication Proficiency is Critical to Human Immunogenicity but May Compromise Safety

Pox vaccines with low or no replication appear safer than vaccines replicate fast in human cells

- Canarypox and Imvamune® (Modified Virus Ankara/MVA) appear to have good tolerability
- Relatively safe in immunocompromised hosts
- Rapidly replicating modern vaccinia vaccines (Dryvax® and ACAM2000®) are associated with myocarditis

Replication correlates positively with immunogenicity

- Jenner's vaccine and modern vaccinia engender strong immunity
- Canarypox and MVA appear to be weak immunogens, suitable for priming of the immune system in healthy human being and potentially safe enough to use in immunocompromised people

Manufacturing and Dosing Requirements

TNX-801 (HPXV) is expected to have similar scalability for mass production as ACAM2000

- TNX-801 grows well in cell lines – immunity is expected after single administration (immunization)
- Only a small dose (replicating live virus) is required for immunization

MVA is hard to scale up for commercial production

- Requires high dose to engender an immune response (non-replicating virus)
- Cumbersome immunization schedule– two doses, 4 weeks apart, are used typically to prime the immune system (slow growth)

Antivirals

- Relatively expensive to manufacture – requires repeated dosing
- May provide logistical challenges to at risk population over the at risk period

Rationale for Developing a Potentially Improved New Smallpox Vaccine Based on Jenner's Vaccine

Vaccination protects against smallpox – both individuals and populations at risk

- Use of Jenner's vaccine resulted in eradication of smallpox

Vaccination can protect AFTER smallpox infection

- Vaccinia can be administered 1-3 days after infection

Vaccination indirectly protects non-immunized people in a population

- "Wetting the forest" or "herd immunity"

Vaccination can be cost effective with safe/low-risk vaccines

- Replication-efficient live virus vaccines can be manufactured and administered for broader use

"The Time is Right"

New synthetic biology technology and new understanding of vaccinia evolution provide an opportunity for a potentially safer vaccine using HPXV

Potential for Use of HPXV as a Vector for Vaccines to Infectious Disease or Cancer

Poxviruses like HPXV can be engineered to express foreign genes and are well recognized platforms for vaccine development

- Large packaging capacity for exogenous DNA inserts (i.e. encoding antigens)
- Precise virus-specific control of exogenous gene insert expression
- Lack of persistence or genomic integration in the host
- Strong immunogenicity as a vaccine
- Ability to rapidly generate vector/insert constructs
- Readily manufacture at scale
- Live, replicating vaccine – direct antigen presentation

Potential advantages of HPXV- strong immunogenicity with good tolerability

Financial Overview

NASDAQ: TNXP	
Cash and cash equivalents, December 31, 2018	$25.0 million
Common stock outstanding as of March 13, 2019	6.1 million

Management Team

Seth Lederman, MD
President & CEO

TARGENT Fusilev (levoleucovorin) for injection 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 Steward pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank svb SiliconValleyBank American Capital

Board of Directors

Seth Lederman, MD Chairman	**Donald Landry, MD, PhD** Chair of Medicine, Columbia University
Margaret Smith Bell Standard Life Investments, Putnam Investments, State Street Research	**Adeoye "Oye" Olukotun, MD** Squibb, BMS, Mallinckrodt, Esperion
Patrick Grace (qp) global family offices, Grace Institute Foundation, WR Grace, Chemed	**John Rhodes** Chair, NYS Public Service Commission, CEO, NYS Dept. of Public Service, Booz Allen
Gen. David Grange (US Army, ret.) Pharm-Olam, PPD, McCormick Foundation	**James Treco** First Chicago, Salomon Brothers/Citigroup

Milestones – Recently Completed and Upcoming

☑	July 2018	Completed P301/HONOR study interim analysis - result did not support study continuation but strengthened new Phase 3 study
☑	August 2018	Presentation of P301/HONOR study results at Military Health System Scientific Symposium
☑	October 2018	Met with FDA and received preliminary agreement on the design of new Phase 3 study of Tonmya for PTSD (P302/RECOVERY study)
☑	November 2018	Received FDA minutes confirming agreement on the design of P302/RECOVERY study
☑	March 2019	FM FDA Clinical Guidance meeting completed
☑	March 2019	P302/RECOVERY study initiated
☐	Second Half 2019	Preliminary human pharmacokinetic and safety data (non-IND study) from selected TNX-601 (tianeptine oxalate) formulation expected
☐	First Half 2020	Topline data from P302/RECOVERY study expected

Summary

Phase 3 development of new bedtime treatment for PTSD, including military-related PTSD

- Major unmet need; ~12 million Americans annually
- Benefited from FDA 505(b)(2) NDA approval requirement

Complimentary day-time PTSD treatment in development

- Leverages development expertise in PTSD, i.e., regulatory, trial recruitment and execution

Fibromyalgia bedtime treatment in development

- IND ready to support Phase 3 potential pivotal efficacy study

New indication in development for agitation in Alzheimer's Disease

- Unmet medical need, no approved drug available
- Fast Track Phase 2/3 ready program

Innovative vaccine in development to prevent Smallpox

- Opportunity to supply stockpiling requirement; short development path
- Studies in mice suggest improved safety profile

TONIX PHARMACEUTICALS

NASDAQ: TNXP

Thank you!

Exhibit 99.03

Investor Presentation

TONIX PHARMACEUTICALS

March 2019

Version P0166 3-11-19 (Doc 0450)

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.

Tonix Development Highlights

TNX-102 SL Cyclobenzaprine Sublingual Tablets

Posttraumatic Stress Disorder (PTSD) – Lead program; new bedtime treatment - Tonmya®[1]

- P302/RECOVERY Phase 3 clinical study initiated in March 2019
- Results from 2 efficacy studies improve the new Phase 3 study design New Phase
- P302/RECOVERY study design features accepted by the FDA[2]

Fibromyalgia Syndrome (FM)

- IND[3] ready to support Phase 3 potential pivotal efficacy study

Agitation in Alzheimer's disease (AAD)

- IND[3] ready to support Phase 2 potential pivotal efficacy study

Pipeline

TNX-601[4] – Daytime PTSD treatment and treatment of neurocognitive dysfunction from corticosteroids

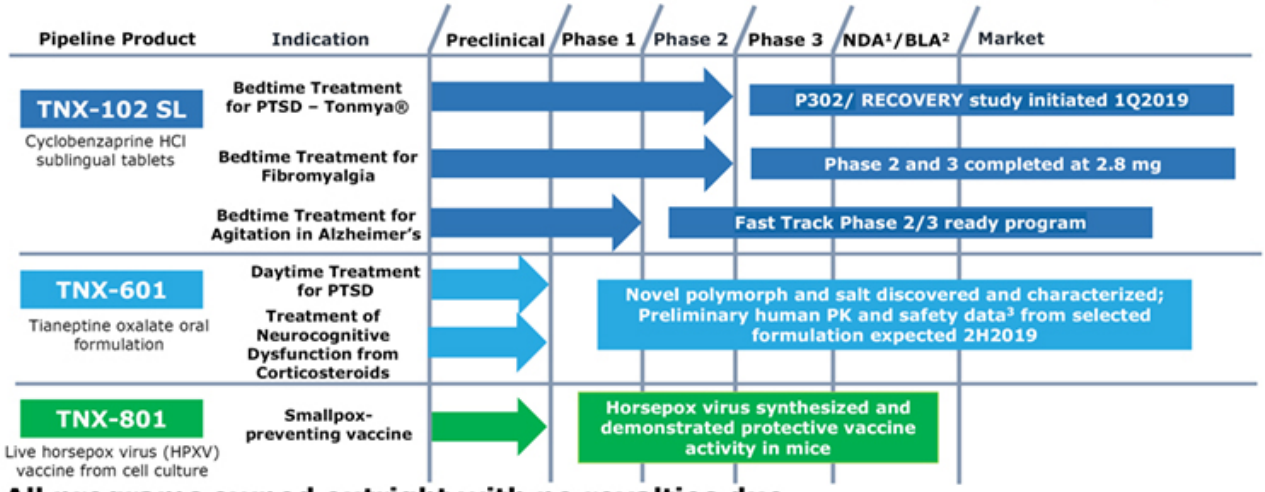
- Pre-IND candidate; nonclinical development ongoing

TNX-801[5] - Smallpox-preventing vaccine candidate

- Efficacy demonstrated in mouse model

[1] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the treatment of PTSD. TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2] FDA Meeting Minutes (November 26, 2018)
[3] IND- Investigational New Drug Application
[4] Tianeptine oxalate
[5] Synthesized live horsepox virus

Candidates in Development



All programs owned outright with no royalties due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³non-IND study

Tonmya: a Potential Bedtime Treatment for PTSD

First investigational new drug to show treatment effect in military-related PTSD in two potential pivotal efficacy studies

- Phase 2 study (P201/AtEase) showed Tonmya 5.6 mg had a strong signal of treatment effect at Week 12 as measured by CAPS-5[1]
- Phase 3 study (P301/HONOR) provided evidence of effectiveness as early as 4 weeks after treatment but diminished over time due to high placebo response
  - Retrospective analysis showed persistent effectiveness at Week 12 in subgroup with trauma ≤9 years from screening
- Both studies can be used as supportive evidence of efficacy and safety for Tonmya NDA submission
- No serious or unexpected adverse events related to Tonmya were reported

FDA feedback and acceptance on new Phase 3 study (P302/RECOVERY) received in November[2]

Patent protection through 2034 in U.S.[3]

- Composition of matter patent for transmucosal delivery of cyclobenzaprine

Novel mechanism targets sleep quality

- Memory processing during sleep is important to recovery from PTSD

[1] CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
[2] FDA Meeting Minutes, November 26, 2018; [3]U.S. Patent No. 9,636,408 for eutectic proprietary Protectic™ formulation

No Recognized Abuse Potential in Clinical Studies

Active ingredient is cyclobenzaprine, which is structurally related to tricyclic antidepressants

- Cyclobenzaprine interacts with receptors that regulate sleep quality: 5-$HT_{2A,}$ α_1-adrenergic and histamine H_1 receptors
- Cyclobenzaprine does **NOT** interact with the same receptors as traditional hypnotic sleep drugs, benzodiazepines or non-benzodiazepines that are associated with retrograde amnesia
- Cyclobenzaprine-containing product was approved 40 years ago and current labeling (May 2018) indicates no abuse or dependence concern

Tonmya NDA can be filed without drug abuse and dependency assessment studies

- Discussed at March 9, 2017 meeting with the FDA

TNX-102 SL Intellectual Property – U.S. Protection until 2034

Composition of matter (eutectic) : Protection expected to 2034

- United States Patent and Trademark Office (USPTO) issued U.S. Patent No. 9,636,408 in May 2017 U.S. Patent No. 9,956,188 in May 2018 and U.S. Patent No. 10,117,936 in November 2018
- Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018
- New Zealand Intellectual Property Office (NZIPO) issued New Zealand Patent No. 631152 in May 2017
- 37 patent applications pending (2 allowed (US and South Africa))

Pharmacokinetics (PK) : Protection expected to 2033

- JPO issued Japanese Patent No. 6259452 in December 2017
- NZIPO issued New Zealand Patent No. 631144 in March 2017
- Taiwanese Intellectual Property Office issued Taiwanese Patent No. I590820 in July 2017
- 21 patent applications pending (1 allowed (Australia))

Method of use for active ingredient cyclobenzaprine : Protection expected to 2030

- USPTO issued U.S. Patent 9,918,948 in March 2018
- European Patent Office issued European Patent No. 2 501 234B1 in September 2017 (validated in 38 countries). Opposition filed in June 2018
- 2 patent applications pending

TNX-102 SL: Sublingual Formulation is Designed for Bedtime Administration

TNX-102 SL: Proprietary sublingual formulation of cyclobenzaprine (CBP) with transmucosal absorption

- Innovation by design with patent protected CBP/mannitol eutectic
- Rapid systemic exposure
- Increases bioavailability during sleep
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, norcyclobenzaprine (norCBP)

CBP undergoes extensive first-pass hepatic metabolism when orally ingested

- Active major metabolite, norCBP[1]
  - Long half-life (~72 hours)
  - Less selective for target receptors (5-$HT_{2A,}$ α_1-adrenergic, histamine H_1)
  - More selective for norepinephrine transporter and muscarinic M_1

TNX-102 SL 505(b)(2) NDA approval can rely on the safety of the reference listed drug (AMRIX®)[2]

[1] Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada
[2] FDA Minutes (November 26, 2018)

Tonmya: Hypothesized Novel Mechanism Targets Sleep Quality for Recovery from PTSD

PTSD is a disorder of recovery

- Most people exposed to extreme trauma recover over a few weeks
- In PTSD, recovery process impeded due to insufficient sleep-dependent memory processing[1,2]

Memory processing is essential to recovery

- Vulnerability to memory intrusions and trauma triggers remains if no consolidation of new learning (extinction)

Tonmya targets sleep quality[3]

- The active ingredient in Tonmya, cyclobenzaprine, interacts with receptors that regulate sleep quality: strongly binds and potently blocks 5-HT_{2A}, α_1-adrenergic and histamine H_1 receptors, permissive to sleep-dependent recovery processes

[1]Straus LD, Acheson DT, Risbrough VB, Drummond SPA. Sleep Deprivation Disrupts Recall of Conditioned Fear Extinction. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017; 2(2):123-129. [2]Murkar ALA, De Koninck J. Consolidative mechanisms of emotional processing in REM sleep and PTSD. Sleep Med Rev. 2018; 41:173-184.
[3]Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada

PTSD: Not Well-Served by Approved Treatments

FDA-approved SSRIs, paroxetine and sertraline, are indicated as a treatment for PTSD

- Neither drug has shown efficacy in military-related PTSD
- Majority of male PTSD patients unresponsive or intolerant to current treatments
- Side effects relating to sexual dysfunction, sleep disturbance and weight gain are commonly reported

Characteristics of an ideal drug therapy that would be compatible and complementary with behavioral therapy

- Lack of retrograde amnesia (e.g., unlike off-label use of benzodiazepines and non-benzodiazepines)
- Lack of interference on sleep (e.g., unlike approved SSRIs)

Tonmya is being investigated in both military and civilian PTSD and is expected to be indicated as a "treatment for PTSD"

Prevalence of PTSD Among Civilians and Veterans

4.7%
Adult population[1]

19-31%
Vietnam veterans[2]

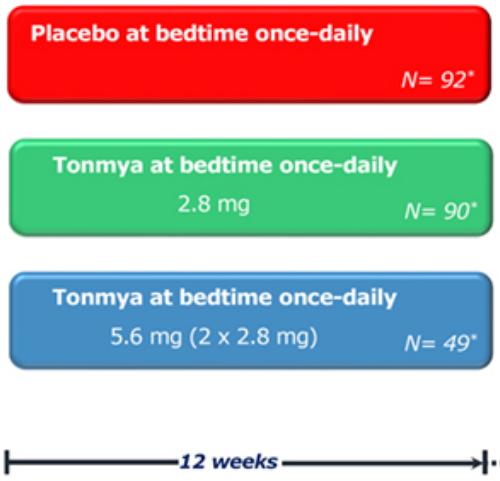
>19%
Iraq/Afghanistan[3]

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.

Phase 2 P201/AtEase[1] Study in Military-Related PTSD



- Randomized, double-blind, placebo-controlled trial in military-related PTSD
- Efficacy analysis from 231* patients; 24 U.S. clinical sites
- Enrolled patients with baseline CAPS-5[2] ≥ 29
- Primary Efficacy Analysis:
  - Difference in CAPS-5 score change from baseline between Tonmya 2.8 mg and placebo at Week 12
- Key Secondary Measures:
  - PROMIS Sleep Disturbance, CGI-I, SDS

[1]ClinicalTrials.gov Identifier: NCT02277704
[2]CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
*Modified intent-to-treat

P201/AtEase Study

P201 was a large adequate well-controlled Phase 2 study in military-related PTSD

- Primary endpoint (Week 12 CAPS-5) did not separate from placebo for TNX-102 SL 2.8 mg
- No safety or tolerability issue discovered
- Retrospective analyses showed TNX-102 SL 5.6 mg had a strong signal of treatment effect at Week 12 CAPS-5 (P=0.053) and CGI-I (P=0.041) scores
- Retrospective analyses suggested CAPS-5 ≥ 33 enrollment criteria for Phase 3

P301/HONOR[1] Study –Evidence of Efficacy at Week 4
Discontinued Due to High Placebo Response at Week 12

General study characteristics:

Randomized, double-blind, placebo-controlled, adaptive design, planned 550 military-related PTSD participants with baseline CAPS-5[2] ≥ 33 in approximately 40 U.S. sites

Tonmya once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets) *N= 125**

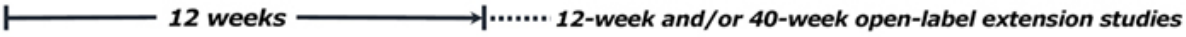
Placebo once-daily at bedtime
*N= 127**

Primary endpoint CAPS-5[2]:

- Mean change from baseline at Week 12 (Tonmya 5.6 mg vs. placebo)

Unblinded interim analysis at 274 randomized participants (mITT* N= 252)

- Study stopped due to not meeting a pre-specified study continuation threshold at Week 12
- Participants discontinued in HONOR or 12-week open-label extension (OLE) studies can enroll in the 40-week OLE study



[1]ClinicalTrials.gov Identifier: NCT03062540
[2]CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
*Modified intent-to-treat

P301/HONOR Study Stopped After Interim Analysis (July 2018)

P301 was a large adequate well-controlled Phase 3 study in military-related PTSD

- Separation on primary endpoint at Week 12 did not cross pre-specified study continuation threshold at Week 12 (p=0.602)
- No safety or tolerability issue discovered
- Retrospective analyses showed Week 4 CAPS-5 (P=0.019) and CGI-I (P=0.015) scores in Tonmya group had a strong signal of treatment effect

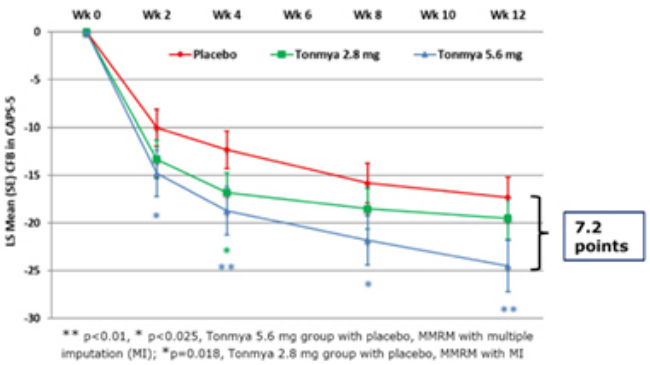
P301 dataset is complex and rich

- Retrospective analyses presented at Military Health System Research Symposium (MHSRS) in Kissimmee, FL on August 22, 2018
- Results discussed with the FDA[1] and helped to design the new Phase 3 P302/RECOVERY study with high probability of success

[1]FDA Meeting Minutes (November 26, 2018)

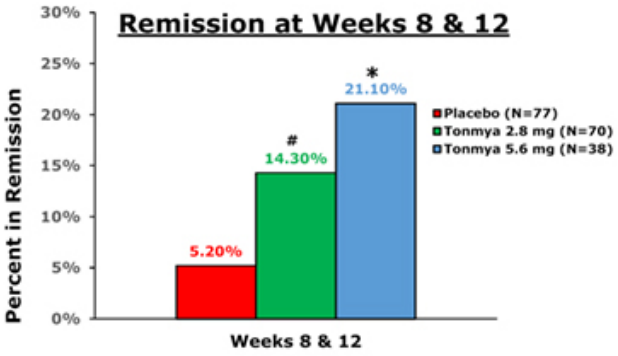
Tonmya Phase 2 Dose-Effect in Military-Related PTSD[1]

PTSD Symptoms (CAPS-5[2] Score)



** p<0.01, * p<0.025, Tonmya 5.6 mg group with placebo, MMRM with multiple imputation (MI); #p=0.018, Tonmya 2.8 mg group with placebo, MMRM with MI

Remission at Weeks 8 & 12



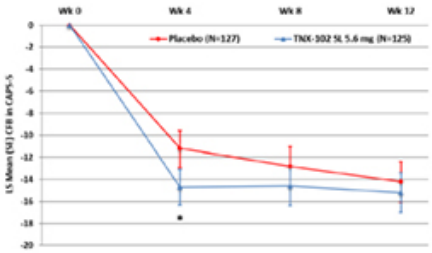
Remission = Loss of Diagnosis and CAPS-5 < 11
Asterisk and hashmark represent pairwise comparisons between Tonmya and Placebo; #p=0.08, Odds Ratio 3.01 (0.89, 10.18)
*p=0.02, Odds Ratio 4.60 (1.27, 16.66); logistic regression

[1]Completed Phase 2 P201/AtEase study: Retrospective analysis of Tonmya 5.6 mg on CAPS-5 ≥33 (high-moderate) subgroup. Primary analysis of P201/AtEase was on Tonmya 2.8 mg in participants with entry CAPS-5 ≥29, moderate PTSD severity.
[2]Clinician administered PTSD Scale for DSM-5

Primary Outcome (CAPS-5) in Phase 3 (mITT) and ≤9 Years Time Since Trauma (TST) Subgroups

Phase 3 P301/HONOR Study[1]

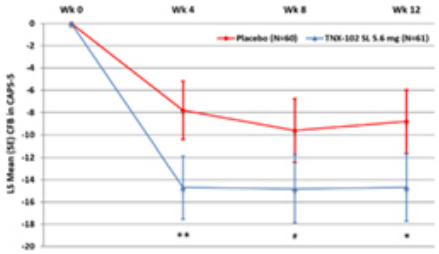
Modified intent to treat (mITT) population



*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

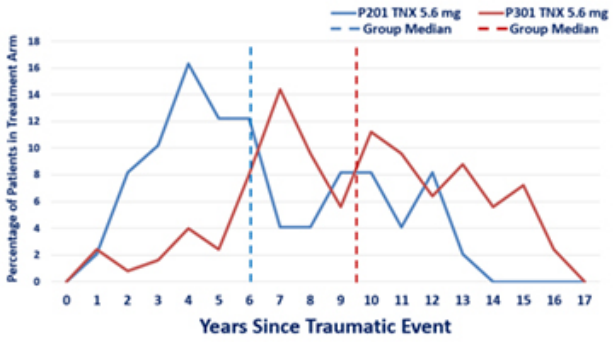
Time Since Trauma ≤9 yrs



**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.

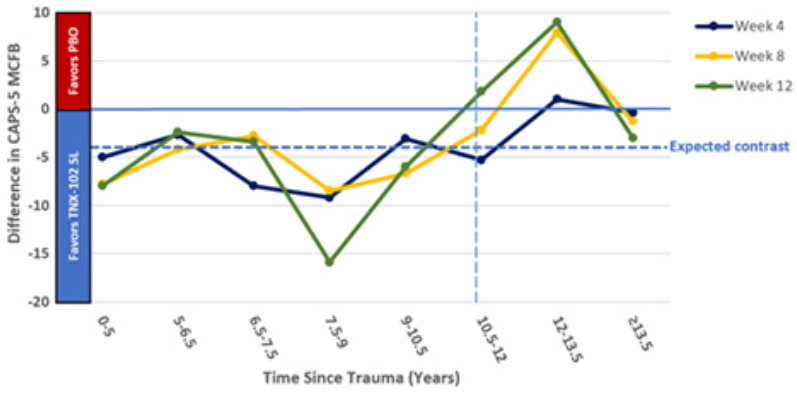
Retrospective Comparison of Time Since Trauma in P201/AtEase versus P301/HONOR (Tonmya 5.6 mg Groups)



P301 study was initiated approximately two years later than Phase 2 P201

- The median time since trauma in Phase 3 was 9.5 years compared to the median time since trauma in Phase 2 of 6.0 years for TNX-102 SL 5.6 mg treated groups

CAPS-5 Mean Change from Baseline Difference from Placebo of Tonmya 5.6 mg in TST Subgroups in P301[1]



Group TST (yrs)	0-5	5-6.5	6.5-7.5	7.5-9	9-10.5	10.5-12	12-13.5	≥ 13.5
Placebo 'N'	12	23	11	13	21	18	13	18
TNX-5.6 mg 'N'	14	17	16	12	22	10	17	18

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

- The mITT population was divided into subgroups based on TST (1.5-2 years each as well as 0-5 years and ≥13.5 years subgroups)
- Graph shows the CAPS-5 differences in MCFB between TNX 5.6 mg and PBO for Weeks 4, 8, and 12 post-baseline timepoints
- "Expected contrast" horizontal dashed line indicates observed effect from Phase 2 P201 study
- For TST <10.5 years groups, TNX 5.6 mg showed good separation from PBO (left side of vertical dashed 10.5 year line)
- For TST >10.5 years groups, separation of TNX 5.6 mg from PBO was either small or worked in the favor of PBO (right side of vertical dashed 10.5 year line)

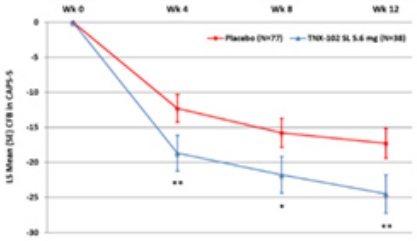
[1]*Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November 1-4, 2018 and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.* https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

PTSD Treatment Response to Tonmya in Phase 2 and Phase 3 Studies: Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

Change in CAPS-5 over course of treatment with Tonmya

CAPS-5 is a structured interview assessing PTSD severity

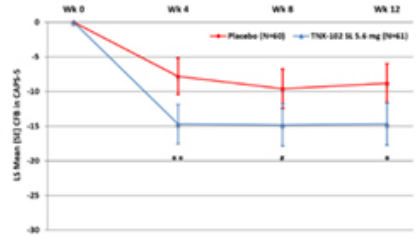
- Required primary endpoint for PTSD drug approval



P201 Baseline CAPS-5 ≥33 *(majority TST[1] ≤9 yr)*

**p<0.01, *p=0.017, TNX-102 SL 5.6 mg group v. placebo, using mixed model repeated measures (MMRM) with multiple imputation (MI)

Decrease in PTSD severity in Phase 3 subgroup ≤9 years since TST is similar to Phase 2 subgroup with baseline CAPS-5 ≥ 33



P301 *TST* ≤9 yr

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

[1]Time since trauma; [2]Majority of P201 participants were ≤9 years since trauma and ~80% of P201 participants and all of P301 participants were ≥33 CAPS-5 at baseline

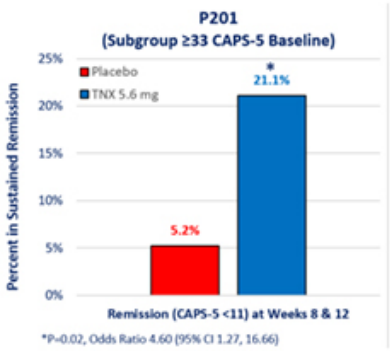
Sustained Remission in Phase 2 and Phase 3 Studies:
Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

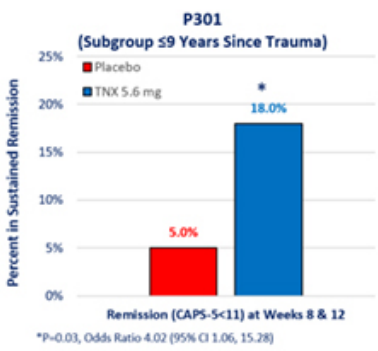
Remission is a clinical state that is essentially asymptomatic

In order to confirm remission:

- Determined rates of participants who met remission status at *both* Week 8 and Week 12

Rate of remission in ≤9 years since trauma group in P301 is similar to baseline CAPS-5 ≥ 33 group in P201[1]





[1]Majority of P201 participants were ≤ 9 years since trauma and ~80% of P201 participants and all of P301 participants were ≥ 33 CAPS-5 at baseline

Retrospective Analyses of ≤9 Years Since Trauma Subgroup on Primary and Secondary Endpoints in P301/HONOR Study

			P301 mITT				P301 ≤9 Year Subgroup			
			PBO (N=127) v. TNX-5.6 (N=125)				PBO (N=60) v. TNX-5.6 (N=61)			
			Week 4		Week 12		Week 4		Week 12	
Measure		Analysis	LSMD	p-value	LSMD	p-value	LSMD	p-value	LSMD	p-value
1°	CAPS-5	MMRM/MI	-3.6	**0.019**	-1.0	0.602	-6.9	**0.004**	-5.9	**0.039**
2°s	CGI-I	MMRM	-0.3	**0.015**	-0.1	0.403	-0.6	**0.002**	-0.5	**0.021**
	SDS	MMRM	-0.2	0.785	-1.6	0.101	-1.8	0.167	-4.3	**0.007**
	PGIC	MMRM	-0.2	0.238	-0.3	**0.020**	-0.4	**0.045**	-0.6	**0.007**
	PROMIS SD	MMRM	-3.1	**0.015**	-2.7	0.082	-4.5	**0.029**	-5.0	**0.042**
	BDI-II	MMRM	-1.1	0.330	-1.4	0.255	-5.2	**0.008**	-6.6	**0.001**

BOLDED p-values are all p<0.05; BDI-II=Beck Depression CAPS-5=Clinician-Administered PTSD Scale for DSM-5; CGI-I=Clinical Global Impression – Improvement scale; mITT=modified Intent-to-Treat sample; MMRM=mixed model repeated measures analysis; MI=multiple imputation; PGIC=Patient Global Impression of Change scale; PROMIS SD=Patient-Reported Outcome Measurement Information System Sleep Disturbance instrument (short form 8a); PBO=placebo; SDS=Sheehan Disability Scale; TNX-5.6=TNX-102 SL 5.6 mg; yrs=years; 1°=primary; 2°s=secondaries

Secondary endpoints also showed strong treatment effects in ≤9 yrs TST

- Support CAPS-5 results and similar to Phase 2 P201 Study results

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

Category of Adverse Reaction Preferred Term	P201 Placebo (N=94)	P201 TNX 2.8 mg (N=93)	P201 TNX 5.6 mg (N=50)	P301 Placebo (N=134)	P301 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 Tonmya

- 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

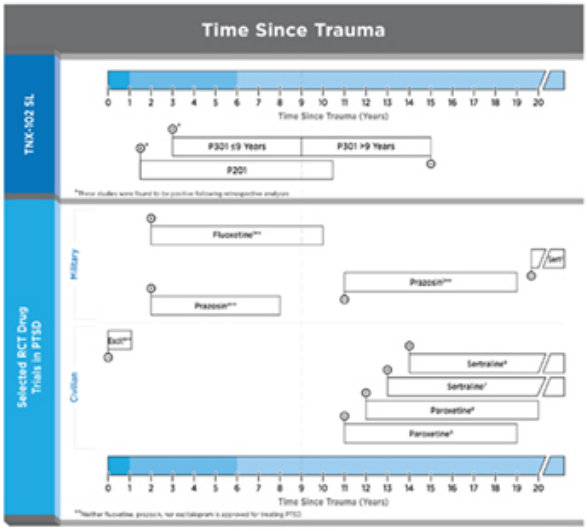
Time Since Trauma – Review of Published Studies

Published studies of prazosin suggested effects in military-PTSD prior to 9 years

- Loss of treatment effect >9 years

Paroxetine and sertraline studies supporting FDA approval were conducted on PTSD > 9 years

- SSRIs have a benefit long after trauma

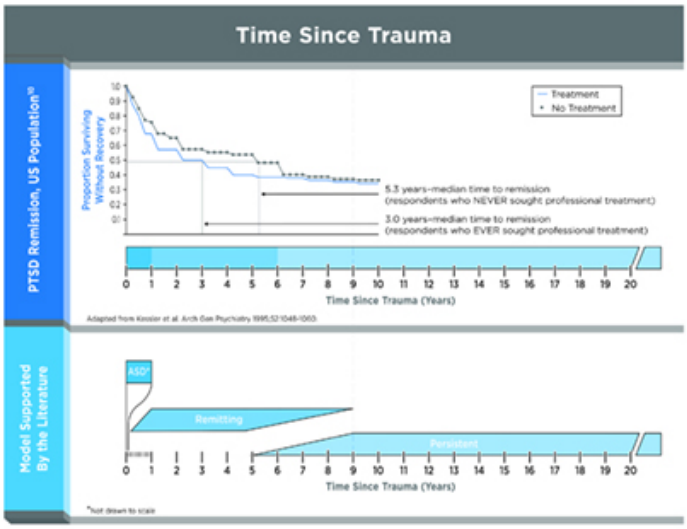


[1]Martenyi et al. *J Clin Psychiatry* 2002;63:199-206.
[2]Friedman et al. *J Clin Psychiatry* 2007;68:711-720.
[3]Raskind et al. *NEJM* 2018;378:507-517.
[4]Raskind et al. *Am J Psychiatry* 2013;170:1003-1010.
[5]Shalev et al. *Arch Gen Psychiatry* 2012;69:166-176.
[6]Davidson et al. *Arch Gen Psychiatry* 2001;58:485-492.
[7]Brady et al. *JAMA* 2000;283:1837-1844.
[8]Marshall et al. *Am J Psychiatry* 2001;158:1982-1988.
[9]Tucker et al. *J Clin Psychiatry* 2001;62:860-868.

Time Since Trauma – Remitting and Persistent Phases of PTSD

Kessler et al[1] studied remission in PTSD with and without therapy

- Identified remitting and persistent phase of PTSD – with transition at approximately 6 years post trauma
- Supported by other studies[2-6]



[1]Kessler et al. *Arch Gen Psychiatry* 1995;52:1048-1060.
[2]Armenta et al. *BMC Psychiatry* 2018;18:48.
[3]Galatzer-Levy et al. *PLOS ONE* 2013;8:e70084.
[4]Perkonigg et al. *Am J Psychiatry* 2005;162:1320-1327.
[5]Santiago et al. *PLOS ONE* 2013;8:e59236.
[6]Davidson & Connor. *Eur Neuropsychopharmacol* 2001;11(Supp3):S148-S149.

Response to Tonmya for Female Participants in P301/HONOR Study[1]

Females made up only 11% of the P301/HONOR study mITT population

Difference in mean change from baseline in CAPS-5 in females between placebo (N=17) and Tonmya 5.6 mg (N=10) was:

- At 4 weeks -11.5 points
- At 12 weeks -9.1 points

Indicates substantial separation from placebo in the small number of female participants

Predicts therapeutic response to Tonmya 5.6 mg likely in mixed civilian and military PTSD population to be studied in upcoming P302/RECOVERY trial

- Civilian PTSD population tends to be about 2/3 female

[1]Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November 1-4, 2018 and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

Response to Tonmya for Non-Combat Traumas in P301/HONOR Study in ≤9 Years Time Since Trauma Subgroup[1]

Non-combat traumas studied are similar to traumas experienced in civilian populations with PTSD

To determine the therapeutic effects of Tonmya 5.6 mg in a mixed civilian and military population, difference in MCFB in CAPS-5 was assessed in non-combat traumas in ≤9 years TST subgroup (placebo N=14, Tonmya 5.6 mg N=10):

- At 4 weeks -4.8 points
- At 12 weeks -4.4 points

Non-combat traumas treated with Tonmya 5.6 mg showed clinically meaningful separation from placebo at Weeks 4 and 12, suggesting a mixed civilian and military sample within 9 years of index trauma may show a therapeutic response to Tonmya

[1]*Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November, 2018; and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.*https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

CAPS-5=Clinician-Administered PTSD Scale for DSM-5; MCFB=mean change from baseline; mITT=modified Intent-to-Treat sample; TST=time since trauma

Summary of Clinical Experience with Tonmya/ TNX-102 SL in PTSD

Median time since trauma (TST) in TNX-102 SL 5.6 mg group in the P301/HONOR study (9.5 years) was longer than P201/AtEase study (6 years)

- Both studied military-related PTSD
- Time has passed since the surge in Iraq

In retrospective analysis, the ≤ 9 year subgroup of P301 study had similar results as the P201 study (primary and secondary)

- TST is important in placebo-controlled clinical study
- Potential enrichment in ≤ 9 years TST subgroup for treatment responders

The ≤ 9 year subgroup of P301 may be enriched for "Remitting Phase" of PTSD[1-4]

- Expect remitting phase of PTSD is more amenable to drug studies

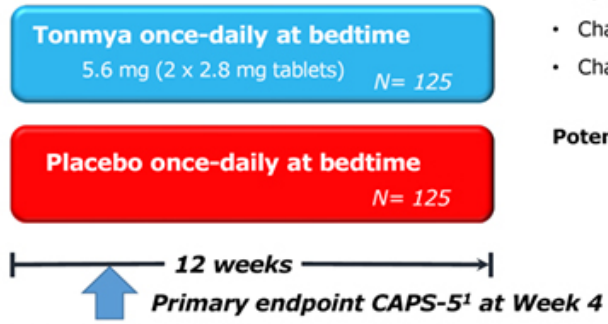
Results from retrospective analyses lead to improved Phase 3 study design

[1]Kessler et al. *Arch Gen Psychiatry* 1995;52:1048-1060.
[2]Armenta et al. *BMC Psychiatry* 2018;18:48.
[3]Galatzer-Levy et al. *PLOS ONE* 2013;8:e70084.
[4]Perkonigg et al. *Am J Psychiatry* 2005;162:1320-1327.

New Phase 3 P302/RECOVERY Study – Initiated 1Q 2019

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 (Tonmya 5.6 mg vs. placebo)

Key Secondary endpoints include:

- CAPS-5 mean change from baseline at Week 12 (Tonmya 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

Late-Stage PTSD Drug Candidates

Tonmya

- Phase 3 development focused on military-related and civilian PTSD; showed activity in treatment of military-related PTSD in large multi-center trials

MDMA-assisted psychotherapy

- Breakthrough therapy that is Phase 3-ready; showed activity in a Phase 2 study of PTSD; enrolling in Phase 3

Other drugs currently (or recently) in Phase 2 development

- Rexulti® (brexpiprazole) - Otsuka/Lundbeck; atypical antipsychotic; positive clinical results from Phase 2 study reported in November 2018 for brexpiprazole, when used in combination with an approved PTSD medication, sertraline, but not as monotherapy
- NYX-783 - Aptinyx; NMDA receptor modulator (enrolling for 8-week Phase 2 study of 144 patients using 50 mg either once daily or once weekly)
- BNC-201 – Bionomics; nicotinic receptor modulator (program planned to resume after reformulation)

TNX-102 SL – Bedtime Treatment for Multiple Potential Indications

Management of Fibromyalgia (FM) – chronic pain condition

- TNX-102 SL studied at low dose (2.8 mg) – half the dose being developed for PTSD – did not separate from placebo on primary endpoint, average pain improvement (responder analysis)
- Retrospective analysis showed average pain improvement (secondary endpoint) after 12 weeks of treatment showed statistical significance (P< 0.05, MMRM)
- Low dose TNX-102 SL (2.8 mg) showed an improvement in sleep quality in Phase 2 and Phase 3 FM trials
- Efficacy of TNX-102 SL 5.6 mg in FM can be studied in a potential pivotal study to support product registration

Agitation in Alzheimer's Disease

- Fast Track designation granted July 2018
- Phase 2/ potential pivotal efficacy study protocol received FDA comments in October 2018

Agitation in Alzheimer's Disease – Additional Indication Being Developed for TNX-102 SL

FDA designated Fast Track development program

Significant unmet need

- No FDA approved drugs for the treatment of agitation in Alzheimer's

Mechanism of improving sleep quality

- Sleep disturbance is a significant and common symptom in Alzheimer's

Pharmacological advantages outweigh potential concerns of using TNX-102 SL in treating agitation in Alzheimer's disease

- Blocks 3 receptors, not just one (e.g., 5-HT_{2A})

g., 5-HT_{2A}) © 2019 Tonix Pharmaceuticals Holding Corp.

TNX-102 SL for Agitation in Alzheimer's – Regulatory Status and Registration Strategy

FDA confirmed no additional study was needed prior to IND submission

- Pre-IND meeting established open dialogue with the FDA on pivotal clinical study design and efficacy endpoints to support product registration

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

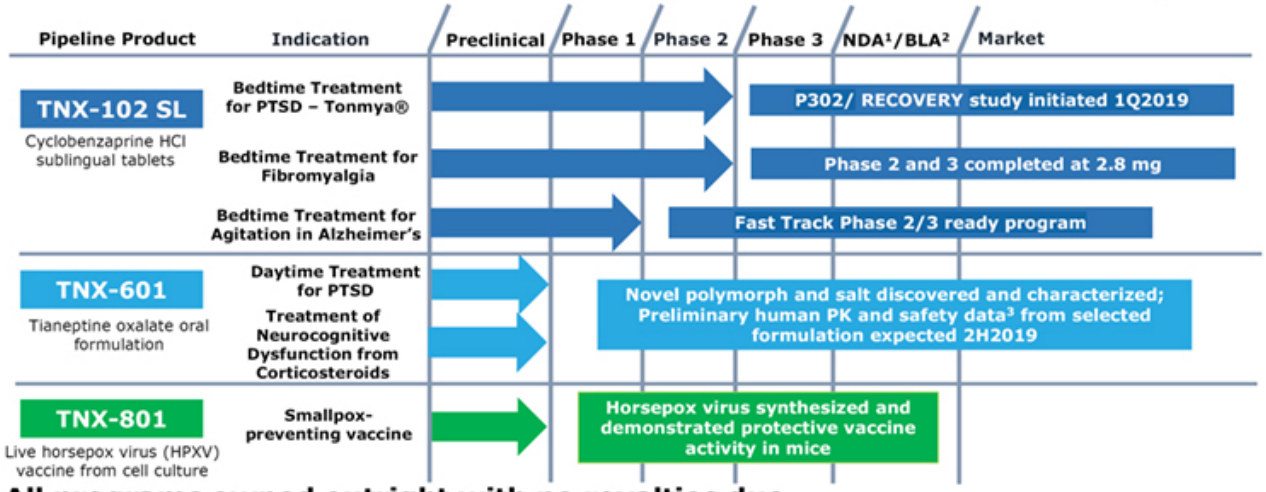
- FDA comments on final protocol received October 2018

Registration Strategy of TNX-102 SL for agitation in Alzheimer's disease

- Efficacy Supplement (sNDA[1]) may be leveraged from the PTSD/FM development program and supported by Initial NDA approval for PTSD/FM

[1]Supplemental New Drug Application

Candidates in Development



All programs owned outright with no royalties due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³non-IND study

TNX-601 (Tianeptine Oxalate): A Potential Clinical Candidate for PTSD

Pre-IND Candidate

Targeting a Condition with Significant Unmet Need

Targeted as a 1st line monotherapy for PTSD: oral formulation for 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
- Preliminary human pharmacokinetic and safety data (non-IND study) from selected formulation expected in second half 2019

Filed patent application on novel salt polymorph

- Issued patent on steroid-induced cognitive impairment and memory loss issues

Clinical evidence for PTSD

- Several studies have shown tianeptine to be 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-801 (Synthesized Live Horsepox Virus): A Smallpox-Preventing Vaccine Candidate

Pre-IND Stage

Potential improvement over current biodefense tools against smallpox

- ✓ Leverages Tonix's government affairs effort
- ✓ Collaboration with Professor David Evans and Dr. Ryan Noyce at University of Alberta
- ✓ Demonstrated protective vaccine activity in mice
- ✓ Patent application on novel vaccine submitted

Regulatory strategy

- We intend to meet with FDA to discuss the most efficient and appropriate investigational plan to support the licensure, either:
  - ✓ Application of the "Animal Rule", or
  - ✓ Conducting an active comparator study using ACAM2000
- Good Manufacturing Practice (GMP) viral production process in development

Targeting a Potential Public Health Issue

Material threat medical countermeasure under 21st Century Cures Act

- Qualifies for **Priority Review Voucher (PRV)** upon licensure*
  - ✓ **PRVs have no expiration date, are transferrable and have sold for ~$125 M**

*BLA/NDA priority 6-month review is expected.

Financial Overview

NASDAQ: TNXP	
Cash and cash equivalents, December 31, 2018	$25.0 million
Common stock outstanding as of March 13, 2019	6.1 million

Management Team

Seth Lederman, MD
President & CEO

Gregory Sullivan, MD
Chief Medical Officer

Bradley Saenger, CPA
Chief Financial Officer

Jessica Morris
Chief Operating Officer

Board of Directors

Seth Lederman, MD Chairman	**Donald Landry, MD, PhD** Chair of Medicine, Columbia University
Margaret Smith Bell Standard Life Investments, Putnam Investments, State Street Research	**Adeoye "Oye" Olukotun, MD** Squibb, BMS, Mallinckrodt, Esperion
Patrick Grace (qp) global family offices, Grace Institute Foundation, WR Grace, Chemed	**John Rhodes** Chair, NYS Public Service Commission, CEO, NYS Dept. of Public Service, Booz Allen
Gen. David Grange (US Army, ret.) Pharm-Olam, PPD, McCormick Foundation	**James Treco** First Chicago, Salomon Brothers/Citigroup

Milestones – Recently Completed and Upcoming

☑	July 2018	Completed P301/HONOR study interim analysis - result did not support study continuation but strengthened new Phase 3 study
☑	August 2018	Presentation of P301/HONOR study results at Military Health System Scientific Symposium
☑	October 2018	Met with FDA and received preliminary agreement on the design of new Phase 3 study of Tonmya for PTSD (P302/RECOVERY study)
☑	November 2018	Received FDA minutes confirming agreement on the design of P302/RECOVERY study
☑	March 2019	FM FDA Clinical Guidance meeting completed
☑	March 2019	P302/RECOVERY study initiated
☐	Second Half 2019	Preliminary human pharmacokinetic and safety data (non-IND study) from selected TNX-601 (tianeptine oxalate) formulation expected
☐	First Half 2020	Topline data from P302/RECOVERY study expected

Summary

Phase 3 development of new bedtime treatment for PTSD, including military-related PTSD

- Major unmet need; ~12 million Americans annually
- Benefited from FDA 505(b)(2) NDA approval requirement

Complimentary day-time PTSD treatment in development

- Leverages development expertise in PTSD, i.e., regulatory, trial recruitment and execution

Fibromyalgia bedtime treatment in development

- IND ready to support Phase 3 potential pivotal efficacy study

New indication in development for agitation in Alzheimer's Disease

- Unmet medical need, no approved drug available
- Fast Track Phase 2/3 ready program

Innovative vaccine in development to prevent Smallpox

- Opportunity to supply stockpiling requirement; short development path
- Studies in mice suggest improved safety profile

TONIX PHARMACEUTICALS

NASDAQ: TNXP

Thank you!

Exhibit 99.04

Investor Presentation

TONIX PHARMACEUTICALS

March 2019

Version P0165 3-18-19 (Doc 0449)

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.

Tonix Development Highlights

TNX-102 SL Cyclobenzaprine Sublingual Tablets

Posttraumatic Stress Disorder (PTSD) – Lead program; new bedtime treatment - Tonmya®[1]

- P302/RECOVERY Phase 3 clinical study initiated in March 2019
- Results from 2 efficacy studies improve the new Phase 3 study design New Phase
- P302/RECOVERY study design features accepted by the FDA[2]

Fibromyalgia Syndrome (FM)

- IND[3] ready to support Phase 3 potential pivotal efficacy study

Agitation in Alzheimer's disease (AAD)

- IND[3] ready to support Phase 2 potential pivotal efficacy study

Pipeline

TNX-601[4] – Daytime PTSD treatment and treatment of neurocognitive dysfunction from corticosteroids

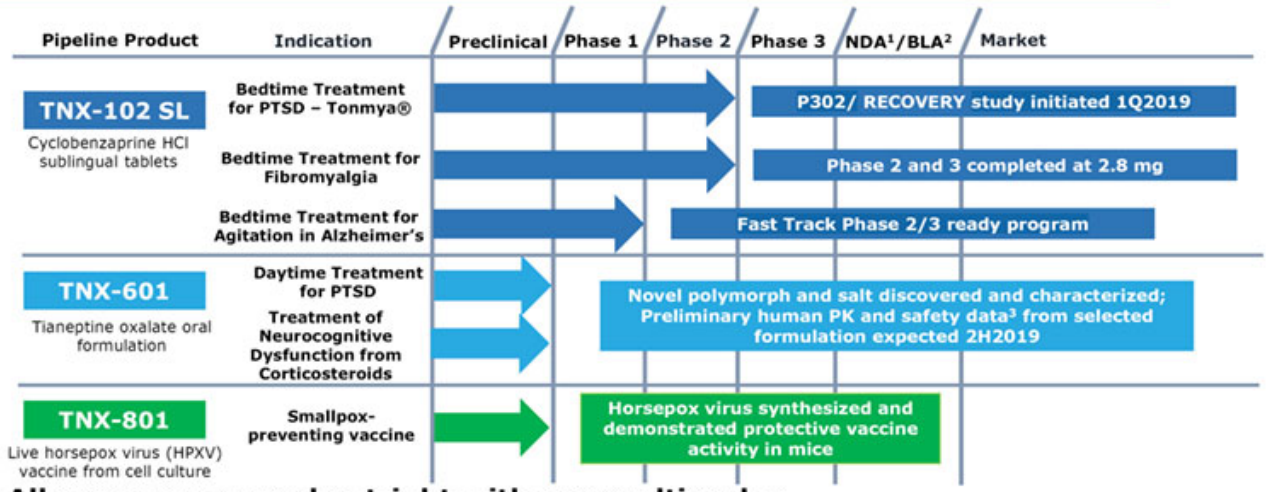
- Pre-IND candidate; nonclinical development ongoing

TNX-801[5] - Smallpox-preventing vaccine candidate

- Efficacy demonstrated in mouse model

[1] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the treatment of PTSD. TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2] FDA Meeting Minutes (November 26, 2018)
[3] IND- Investigational New Drug Application
[4] Tianeptine oxalate
[5] Synthesized live horsepox virus

Candidates in Development



All programs owned outright with no royalties due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³non-IND study

Tonmya: a Potential Bedtime Treatment for PTSD

First investigational new drug to show treatment effect in military-related PTSD in two potential pivotal efficacy studies

- Phase 2 study (P201/AtEase) showed Tonmya 5.6 mg had a strong signal of treatment effect at Week 12 as measured by CAPS-5[1]
- Phase 3 study (P301/HONOR) provided evidence of effectiveness as early as 4 weeks after treatment but diminished over time due to high placebo response
  - Retrospective analysis showed persistent effectiveness at Week 12 in subgroup with trauma ≤9 years from screening
- Both studies can be used as supportive evidence of efficacy and safety for Tonmya NDA submission
- No serious or unexpected adverse events related to Tonmya were reported

FDA feedback and acceptance on new Phase 3 study (P302/RECOVERY) received in November[2]

[1] CAPS-5 = Clinician-Administered PTSD Scale for DSM-5
[2] FDA Meeting Minutes, November 26, 2018

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 Military PTSD

PTSD is signature wound of last 25 years of war

- Affects servicemember health and performance, force readiness, retention
- Believed to be the underlying cause of suicide in many cases

No FDA-approved products for PTSD since Pfizer's Zoloft® (sertraline) and GSK's Paxil® (paroxetine) circa 2000

- Neither has shown efficacy in military-related PTSD
- Male PTSD patients often unresponsive or intolerant of current treatments
- Side effects relating to sexual dysfunction, sleep and weight gain are commonly reported

U.S. Department of Defense (DoD) is working to understand and treat PTSD

- Increased scrutiny of PTSD-related discharges for behavioral problems
- Wider recognition that PTSD is a service-related disability
- Collaboration with Army: Tonix-USAMMDA CRADA signed in 2015

TNX-102 SL Intellectual Property – U.S. Protection until 2034

Composition of matter (eutectic) : Protection expected to 2034

- United States Patent and Trademark Office (USPTO) issued U.S. Patent No. 9,636,408 in May 2017 U.S. Patent No. 9,956,188 in May 2018 and U.S. Patent No. 10,117,936 in November 2018
- Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018
- New Zealand Intellectual Property Office (NZIPO) issued New Zealand Patent No. 631152 in May 2017
- 37 patent applications pending (2 allowed (US and South Africa))

Pharmacokinetics (PK) : Protection expected to 2033

- JPO issued Japanese Patent No. 6259452 in December 2017
- NZIPO issued New Zealand Patent No. 631144 in March 2017
- Taiwanese Intellectual Property Office issued Taiwanese Patent No. I590820 in July 2017
- 21 patent applications pending (1 allowed (Australia))

Method of use for active ingredient cyclobenzaprine : Protection expected to 2030

- USPTO issued U.S. Patent 9,918,948 in March 2018
- European Patent Office issued European Patent No. 2 501 234B1 in September 2017 (validated in 38 countries). Opposition filed in June 2018
- 2 patent applications pending

Potential Therapeutic Advantages of Tonmya

Tonmya 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
- Tonmya is believed to normalize memory processing and facilitate extinction consolidation (breaking the link between "triggers" and PTSD symptoms)

Tonmya is *NEITHER* a benzodiazepine nor a narcotic

- The active ingredient of Tonmya, cyclobenzaprine, does **NOT** interact with the same receptors as traditional hypnotic sleep drugs associated with retrograde amnesia; is **NOT** an opiate

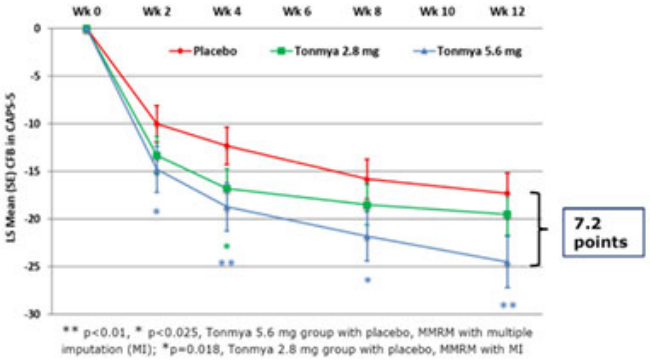
Tonmya is non-addictive

- 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 Tonmya (15-30 mg/day v. 5.6 mg/day); NDA can be filed without drug abuse and dependency assessment studies

Once-daily sublingual dose taken at bedtime enhances patient adherence

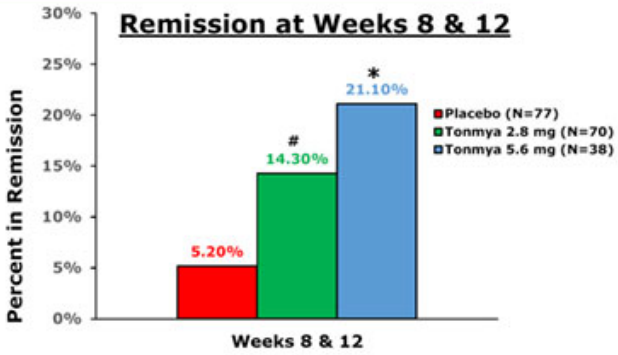
Tonmya Phase 2 Dose-Effect in Military-Related PTSD[1]

PTSD Symptoms (CAPS-5[2] Score)



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

Remission at Weeks 8 & 12



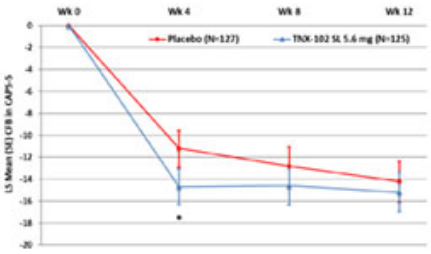
Remission = Loss of Diagnosis and CAPS-5 < 11
Asterisk and hashmark represent pairwise comparisons between Tonmya and Placebo; #p=0.08, Odds Ratio 3.01 (0.89, 10.18)
*p=0.02, Odds Ratio 4.60 (1.27, 16.66); logistic regression

[1]Completed Phase 2 P201/AtEase study: Retrospective analysis of Tonmya 5.6 mg on CAPS-5 ≥33 (high-moderate) subgroup. Primary analysis of P201/AtEase was on Tonmya 2.8 mg in participants with entry CAPS-5 ≥29, moderate PTSD severity.
[2]Clinician administered PTSD Scale for DSM-5

Primary Outcome (CAPS-5) in Phase 3 (mITT) and ≤9 Years Time Since Trauma (TST) Subgroups

Phase 3 P301/HONOR Study[1]

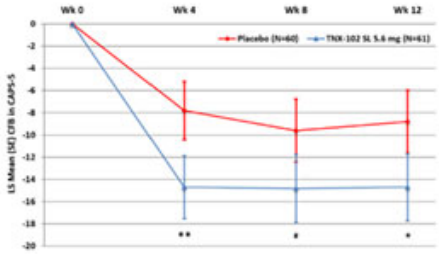
Modified intent to treat (mITT) population



*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

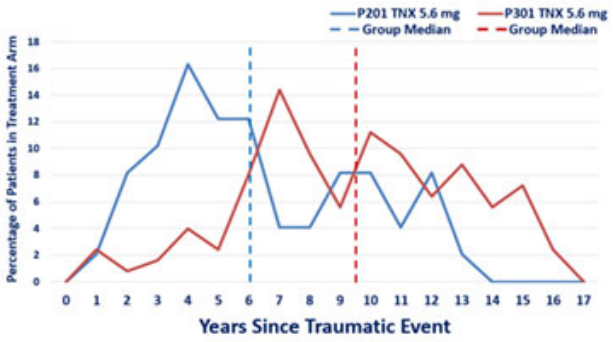
Time Since Trauma ≤9 yrs



**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.

Retrospective Comparison of Time Since Trauma in P201/AtEase versus P301/HONOR (Tonmya 5.6 mg Groups)



P301 study was initiated approximately two years later than Phase 2 P201

- The median time since trauma in Phase 3 was 9.5 years compared to the median time since trauma in Phase 2 of 6.0 years for TNX-102 SL 5.6 mg treated groups

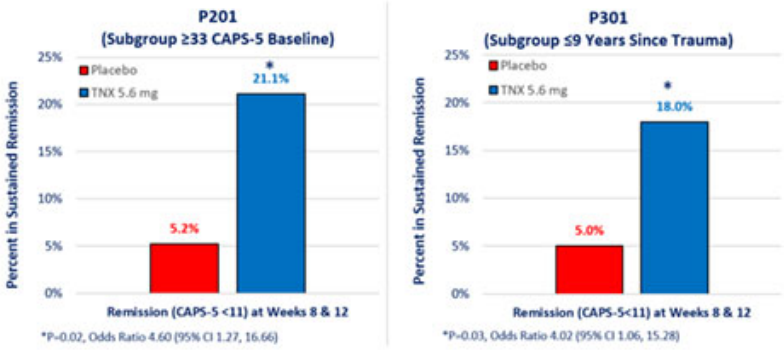
Sustained Remission in Phase 2 and Phase 3 Studies:
Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

Remission is a clinical state that is essentially asymptomatic

In order to confirm remission:

- Determined rates of participants who met remission status at *both* Week 8 and Week 12

Rate of remission in ≤9 years since trauma group in P301 is similar to baseline CAPS-5 ≥ 33 group in P201[1]



[1]Majority of P201 participants were ≤ 9 years since trauma and ~80% of P201 participants and all of P301 participants were ≥ 33 CAPS-5 at baseline

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

Category of Adverse Reaction Preferred Term	P201 Placebo (N=94)	P201 TNX 2.8 mg (N=93)	P201 TNX 5.6 mg (N=50)	P301 Placebo (N=134)	P301 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 Tonmya

- 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

Response to Tonmya for Female Participants in P301/HONOR Study[1]

Females made up only 11% of the P301/HONOR study mITT population

Difference in mean change from baseline in CAPS-5 in females between placebo (N=17) and Tonmya 5.6 mg (N=10) was:

- At 4 weeks -11.5 points
- At 12 weeks -9.1 points

Indicates substantial separation from placebo in the small number of female participants

Predicts therapeutic response to Tonmya 5.6 mg likely in mixed civilian and military PTSD population to be studied in upcoming P302/RECOVERY trial

- Civilian PTSD population tends to be about 2/3 female

[1]*Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November 1-4, 2018 and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.* https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

Response to Tonmya for Non-Combat Traumas in P301/HONOR Study in ≤9 Years Time Since Trauma Subgroup[1]

Non-combat traumas studied are similar to traumas experienced in civilian populations with PTSD

To determine the therapeutic effects of Tonmya 5.6 mg in a mixed civilian and military population, difference in MCFB in CAPS-5 was assessed in non-combat traumas in ≤9 years TST subgroup (placebo N=14, Tonmya 5.6 mg N=10):

- At 4 weeks -4.8 points
- At 12 weeks -4.4 points

Non-combat traumas treated with Tonmya 5.6 mg showed clinically meaningful separation from placebo at Weeks 4 and 12, suggesting a mixed civilian and military sample within 9 years of index trauma may show a therapeutic response to Tonmya

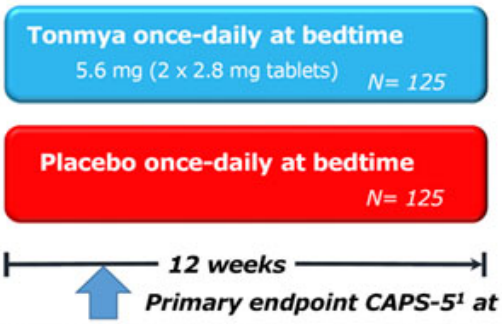
[1] *Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November, 2018 and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12,suppl):S10.* https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

CAPS-5=Clinician-Administered PTSD Scale for DSM-5; MCFB=mean change from baseline; mITT=modified Intent-to-Treat sample; TST=time since trauma

New Phase 3 P302/RECOVERY Study – Initiated 1Q 2019

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 (Tonmya 5.6 mg vs. placebo)

Key Secondary endpoints include:

- CAPS-5 mean change from baseline at Week 12 (Tonmya 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

Late-Stage PTSD Drug Candidates

Tonmya

- Phase 3 development focused on military-related and civilian PTSD; showed activity in treatment of military-related PTSD in large multi-center trials

MDMA-assisted psychotherapy

- Breakthrough therapy that is Phase 3-ready; showed activity in a Phase 2 study of PTSD; enrolling in Phase 3

Other drugs currently (or recently) in Phase 2 development

- Rexulti® (brexpiprazole) - Otsuka/Lundbeck; atypical antipsychotic; positive clinical results from Phase 2 study reported in November 2018 for brexpiprazole, when used in combination with an approved PTSD medication, sertraline, but not as monotherapy
- NYX-783 - Aptinyx; NMDA receptor modulator (enrolling for 8-week Phase 2 study of 144 patients using 50 mg either once daily or once weekly)
- BNC-201 – Bionomics; nicotinic receptor modulator (program planned to resume after reformulation)

TNX-102 SL – Bedtime Treatment for Multiple Potential Indications

Management of Fibromyalgia (FM) – chronic pain condition

- TNX-102 SL studied at low dose (2.8 mg) – half the dose being developed for PTSD – did not separate from placebo on primary endpoint, average pain improvement (responder analysis)
- Retrospective analysis showed average pain improvement (secondary endpoint) after 12 weeks of treatment showed statistical significance ($P < 0.05$, MMRM)
- Low dose TNX-102 SL (2.8 mg) showed an improvement in sleep quality in Phase 2 and Phase 3 FM trials
- Efficacy of TNX-102 SL 5.6 mg in FM can be studied in a potential pivotal study to support product registration

Agitation in Alzheimer's Disease

- Fast Track designation granted July 2018
- Phase 2/ potential pivotal efficacy study protocol received FDA comments in October 2018

TNX-102 SL for Agitation in Alzheimer's – Regulatory Status and Registration Strategy

FDA confirmed no additional study was needed prior to IND submission

- Pre-IND meeting established open dialogue with the FDA on pivotal clinical study design and efficacy endpoints to support product registration

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

- FDA comments on final protocol received October 2018

Registration Strategy of TNX-102 SL for agitation in Alzheimer's disease

- Efficacy Supplement (sNDA[1]) may be leveraged from the PTSD/FM development program and supported by Initial NDA approval for PTSD/FM

[1]Supplemental New Drug Application

TNX-601 (Tianeptine Oxalate): A Potential Clinical Candidate for PTSD

Pre-IND Candidate

Targeting a Condition with Significant Unmet Need

Targeted as a 1st line monotherapy for PTSD: oral formulation for 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
- Preliminary human pharmacokinetic and safety data (non-IND study) from selected formulation expected in second half 2019

Filed patent application on novel salt polymorph

- Issued patent on steroid-induced cognitive impairment and memory loss issues

Clinical evidence for PTSD

- Several studies have shown tianeptine to be 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-801 (Synthesized Live Horsepox Virus): A Smallpox-Preventing Vaccine Candidate

Pre-IND Stage

Potential improvement over current biodefense tools against smallpox

- ✓ Leverages Tonix's government affairs effort
- ✓ Collaboration with Professor David Evans and Dr. Ryan Noyce at University of Alberta
- ✓ Demonstrated protective vaccine activity in mice
- ✓ Patent application on novel vaccine submitted

Regulatory strategy

- We intend to meet with FDA to discuss the most efficient and appropriate investigational plan to support the licensure, either:
  - ✓ Application of the "Animal Rule", or
  - ✓ Conducting an active comparator study using ACAM2000
- Good Manufacturing Practice (GMP) viral production process in development

Targeting a Potential Public Health Issue

Material threat medical countermeasure under 21st Century Cures Act

- Qualifies for **Priority Review Voucher (PRV)** upon licensure*
  - ✓ **PRVs have no expiration date, are transferrable and have sold for ~$125 M**

*BLA/NDA priority 6-month review is expected.

Financial Overview

NASDAQ: TNXP	
Cash and cash equivalents, December 31, 2018	$25.0 million
Common stock outstanding as of March 13, 2019	6.1 million

Management Team

Seth Lederman, MD
President & CEO

TARGENT · Fusilev (levoleucovorin) for injection · 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 · Steward · pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank · svb Silicon Valley Bank · American Capital

Milestones – Recently Completed and Upcoming

☑	July 2018	Completed P301/HONOR study interim analysis - result did not support study continuation but strengthened new Phase 3 study
☑	August 2018	Presentation of P301/HONOR study results at Military Health System Scientific Symposium
☑	October 2018	Met with FDA and received preliminary agreement on the design of new Phase 3 study of Tonmya for PTSD (P302/RECOVERY study)
☑	November 2018	Received FDA minutes confirming agreement on the design of P302/RECOVERY study
☑	March 2019	FM FDA Clinical Guidance meeting completed
☑	March 2019	P302/RECOVERY study initiated
☐	Second Half 2019	Preliminary human pharmacokinetic and safety data (non-IND study) from selected TNX-601 (tianeptine oxalate) formulation expected
☐	First Half 2020	Topline data from P302/RECOVERY study expected

Summary

Phase 3 development of new bedtime treatment for PTSD, including military-related PTSD

- Major unmet need; ~12 million Americans annually
- Benefited from FDA 505(b)(2) NDA approval requirement

Complimentary day-time PTSD treatment in development

- Leverages development expertise in PTSD, i.e., regulatory, trial recruitment and execution

Fibromyalgia bedtime treatment in development

- IND ready to support Phase 3 potential pivotal efficacy study

New indication in development for agitation in Alzheimer's Disease

- Unmet medical need, no approved drug available
- Fast Track Phase 2/3 ready program

Innovative vaccine in development to prevent Smallpox

- Opportunity to supply stockpiling requirement; short development path
- Studies in mice suggest improved safety profile

TONIX PHARMACEUTICALS

NASDAQ: TNXP

Thank you!