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): August 21, 2018

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

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

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

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

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

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

Item 7.01 Regulation FD Disclosure.

On August 21, 2018, Tonix Pharmaceuticals Holding Corp. (the "Company") presented the results of the Phase 3 HONOR P301 Study and Phase 2 AtEase P201 Study in a Poster Presentation (the "Poster Presentation") at the 2018 Military Health System Research Symposium. Copies of the Poster Presentation and the press release that discusses this matter are filed as Exhibits 99.01 and 99.02, respectively, to, and incorporated by reference in, this report.

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 investor presentations are filed as Exhibits 99.03 and 99.04, and incorporated by reference in, this report.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Poster Presentation
99.02	Press Release, dated August 21, 2018, issued by the Company
99.03	Corporate Presentation by the Company for August 2018 (Long Form)
99.04	Corporate Presentation by the Company for August 2018 (Short 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: August 21, 2018

By: /s/ Seth Lederman
Seth Lederman
President & Chief Executive Officer

Exhibit 99.01

Exhibit 99.02

Tonix Pharmaceuticals Presents Results and Retrospective Analyses of Two Double-Blind, Randomized Placebo-Controlled 12-Week Studies of Tonmya® in Military-Related PTSD at the 2018 Military Health System Research Symposium

Retrospective Analysis of the Discontinued Phase 3 P301 "HONOR" Study Revealed Clinically Meaningful Response to Tonmya in PTSD Participants with Trauma Experienced Within Nine Years Prior to Screening but Not in Participants with Trauma Experienced More Than Nine Years Prior to Screening

Treatment Effect Seen in Phase 3 P301 Participants with Trauma Experienced Within Nine Years Replicated the Results of the Tonmya 5.6 mg Group in the Phase 2 P201 "AtEase" Study

NEW YORK, August 21, 2018 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix) is presenting a poster today at the 2018 Military Health System Research Symposium (MHSRS) in Kissimmee, Fla. The poster, entitled "Effect of Time Since Trauma on Response to TNX-102 SL* (Cyclobenzaprine Sublingual Tablets) in Military-Related PTSD: Results of Two Double-Blind Randomized Placebo-Controlled Studies" includes results and retrospective analyses from the Phase 3 P301 study ("HONOR") and the Phase 2 P201 study ("AtEase"). TNX-102 SL, or Tonmya*, is being developed for the treatment of posttraumatic stress disorder (PTSD). The poster can be found on the Scientific Presentations page of Tonix's website.

Tonix recently reported that the Phase 3 P301 study was stopped at the pre-planned interim analysis because it did not achieve a study continuation threshold on the primary outcome of improvement in the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) at Week 12 in the modified intent-to-treat (mITT) population. Today's poster presentation reports that a retrospective analysis revealed a treatment effect in participants who experienced trauma less than or equal to nine years prior to screening (approximately 50% of the mITT population). For this subgroup, the p-value of the primary endpoint at Week 12, using mixed model repeated measures with multiple imputation (MMRM with MI), was 0.039. In contrast, there was no benefit in the participants who experienced trauma more than nine years prior to screening. The impact of time since trauma on Tonmya treatment response was not evident in the Phase 2 P201 trial, which might relate to the fact that P201 had relatively fewer participants who experienced trauma greater than nine years before screening. There were no serious and unexpected adverse events (AEs) in P301 or P201. The AEs observed in both studies were comparable and also consistent with the experience in prior studies in fibromyalgia. Observed systemic AEs were consistent with those described in approved oral cyclobenzaprine product labels. Similar severity and incidence of oral hypoesthesia (tongue/mouth numbness) has been observed across studies (37% in P301; 36% in P201) for Tonmya 5.6 mg.

Dr. Seth Lederman, CEO of Tonix commented, "The P301 and P201 studies help to advance the clinical development of TNX-102 SL for PTSD. Future studies will focus on patients with more recent trauma (less than nine years). The finding that treatment response to Tonmya in P301 decreases as the time since trauma gets longer, suggests that military service members and veterans with PTSD are transitioning from a Tonmya-treatment responsive state to a non-responsive state after approximately nine years. These results emphasize the urgency for early diagnosis and treatment for PTSD, especially for military-related PTSD."

Dr. Gregory Sullivan, Chief Medical Officer of Tonix commented, “Trauma is the cause of PTSD, but PTSD is a complex condition with clear evidence of a dynamic pathophysiology which changes over time. Treatment responsiveness over the course of the disease may vary with different pharmacological classes, and may also differ between PTSD from combat versus other types of trauma. Yet it is unclear what specific features of PTSD change over time and make it less treatment responsive. These findings of P301 and P201 show that in PTSD, time since trauma is important in the treatment response to Tonmya. Other aspects of PTSD have been observed to depend on time since trauma, such as a decrease in the rates of remission the more years out from the trauma.[1] The subgroup with trauma less than nine years prior to screening in P301 may include more participants within the ’remitting‘ phase of PTSD, while the greater than nine years since trauma subgroup in P301 may include more participants in the ’persistent‘ phase of PTSD, which have been described in longitudinal studies of PTSD in the literature.[1-6],,

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

[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.

The Phase 3 HONOR Study (P301)

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

About Tonmya and PTSD

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

About Tonix Pharmaceuticals Holding Corp.

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

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

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2017, as filed with the Securities and Exchange Commission (the "SEC") on March 9, 2018, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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Exhibit 99.03

Investor Presentation

TONIX PHARMACEUTICALS

August 2018

Version P0126 8-21-18 (Doc 0381)

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, 2017, as filed with the Securities and Exchange Commission (the "SEC") on March 9, 2018, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.

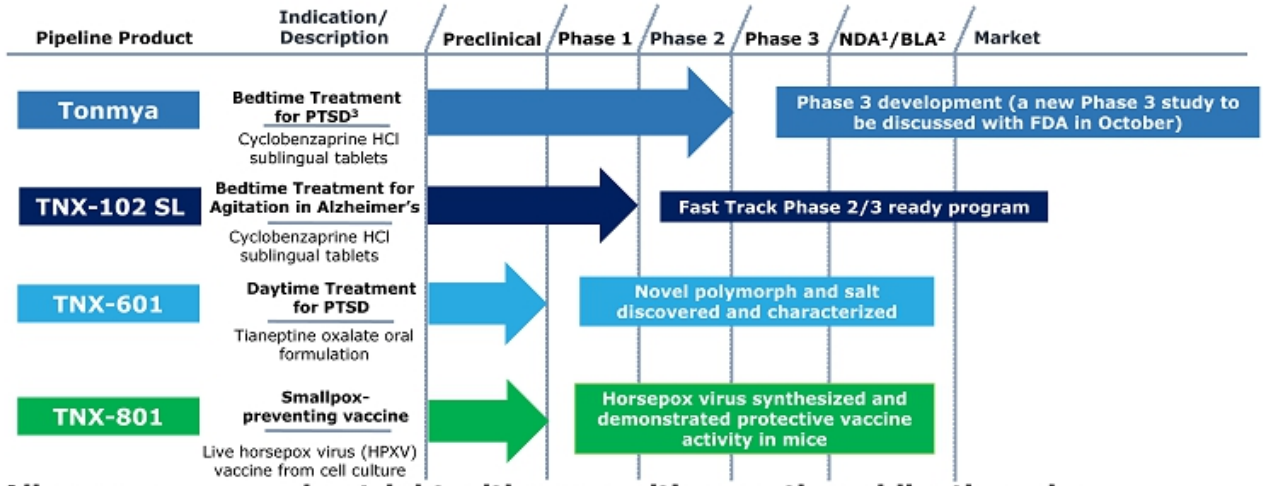
Who we are:

- 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

Candidates in Development



All programs owned outright with no royalties or other obligations due

[1]NDA- New Drug Application; [2]BLA –Biologic Licensing Application; [3]PTSD-Posttraumatic Stress Disorder

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

Tonix Development Highlights

Cyclobenzaprine Sublingual Tablets

Lead Program Tonmya®[1] –FDA Breakthrough Therapy in PTSD– Bedtime treatment in Phase 3 Development

- Results from 2 efficacy studies can improve a new Phase 3 study design
- FDA feedback and agreement are expected 4Q2018
- Pivotal efficacy study may initiate as early as 2019

TNX-102 SL – FDA Fast Track development program for agitation in Alzheimer's (AAD) disease

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

Pipeline

TNX-601[3] - Pre-IND candidate for daytime treatment for PTSD

- Nonclinical development ongoing

TNX-801[4] - Smallpox-preventing vaccine candidate

- Efficacy demonstrated in mouse model
- cGMP process development underway

[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 PTSD. TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2] IND- Investigational New Drug Application
[3] Tianeptine oxalate
[4] Synthesized live horsepox virus

Tonmya for PTSD

Breakthrough Therapy (BT) designation from the FDA

- Expedited development and accelerated approval are expected

One Phase 2 study completed and one Phase 3 study stopped early due to inadequate separation from placebo

- Both studies were accepted by the FDA as potential pivotal efficacy studies in military-related PTSD if successful
- No safety or tolerability concerns
- Phase 2 study (P201) formed the basis of BT designation
- Phase 3 study (P301) provided evidence of effectiveness as early as 4 weeks after treatment but diminished over time due to high placebo response
  - Retrospective analysis showed Tonmya response in subgroup with trauma ≤9 years from screening

Expecting FDA feedback and agreement on second Phase 3 trial in 4Q2018

- Potential NDA[1] approval can be based on one Phase 3 study

Patent protection through 2034 in U.S.[2]

- 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] NDA = New Drug Application
[2] U.S. Patent No. 9,636,408 for eutectic proprietary Protectic™ formulation

Breakthrough Therapy Designation

FDA granted Tonmya Breakthrough Therapy designation – reported December 19, 2016

- PTSD is a serious condition
- Tonmya has potential advantages over existing therapies in military-related PTSD

Benefits of Breakthrough Therapy designation

- Eligibility for priority review of the NDA within 6 months instead of 10-12 months
- Option to submit completed portions of the NDA for rolling review
- An organizational commitment involving FDA's senior managers to accelerate the development and approval process, an opportunity to compress development time

NDA approval based on single-study is possible if results are statistically very persuasive

- Discussed at March 9, 2017 Initial Cross-disciplinary Breakthrough Meeting with the FDA

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 Initial Cross-disciplinary Breakthrough 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 and U.S. Patent No. 9,956,188 in May 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

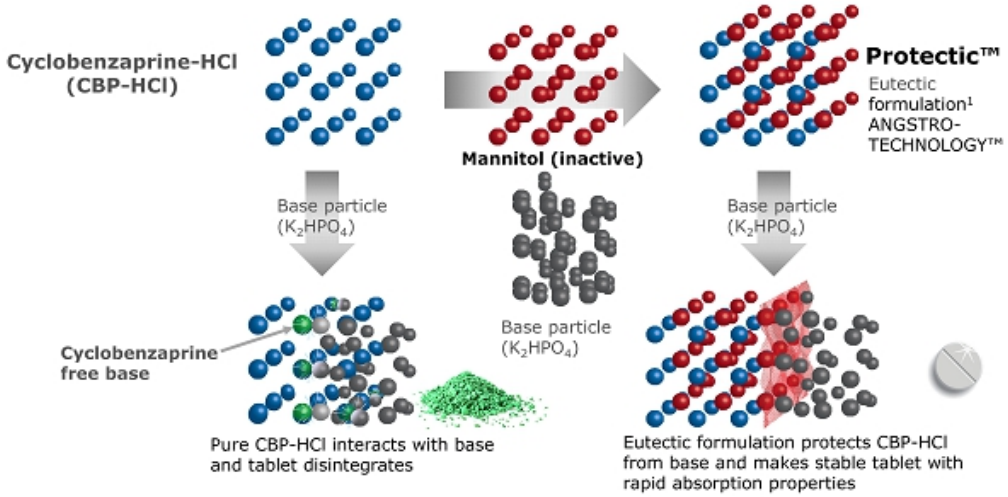
- Innovation by design with patent protected CBP/mannitol eutectic
- Rapid systemic exposure
- Increases bioavailability during sleep
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, norcyclobenzaprine (norCBP)

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

[1] Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada

Proprietary Cyclobenzaprine Hydrochloride Eutectic Mixture Stabilizes Sublingual Tablet Formulation



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

Tonmya: 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

Memory processing is essential to recovery

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

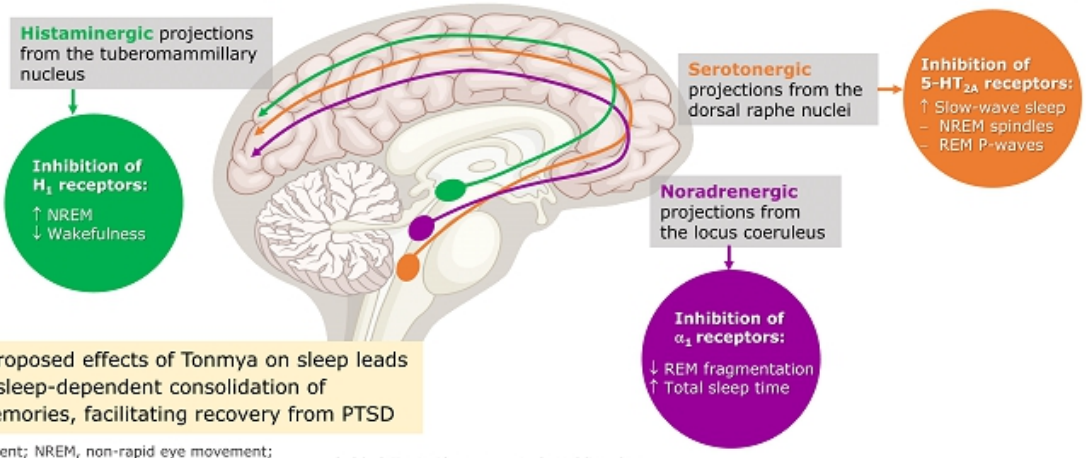
Tonmya targets sleep quality[1]

- 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] 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

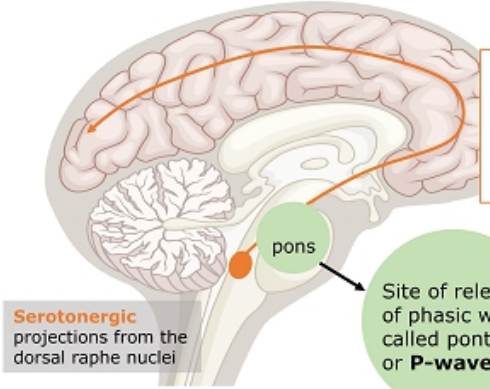
REM, rapid eye movement; NREM, non-rapid eye movement; P-waves, ponto-geniculo-occipital waves

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



- **Serotonergic** activity normally inhibits P-wave release during REM sleep[2]
- This is thought to be done primarily through activity at **5-HT$_{2A}$** receptors[3]

P-wave activity is highest right before and during **REM sleep**[1]

- 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

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.

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

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%* (11 million adults)[2]
  EU 2.3% (~10.0 million adults)[3]

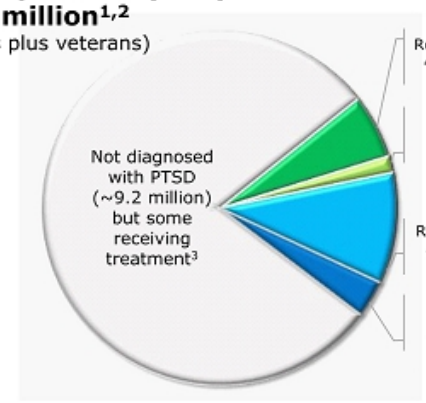
Most common forms of trauma[1]

- 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
[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.)
~11 million[1,2]
(civilians plus veterans)



~620k Veterans Diagnosed in Veterans Administration (VA)[2,4]

~1.2 million Civilians Diagnosed[3]

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

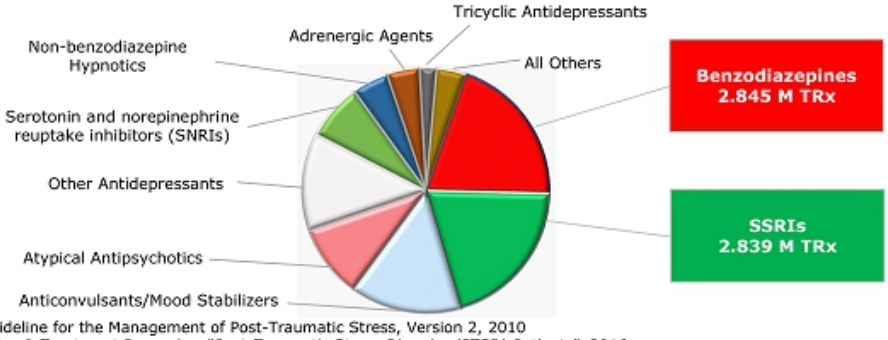
[1] Goldstein et al., 2016 (civilians)
[2] Veterans: VA/DOD Clinical Practice Guidelines for the Managements of PTSD and Acute Stress Disorder, 2017, page 15 (619,493 vets diagnosed with PTSD in VA for 2016)
[3] IMS Consulting, *Market Sizing & Treatment Dynamics: Post-Traumatic Stress Disorder (PTSD) 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 patients unresponsive or intolerant to current treatments
- Side effects relating to sexual dysfunction (particularly in males), sleep 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 developed as a "treatment for PTSD"

- FDA does not distinguish between military and civilian PTSD

Why Initially Target 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

High Prevalence of PTSD Among Combat Veterans

4.7%
General population[1]

19-31%
Vietnam veterans[2]

>19%
Iraq/Afghanistan[3]

11 million American adults affected[4,5]

Women more likely to develop than men[1]

Susceptibility may **run in families**[1]

[1]Goldstein et al., 2016; [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; [4] Goldstein et al., 2016; [5] Veterans: VA/DOD Clinical Practice Guidelines for the Managements of PTSD and Acute Stress Disorder, 2017, page 15

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]

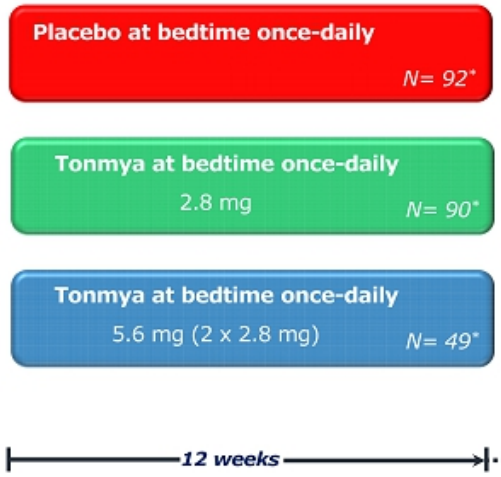
Indirect costs

$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 AtEase/P201[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

AtEase/P201 Study

AtEase was a large adequate well-controlled study in military-related PTSD

- Separation on primary endpoint at Week 12 did not meet primary endpoint at Week 12 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 - Week 12 CAPS-5 (P=0.053) and CGI-I (P=0.041) scores in TNX-102 SL group
- Retrospective analyses suggested CAPS-5 ≥ 33 enrollment criteria for Phase 3
- Additional retrospective analyses are part of planning for FDA meeting in October to discuss a new Phase 3 study

AtEase/P201 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

HONOR/P301[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 (IA) at 274 randomized participants (mITT* N= 252)

- Study stopped based on 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

HONOR/P301 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 due high placebo response at week 12

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

CI = Confidence Interval

MCFB = Mean Change From Baseline

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

HONOR was a large adequate well-controlled study in military-related PTSD

- Separation on primary endpoint at Week 12 did not cross pre-specified study continuation threshold at Week 12
- 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

HONOR dataset is complex and rich

- Retrospective analyses presented at Military Health System Research Symposium (MHSRS) in Kissimmee, FL on August 22, 2018
- Helps to design a better Phase 3 study with high probability of success

Differences Between AtEase/P201 and HONOR/P301 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

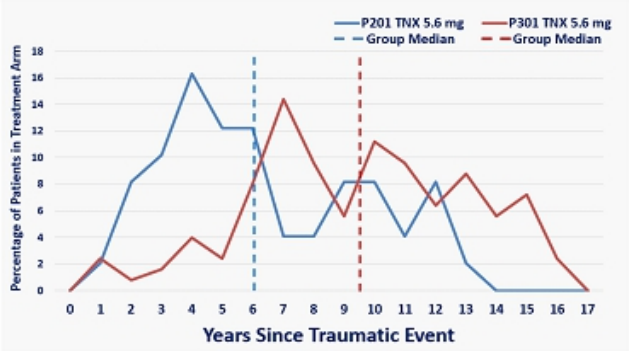
AtEase/P201 and HONOR/P301 Demographics and Characteristics

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

Retrospective Comparison of Time Since Trauma in AtEase/P201 versus HONOR/P301 (TNX 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

Retrospective Analysis of Treatment Response in ≤9 & >9 Years since Trauma in HONOR/P301 Study

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

MMRM with Multiple Imputation

The ≤9 years since trauma group in P301 replicated results from P201

- Retrospective analysis of P201 showed 5.6 mg treatment group difference over placebo of 5.0 points (MMRM with MI, p = 0.031)

LS Mean = Least Squares Mean
MCFB = Mean Change From Baseline

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

		P301 mITT				P301 ≤9 Year Subsample			
		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
- Support results on CAPS-5 and replicate results of Phase 2 P201 Study

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 AtEase/P201 and HONOR/P301*#

	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 Reaction					
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 and unexpected AEs in P301 or P201

- Systemic AEs comparable between studies and also consistent with those described in approved product labeling
- Similar severity and incidence of oral hypoesthesia (oral numbness)

Sustained Remission in HONOR/P301 and AtEase/P201 Studies

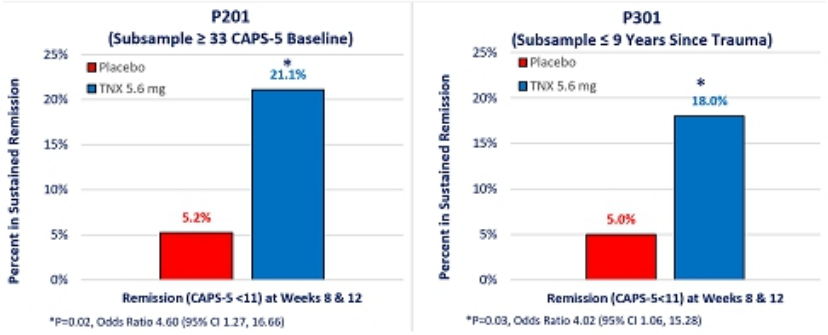
Retrospective Analyses of Phase 2 Subgroup with Entry CAPS-5 ≥33 and Phase 3 subgroup ≤9 Years Since Trauma

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



Sustained Remission in HONOR/P301 and AtEase/P201

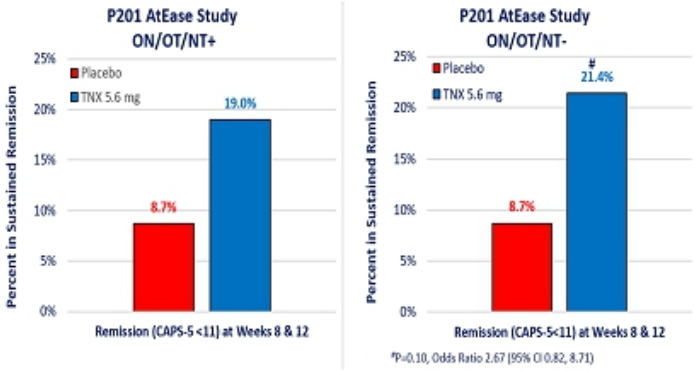
Retrospective Analyses of Phase 2 Subgroups with and without Oral AE's (ON/OT/NT)

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



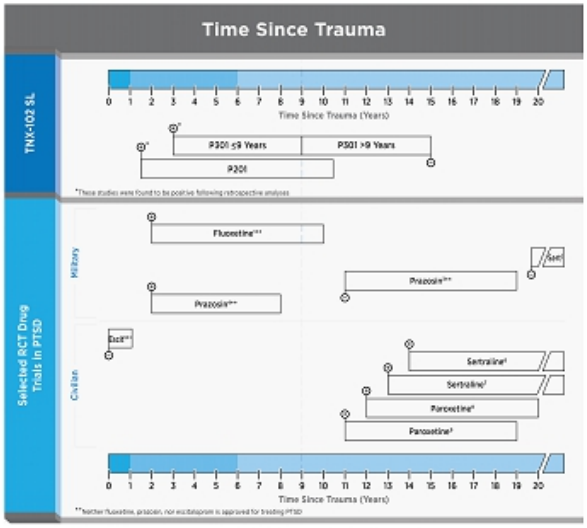
Time Since Trauma – Review of Published Studies

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; Sert=sertraline;

[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.

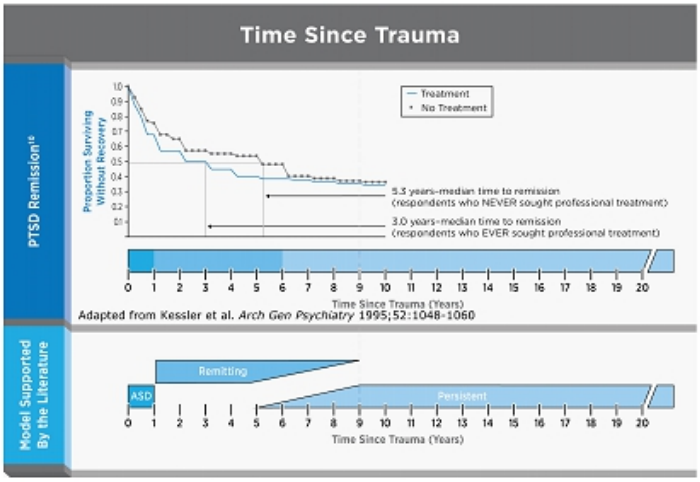
Time Since Trauma – Remitting and Persistent Phases of PTSD

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]

TNX-102 SL responsiveness may be limited to the remitting phase of PTSD

- Consistent with sleep mechanism of facilitating natural recovery



[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.

Tonmya/TNX-102 SL – Summary

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

- Time has passed since the surge in Iraq

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

- Time since trauma is important in the treatment response and PTSD >9 years does not appear to respond to TNX-102 SL

The TNX-102 SL responsive phase of PTSD may correspond to the "Remitting Phase" of PTSD[1-4]

- Persistent phase of PTSD may be non-responsive to TNX-102 SL therapy

[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.

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

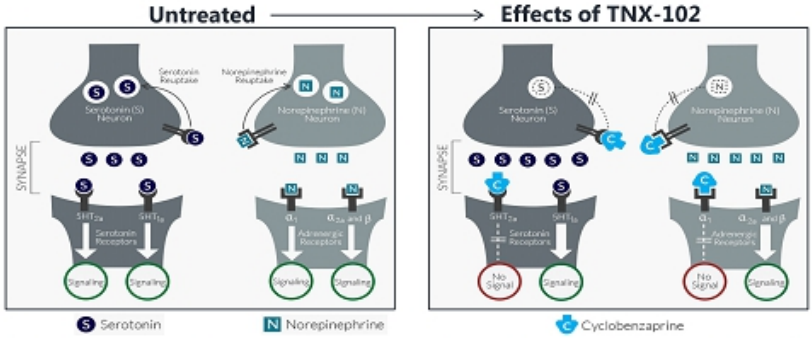
Multi-functional activity suggests potential for other indications

- 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

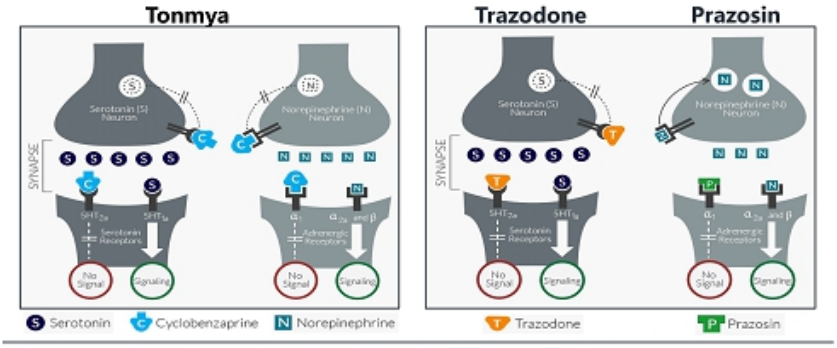


SNARI = Serotonin and Norepinephrine receptor Antagonist and Reuptake Inhibitor

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 – 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

Agitation in Alzheimer's Disease

- Phase 2 study can be a pivotal efficacy study
- Fast Track designation granted July 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 is 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

Phase 2 IND cleared in April 2018

- Proposed Phase 2 IND study can potentially serve as a pivotal efficacy study

Potential approval of TNX-102 SL in agitation in Alzheimer's disease

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

[1]Supplemental New Drug Application

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.

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

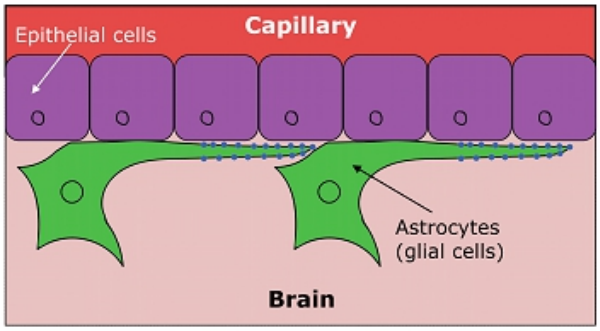
- Animal studies have shown debris clearance from the brain during sleep including toxic proteins associated with Alzheimer's progression[1]

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

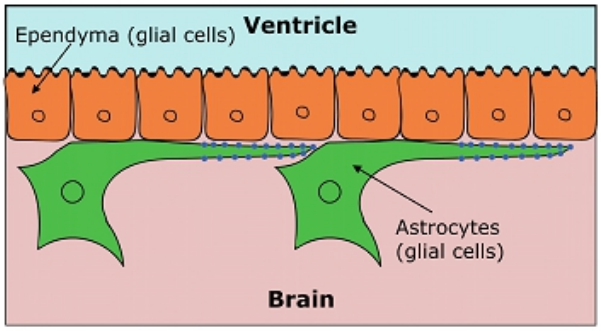
Protective Barriers in the Central and Peripheral Nervous Systems

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]



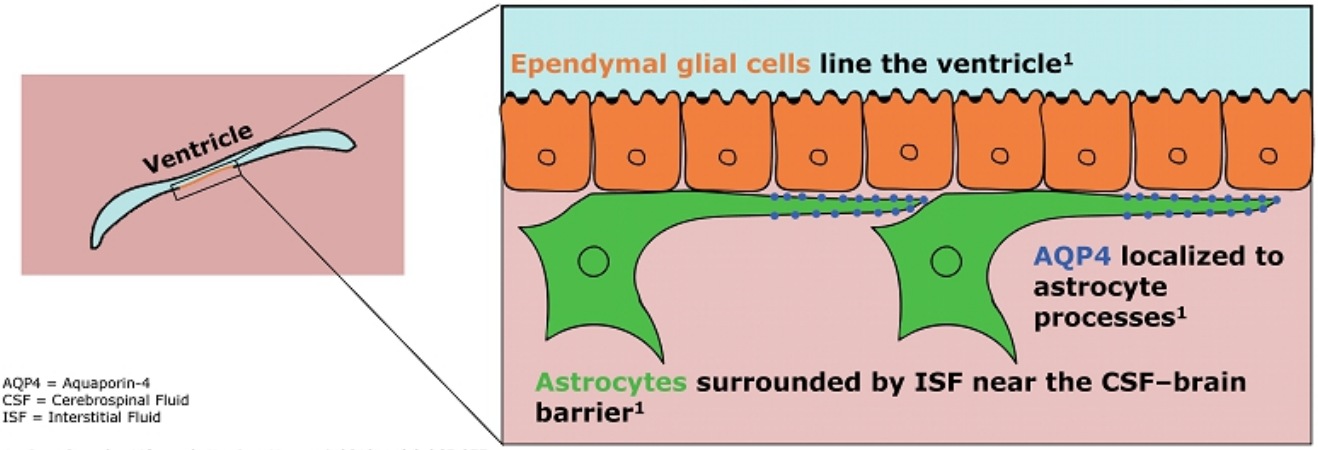
Cerebrospinal Fluid (CSF)–Brain Barrier/Glymphatic System:
extracts toxins from the brain[2]



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]



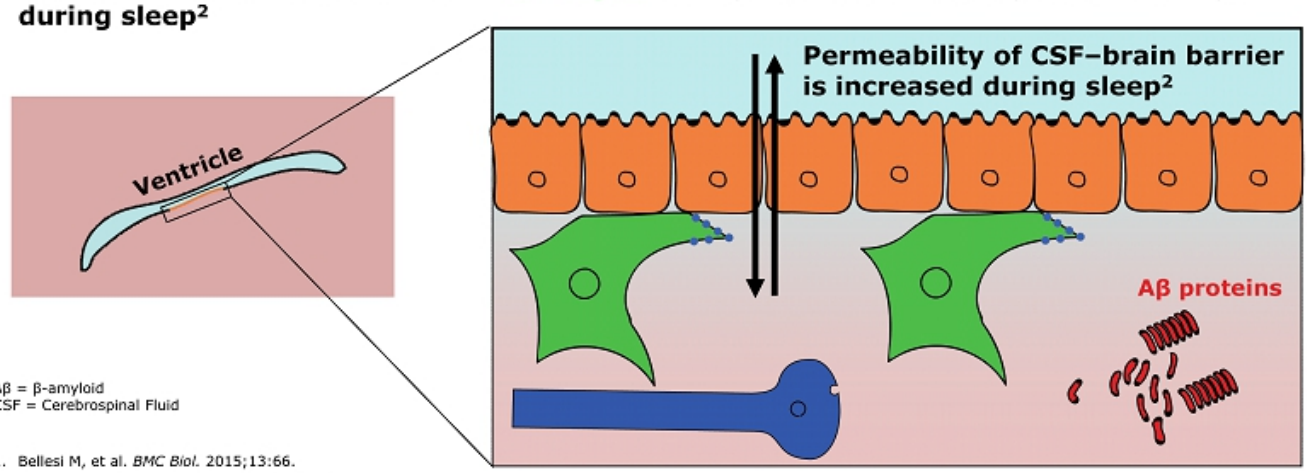
AQP4 = Aquaporin-4
CSF = Cerebrospinal Fluid
ISF = Interstitial Fluid

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]



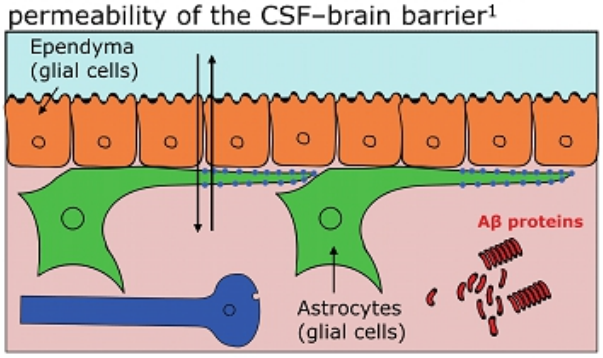
Aβ = β-amyloid
CSF = Cerebrospinal Fluid

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

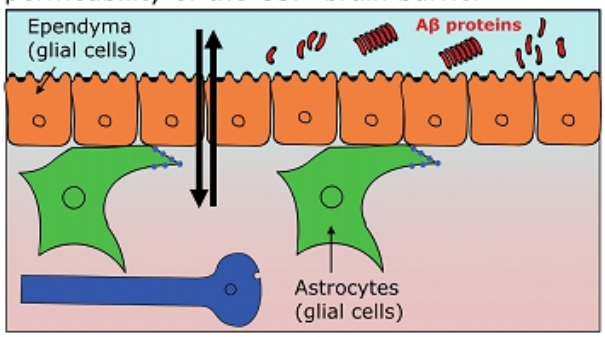
Sleep–Wake Cycles Alter Permeability of the CSF–Brain Barrier

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

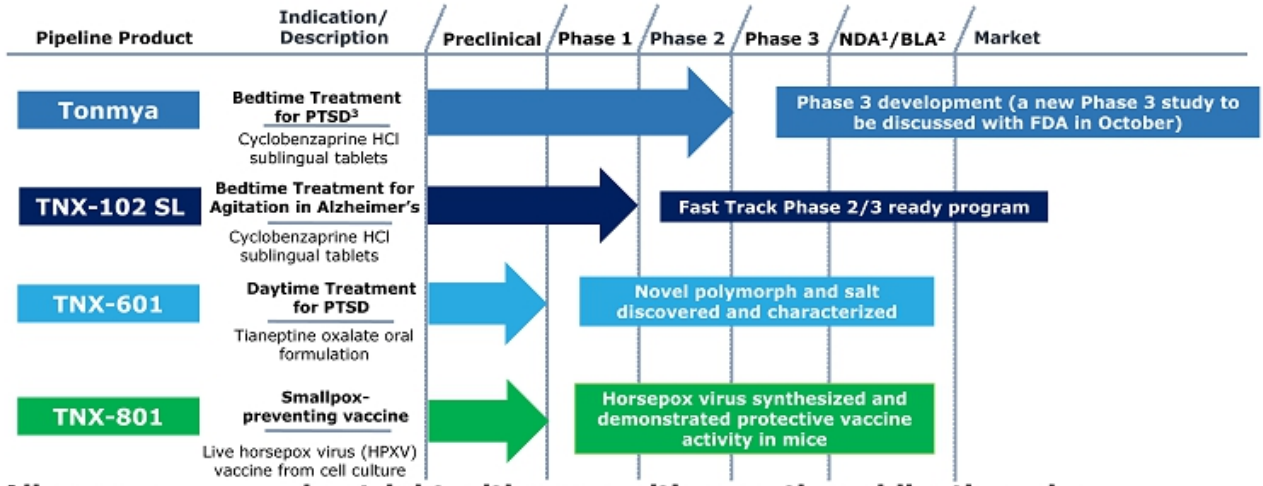
Competitive landscape

- $5HT_{2A}$ Antagonists/inverse agonists
  - Nelotanserin (Axovant)
- Atypical Antipsychotics (also have $5HT_{2A}$ antagonism)
  - Rexulti® brexpiprazole (Otsuka/Lundbeck)
  - Lumateperone (InterCellular)
- 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

Candidates in Development



All programs owned outright with no royalties or other obligations due

[1]NDA- New Drug Application; [2]BLA –Biologic Licensing Application; [3]PTSD-Posttraumatic Stress Disorder

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 Tonmya**

- Tianeptine sodium (amorphous) has been approved in EU, Russia, Asia and Latin America for depression since 1987 with established post-marketing experience
- Identified new oxalate salt polymorph with improved pharmaceutical properties ideal for reformulation

Filed patent application on novel salt polymorph

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

Clinical evidence for PTSD

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

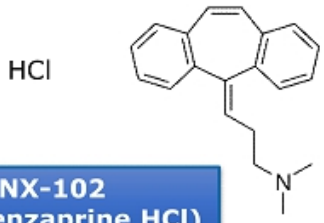
[1] Frančišković T, et al. Psychiatr Danub. 2011 Sep;23(3):257-63. PMID: 21963693
[2] Rumyantseva GM and, Stepanov AL. Neurosci Behav Physiol. 2008 Jan;38(1):55-61. PMID: 18097761
[3] Aleksandrovskiĭ IA, et al. Zh Nevrol Psikhiatr Im S S Korsakova. 2005;105(11):24-9. PMID: 16329631 [Russian]
[4] Onder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

Structural Comparison: TNX-102 and TNX-601

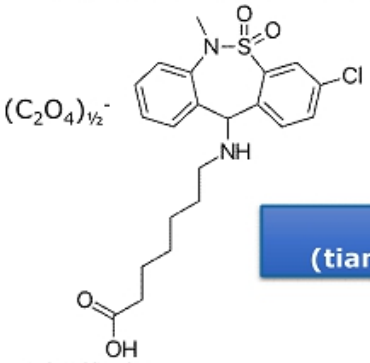
Cyclobenzaprine and tianeptine share structural similarities with classic tricyclic antidepressants (TCAs) and to each other, but each has unique pharmacological properties

- 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**

[1]PRV can be applied to any BLA/NDA for priority 6-month review

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

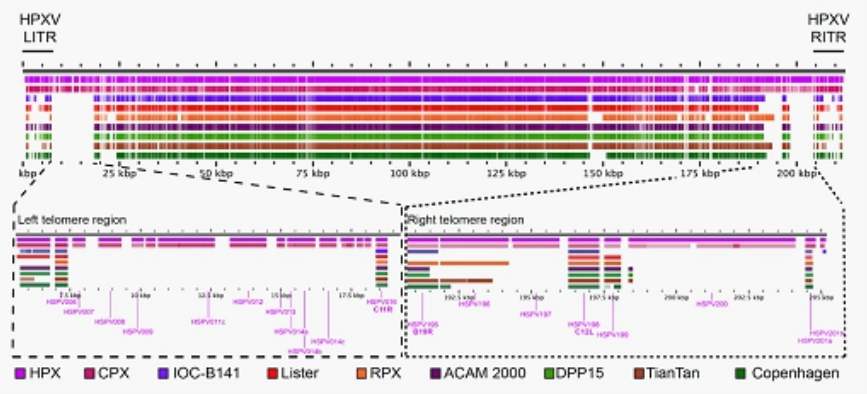
Vaccinia (VACV) strains have demonstrated potential for zoonotic infections and re-infection of humans[2-5]

- 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

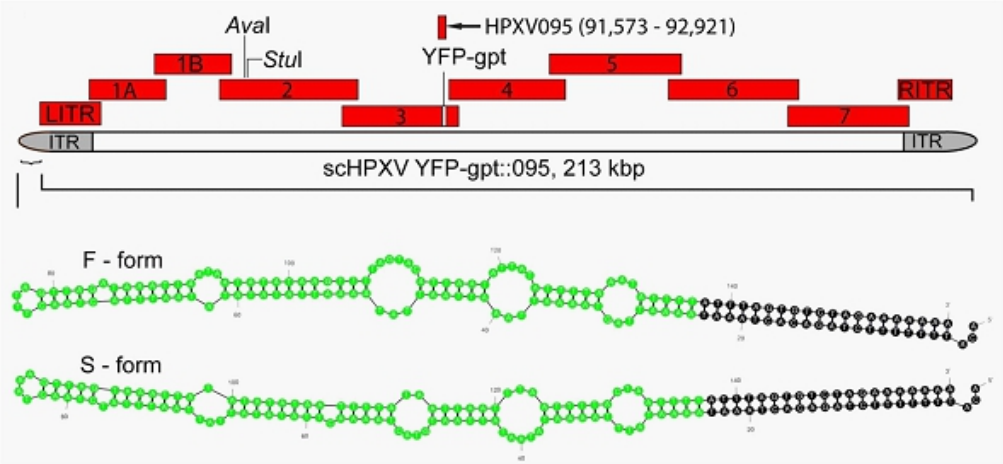
HPXV and its Relationship to Other Orthopoxviruses



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

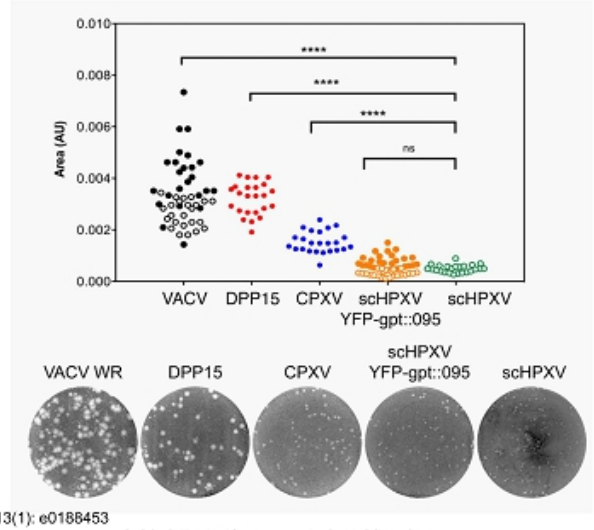
Genome Assembly (212 kbp) by Synthesis of Fragments and Construction of Telomeres



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

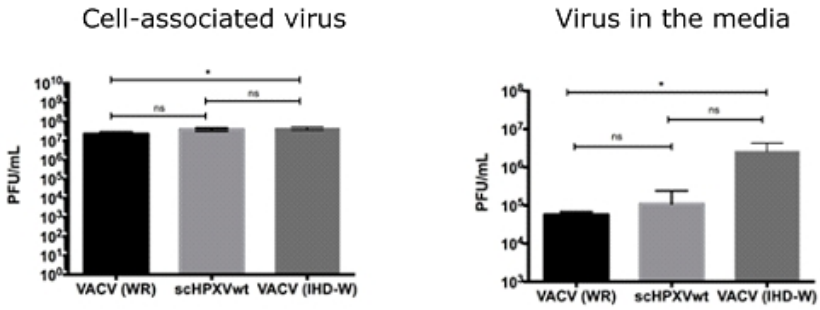
Sequence: GenBank entry DQ792504; DNA: GeneArt

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



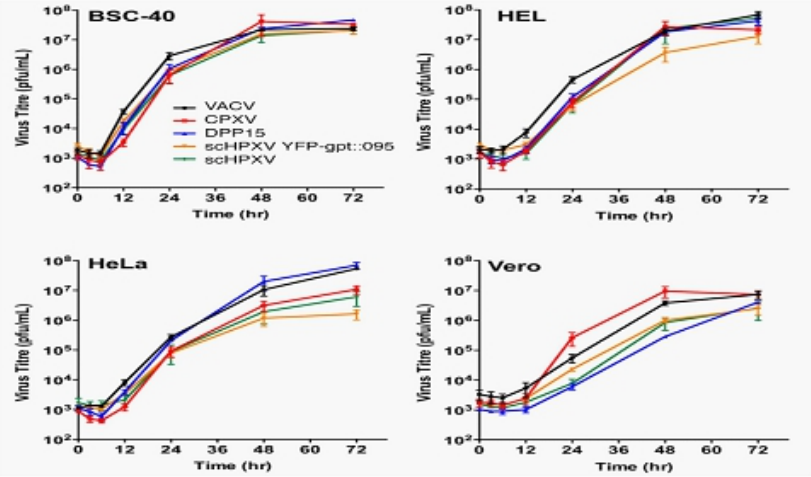
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Production of Cell-Associated and Extracellular Virus



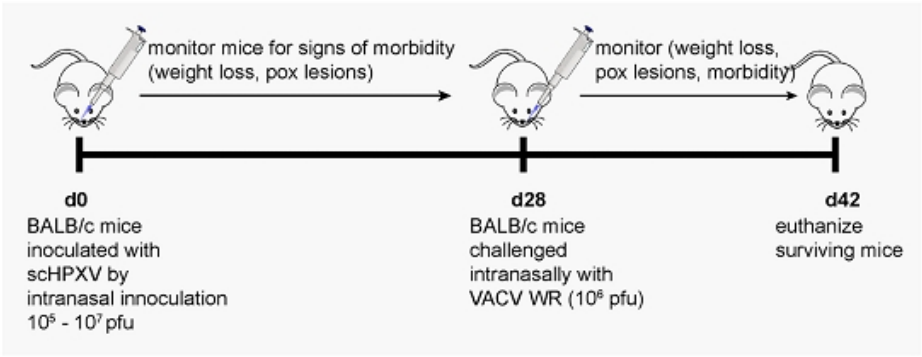
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

HPXV Growth Characteristics



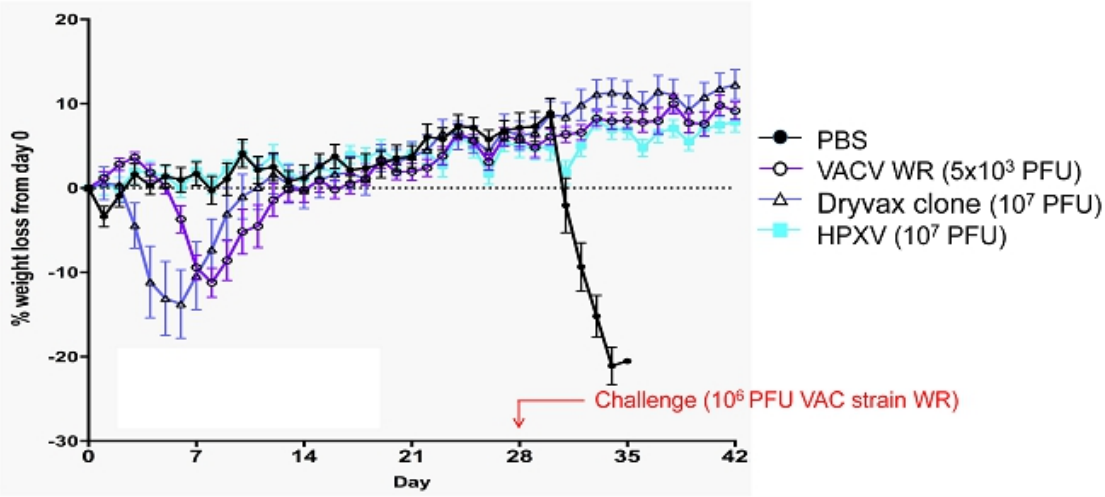
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Testing Vaccine Protective Activity of HPXV in Mice Model



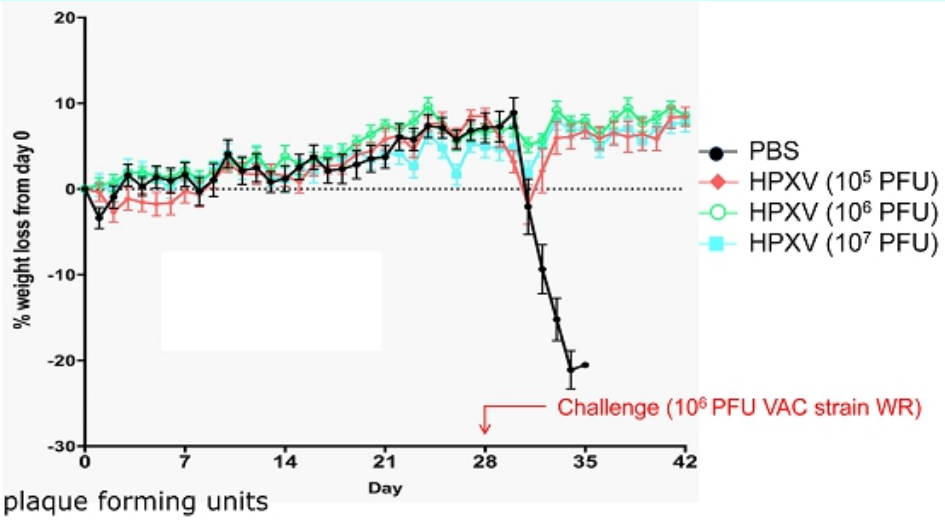
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

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

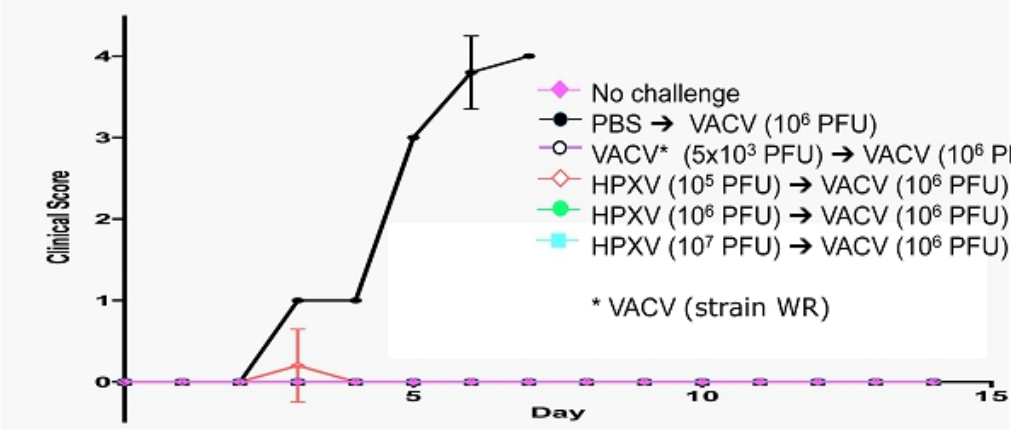
HPXV Vaccine Protection Activity Observed As Low As 10^5 PFU*



*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

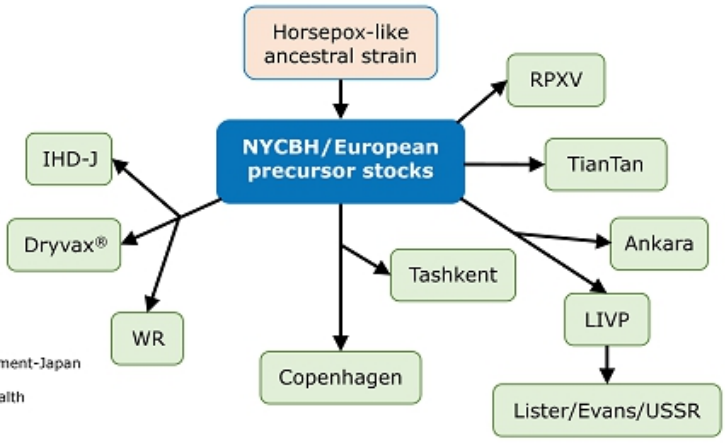
Modern VACV vaccination safety studied in 1081 VACV (Dryvax [62.5%] and ACAM2000 [37.5%]) vaccinees[1]

- 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

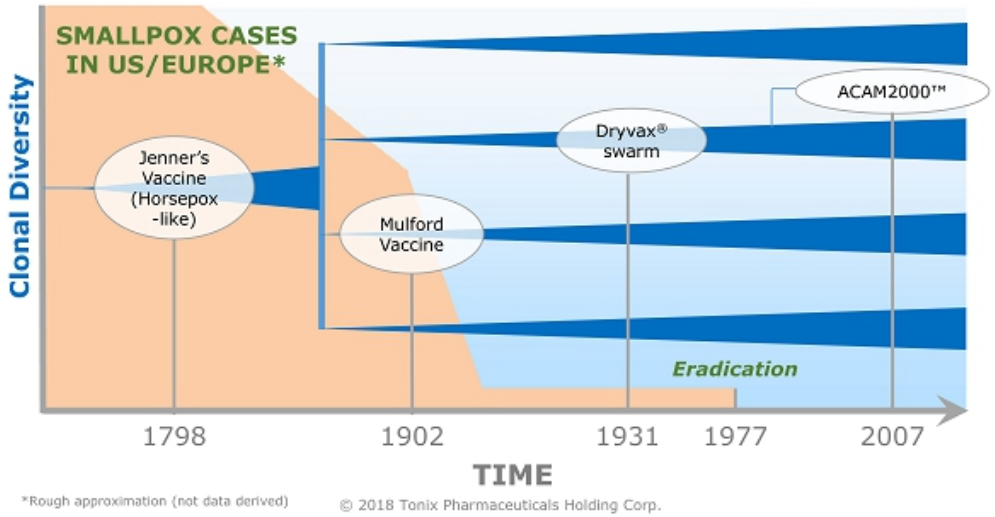


IHD-J=International Health Department-Japan
LIVP=Lister Vaccine Strain
NYCBH=New York City Board of Health
RPXV=Rabbitpox Virus
WR=Western Reserve

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

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

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Milestones – Recently Completed and Upcoming

Tonmya – Posttraumatic Stress Disorder

☑	July 2018	Completed HONOR/P301 study interim analysis - result did not support study continuation
☑	August 2018	Presentation of HONOR/P301 study results at Military Health System Scientific Symposium
☐	October 2018	Meetings with FDA to discuss next Phase 3 study design and finalize commercial product CMC plan

Summary

Phase 3 Breakthrough Therapy development for PTSD focused on military-related PTSD

- Major unmet need; ~11 million Americans affected
- Potential single-study NDA submission

New indication in development for agitation in Alzheimer's Disease

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

Complimentary day-time PTSD treatment in development

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

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

August 2018

Version P0125 8-21-18 (Doc 0380)

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, 2017, as filed with the Securities and Exchange Commission (the "SEC") on March 9, 2018, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.

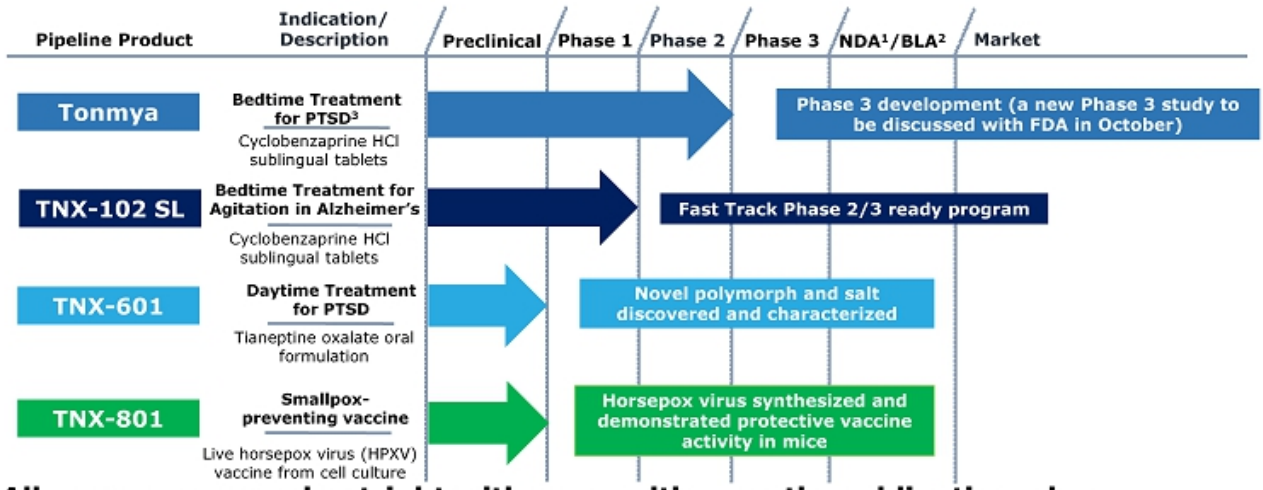
Who we are:

- 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 pathways and established clinical endpoints
  - Built on a foundation of proprietary intellectual property

Candidates in Development



All programs owned outright with no royalties or other obligations due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³PTSD-Posttraumatic Stress Disorder

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

Tonix Development Highlights

Cyclobenzaprine Sublingual Tablets

Lead Program Tonmya®[1] –FDA Breakthrough Therapy in PTSD– Bedtime treatment in Phase 3 Development

- Results from 2 efficacy studies can improve a new Phase 3 study design
- FDA feedback and agreement are expected 4Q2018
- Pivotal efficacy study may initiate as early as 2019

TNX-102 SL – FDA Fast Track development program for agitation in Alzheimer's (AAD) disease

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

Pipeline

TNX-601[3] - Pre-IND candidate for daytime treatment for PTSD

- Nonclinical development ongoing

TNX-801[4] - Smallpox-preventing vaccine candidate

- Efficacy demonstrated in mouse model
- cGMP process development underway

[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 PTSD. TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2] IND- Investigational New Drug Application
[3] Tianeptine oxalate
[4] Synthesized live horsepox virus

Tonmya for PTSD

Breakthrough Therapy (BT) designation from the FDA

- Expedited development and accelerated approval are expected

One Phase 2 study completed and one Phase 3 study stopped early due to inadequate separation from placebo

- Both studies were accepted by the FDA as potential pivotal efficacy studies in military-related PTSD if successful
- No safety or tolerability concerns
- Phase 2 study (P201) formed the basis of BT designation
- Phase 3 study (P301) provided evidence of effectiveness as early as 4 weeks after treatment but diminished over time due to high placebo response
  - Retrospective analysis showed Tonmya response in subgroup with trauma ≤9 years from screening

Expecting FDA feedback and agreement on second Phase 3 trial in 4Q2018

- Potential NDA[1] approval can be based on one Phase 3 study

Patent protection through 2034 in U.S.[2]

- 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] NDA = New Drug Application
[2] U.S. Patent No. 9,636,408 for eutectic proprietary Protectic™ formulation

Breakthrough Therapy Designation

FDA granted Tonmya Breakthrough Therapy designation – reported December 19, 2016

- PTSD is a serious condition
- Tonmya has potential advantages over existing therapies in military-related PTSD

Benefits of Breakthrough Therapy designation

- Eligibility for priority review of the NDA within 6 months instead of 10-12 months
- Option to submit completed portions of the NDA for rolling review
- An organizational commitment involving FDA's senior managers to accelerate the development and approval process, an opportunity to compress development time

NDA approval based on single-study is possible if results are statistically very persuasive

- Discussed at March 9, 2017 Initial Cross-disciplinary Breakthrough Meeting with the FDA

Tonmya: Features in PTSD Therapy

Designed for bedtime use

- Every night, sublingual therapy

Targets sleep quality[1]

- The active ingredient 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

No recognized abuse potential

- Not a benzo or non-benzo class drug

U.S. patent protection through 2034

- Composition of matter and method of use patents issued – Pharmacokinetic patent application in review

[1] Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada

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 Initial Cross-disciplinary Breakthrough 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 and U.S. Patent No. 9,956,188 in May 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

[1] Daugherty et al., Abstract 728, Society of Biological Psychiatry 70th Annual Scientific Convention, May 14-16, 2015, Toronto Ontario, Canada

Tonmya: 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

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[1]

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

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: 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 patients unresponsive or intolerant to current treatments
- Side effects relating to sexual dysfunction (particularly in males), sleep 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 developed as a "treatment for PTSD"

- FDA does not distinguish between military and civilian PTSD

High Prevalence of PTSD Among Combat Veterans

4.7%
General population[1]

19-31%
Vietnam veterans[2]

>19%
Iraq/Afghanistan[3]

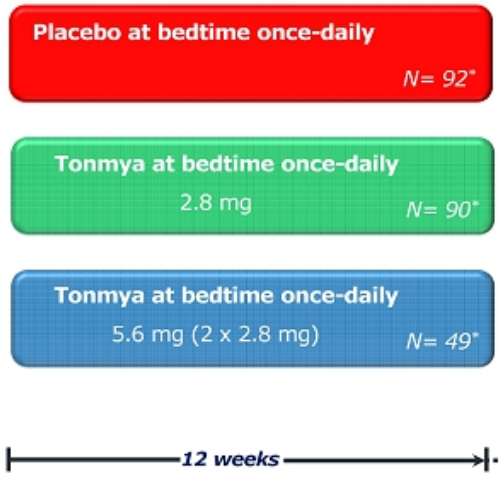
11 million American adults affected[4,5]

Women more likely to develop than men[1]

Susceptibility may **run in families**[1]

[1]Goldstein et al., 2016; [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; [4] Goldstein et al., 2016; [5] Veterans: VA/DOD Clinical Practice Guidelines for the Managements of PTSD and Acute Stress Disorder, 2017, page 15

Phase 2 AtEase/P201[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

AtEase/P201 Study

AtEase was a large adequate well-controlled study in military-related PTSD

- Separation on primary endpoint at Week 12 did not meet primary endpoint at Week 12 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 - Week 12 CAPS-5 (P=0.053) and CGI-I (P=0.041) scores in TNX-102 SL group
- Retrospective analyses suggested CAPS-5 ≥ 33 enrollment criteria for Phase 3
- Additional retrospective analyses are part of planning for FDA meeting in October to discuss a new Phase 3 study

AtEase/P201 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

HONOR/P301[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 (IA) at 274 randomized participants (mITT* N= 252)

- Study stopped based on 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

HONOR/P301 Study- Primary Analysis in mITT Population

	Placebo		TNX-102 SL 5.6 mg		
Visit	N=127		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 due high placebo response at week 12

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

CI = Confidence Interval

MCFB = Mean Change From Baseline

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

HONOR was a large adequate well-controlled study in military-related PTSD

- Separation on primary endpoint at Week 12 did not cross pre-specified study continuation threshold at Week 12
- No safety or tolerability issues 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

HONOR dataset is complex and rich

- Retrospective analyses presented at Military Health System Research Symposium (MHSRS) in Kissimmee, FL on August 22, 2018
- Helps to design a better Phase 3 study with high probability of success

Differences Between AtEase/P201 and HONOR/P301 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

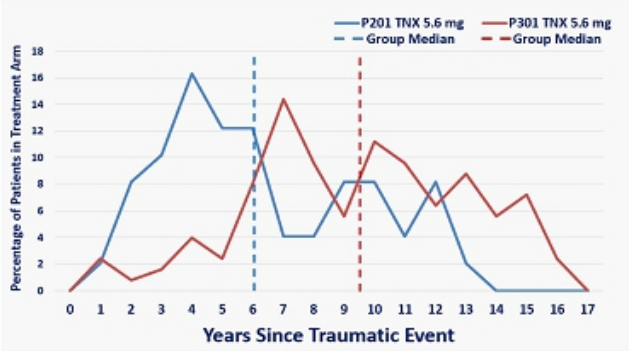
AtEase/P201 and HONOR/P301 Demographics and Characteristics

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

Retrospective Comparison of Time Since Trauma in AtEase/P201 versus HONOR/P301 (TNX 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

Retrospective Analysis of Treatment Response in ≤9 & >9 Years since Trauma in HONOR/P301 Study

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

MMRM with Multiple Imputation

The ≤9 years since trauma group in P301 replicated results from P201

- Retrospective analysis of P201 showed 5.6 mg treatment group difference over placebo of 5.0 points (MMRM with MI, p = 0.031)

LS Mean = Least Squares Mean
MCFB = Mean Change From Baseline

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

		P301 mITT				P301 ≤9 Year Subsample			
		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
- Support results on CAPS-5 and replicate results of Phase 2 P201 Study

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 AtEase/P201 and HONOR/P301*#

	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 Reaction					
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 and unexpected AEs in P301 or P201

- Systemic AEs comparable between studies and also consistent with those described in approved product labeling
- Similar severity and incidence of oral hypoesthesia (oral numbness)

Sustained Remission in HONOR/P301 and AtEase/P201 Studies

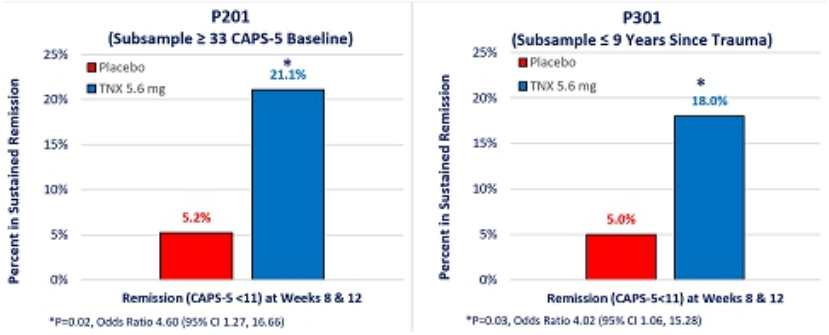
Retrospective Analyses of Phase 2 Subgroup with Entry CAPS-5 ≥33 and Phase 3 subgroup ≤9 Years Since Trauma

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



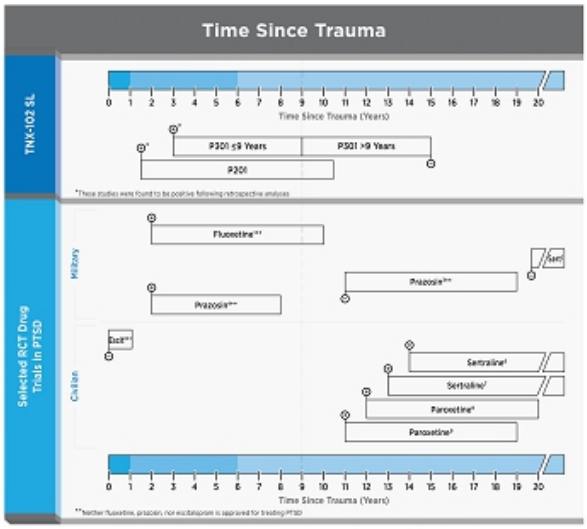
Time Since Trauma – Review of Published Studies

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



Esct=escitalopram; Sert=sertraline;

[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.

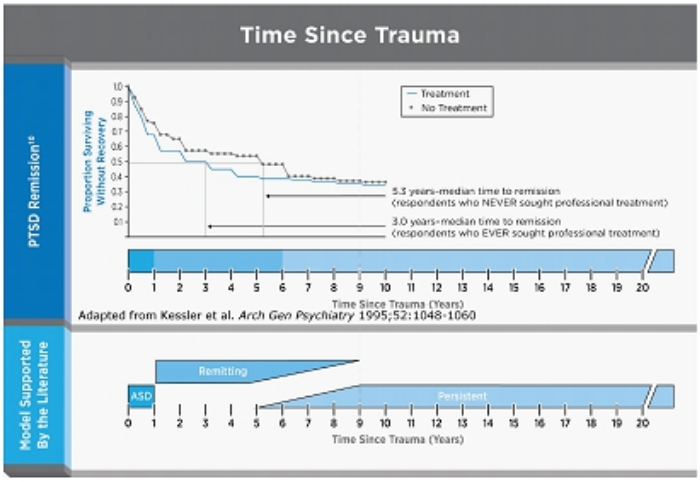
Time Since Trauma – Remitting and Persistent Phases of PTSD

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]

TNX-102 SL responsiveness may be limited to the remitting phase of PTSD

- Consistent with sleep mechanism of facilitating natural recovery



[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.

Tonmya/TNX-102 SL – Summary

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

- Time has passed since the surge in Iraq

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

- Time since trauma is important in the treatment response and PTSD >9 years does not appear to respond to TNX-102 SL

The TNX-102 SL responsive phase of PTSD may correspond to the "Remitting Phase" of PTSD[1-4]

- Persistent phase of PTSD may be non-responsive to TNX-102 SL therapy

[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.

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 – 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

Agitation in Alzheimer's Disease

- Phase 2 study can be a pivotal efficacy study
- Fast Track designation granted July 2018

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})

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

Connection between Sleep Disturbance and Agitation

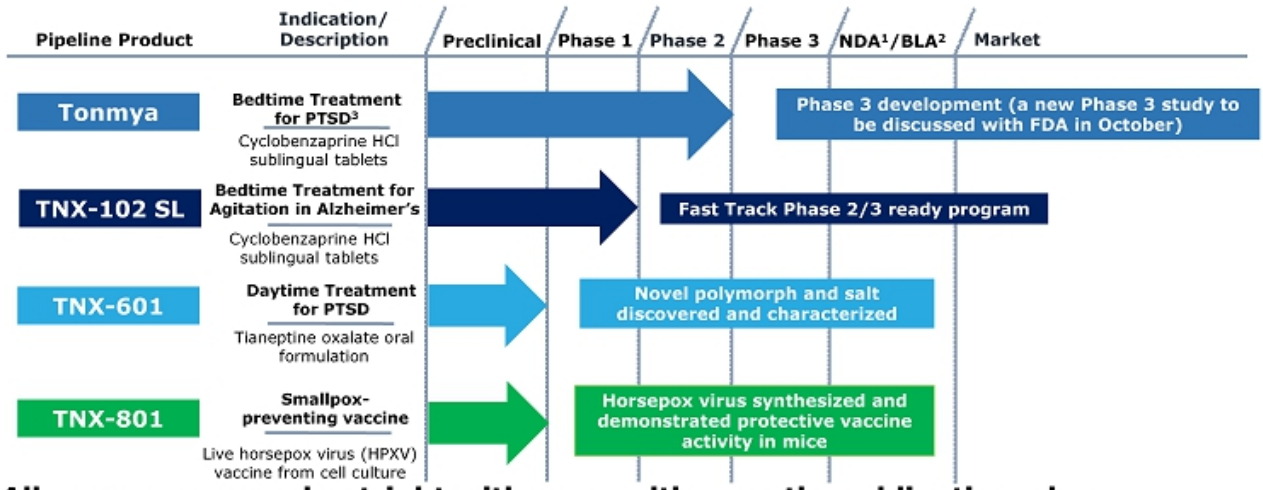
- Agitation in Alzheimer's Disease is associated with sleep disturbance[1,2]
- Evidence that improving sleep could improve agitation[3]

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.

Candidates in Development



All programs owned outright with no royalties or other obligations due

¹NDA- New Drug Application; ²BLA –Biologic Licensing Application; ³PTSD-Posttraumatic Stress Disorder

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

Pre-IND Candidate

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 Tonmya**

- Tianeptine sodium (amorphous) has been approved in EU, Russia, Asia and Latin America for depression since 1987 with established post-marketing experience
- Identified new oxalate salt polymorph with improved pharmaceutical properties ideal for reformulation

Filed patent application on novel salt polymorph

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

Targeting a Condition with Significant Unmet Need

Clinical evidence for PTSD

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

IND enabling non-clinical study underway

[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**

[1]PRV can be applied to any BLA/NDA for priority 6-month review

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

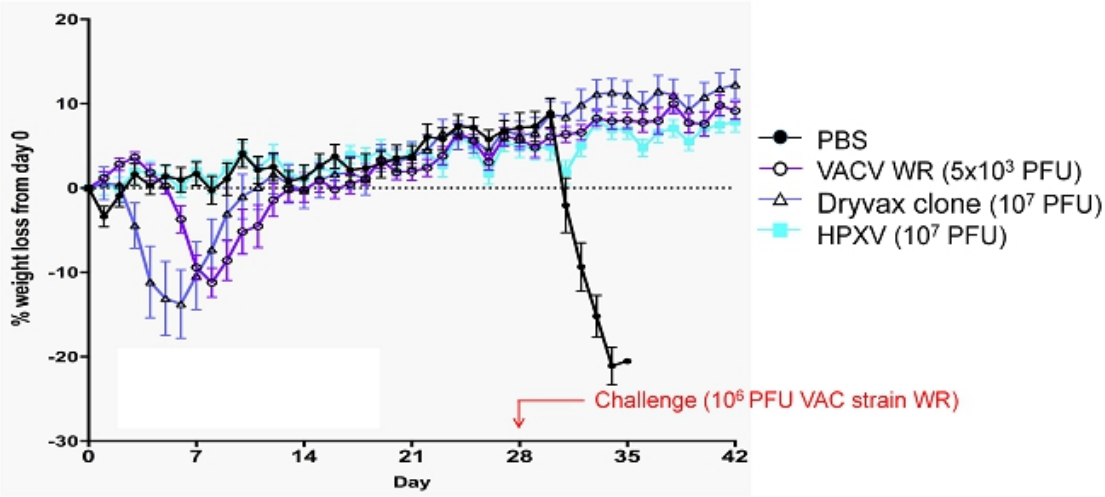
- Vaccinia is the term used to classify the live poxviruses that are used as smallpox vaccines, including ACAM2000, which is the latest smallpox vaccine licensed in the U.S.

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

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

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

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

Management Team

Seth Lederman, MD
President & CEO

Gregory Sullivan, MD
Chief Medical Officer

Bradley Saenger, CPA
Chief Financial Officer

Jessica Morris
Chief Operating Officer

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Seth Lederman, MD Chairman	**Ernest Mario, PhD** ALZA, Glaxo, Reliant Pharma
Margaret Smith Bell Standard Life Investments, Putnam Investments, State Street Research	**Charles Mather** BTIG, Janney, Jefferies, Cowen, Smith Barney
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Gen. David Grange (ret.) Pharm-Olam, PPD, McCormick Foundation	**Samuel Saks, MD** Jazz Pharma, ALZA, Johnson & Johnson
Donald Landry, MD, PhD Chair of Medicine, Columbia University	

Milestones – Recently Completed and Upcoming

Tonmya – Posttraumatic Stress Disorder

☑	July 2018	Completed HONOR/P301 study interim analysis - result did not support study continuation
☑	August 2018	Presentation of HONOR/P301 study results at Military Health System Scientific Symposium
☐	October 2018	Meetings with FDA to discuss next Phase 3 study design and finalize commercial product CMC plan

Summary

Phase 3 Breakthrough Therapy development for PTSD focused on military-related PTSD

- Major unmet need; ~11 million Americans affected
- Potential single-study NDA submission

New indication in development for agitation in Alzheimer's Disease

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

Complimentary day-time PTSD treatment in development

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

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!