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): October 16, 2019

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

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

509 Madison Avenue, Suite 1608, New York, New York 10022
(Address of principal executive offices) (Zip Code)

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

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

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

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Global Market

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

Emerging growth company ☐

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

Item 7.01 Regulation FD Disclosure.

The Company updated its investor presentations, which are used to conduct meetings with investors, stockholders and analysts and at investor conferences, and which the Company intends to place on its website, which may contain nonpublic information. Copies of the presentations are filed as Exhibit 99.01 and 99.02 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.01 and 99.02 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Corporate Presentation by the Company for October 2019 (Long Form)
99.02	Corporate Presentation by the Company for October 2019 (Abbreviated Form)

SIGNATURE

Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: October 16, 2019

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

Exhibit 99.01

Investor Presentation

TONIX PHARMACEUTICALS

October 2019

Version P0201 10-16-19 (Doc 0544)

Cautionary Note on Forward-Looking Statements

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

Tonix Pharmaceuticals

Who we are:

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

- Focusing on small molecules and biologics to treat psychiatric, pain and addiction conditions, to improve biodefense through potential medical counter-measures and to prevent and treat organ transplant rejection

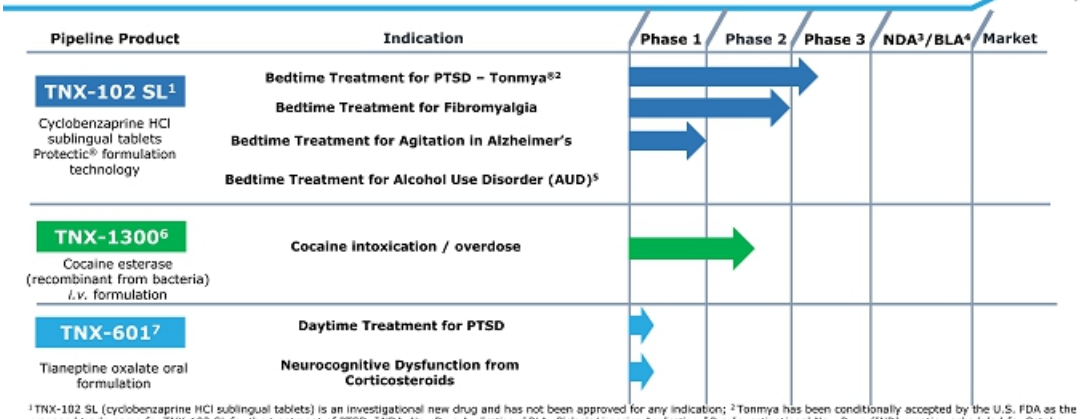
What we do:

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

CNS Candidates in Clinical Development

Psychiatry, Pain and Addiction

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



[1] TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication; [2] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL for the treatment of PTSD. [3] NDA- New Drug Application; [4] BLA –Biologic Licensing Application; [5] Pre-Investigational New Drug (IND) meeting scheduled for October with FDA. Upon receiving FDA clearance of an IND application, TNX-102 SL for AUD will be Phase 2 ready as it is expected to qualify for the 505(b)(2) pathway for approval; [6] TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication; [7] TNX-601 is in the pre-IND stage in the U.S., but a Phase 1 study for formulation development is currently being conducted outside of the U.S.

Preclinical Pipeline[1]

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

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

TNX-102 SL Proposed Mechanism: Improving Sleep Quality

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

Therapeutic Area	Target Indication	Status
Psychiatry	Posttraumatic stress disorder (PTSD)	Phase 3
Rheumatology	Fibromyalgia (FM)	Phase 3
Psychiatry / Neurology	Agitation in Alzheimer's Disease (AAD)	Phase 2 ready
Addiction	Alcohol Use Disorder (AUD)	Pre-IND
Chronic pain	TBD	Life-cycle opportunity
Sleep disorders	TBD	Life-cycle opportunity

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

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

Overview of Posttraumatic Stress Disorder (PTSD)

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

Symptoms of PTSD fall into four clusters:

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

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

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

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

Impact of PTSD on People

Consequences:

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

PTSD as a risk factor for:

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

PTSD: U.S. Prevalence and Index Traumas

PTSD is a chronic response to traumatic event(s)

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

Adult Civilians:

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

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

Most common forms of trauma[1]

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

[1] Kessler et al., Arch Gen Psychiatry 1995; 52:1048
[2] Goldstein et al., 2016 (adjusted for 2019)
[3] The European Union Market Potential for a New PTSD Drug. Prepared for Tonix Pharmaceuticals by Procela Consultants Ltd, September 2016

Prevalence of PTSD Among Civilians and Veterans

4.7%
Adult population[1]

19-31%
Vietnam veterans[2]

>19%
Iraq/Afghanistan[3]

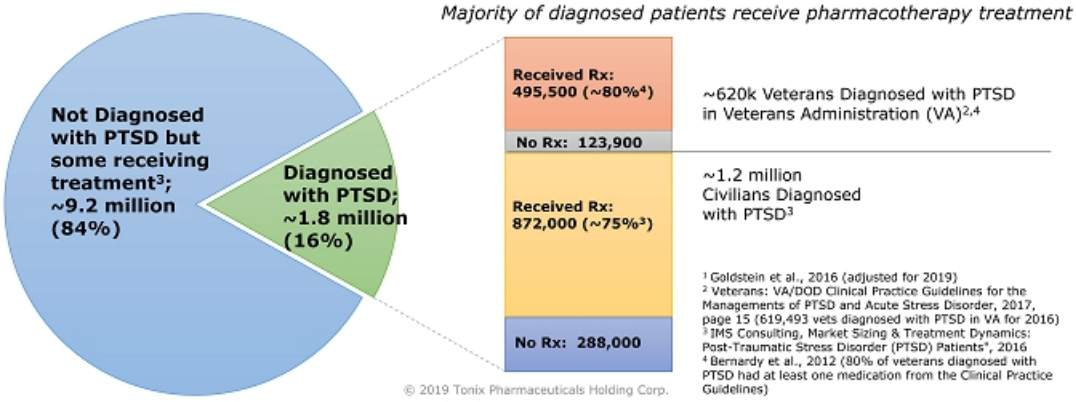
12 million American adults annually[1]

Women more likely to develop than men[1]

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

PTSD Prevalence and Market Characteristics

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



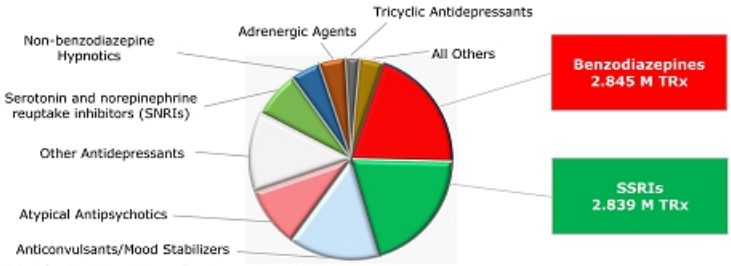
[1] Goldstein et al., 2016 (adjusted for 2019)
[2] Veterans: VA/DOD Clinical Practice Guidelines for the Managements of PTSD and Acute Stress Disorder, 2017, page 15 (619,493 vets diagnosed with PTSD in VA for 2016)
[3] IMS Consulting, Market Sizing & Treatment Dynamics: Post-Traumatic Stress Disorder (PTSD) Patients', 2016
[4] Bernardy et al., 2012 (80% of veterans diagnosed with PTSD had at least one medication from the Clinical Practice Guidelines)

What Drug Classes are Used to Treat PTSD?

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

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

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



* TRx = Total prescriptions

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

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

PTSD: Not Well-Served by Approved Treatments

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

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

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

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

TNX-102 SL is being investigated in both military and civilian PTSD and is expected to be indicated as a "treatment for PTSD"

Why Initially Targeted Military-Related PTSD?

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

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

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

- **Inconsistent treatment response observed in males**

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

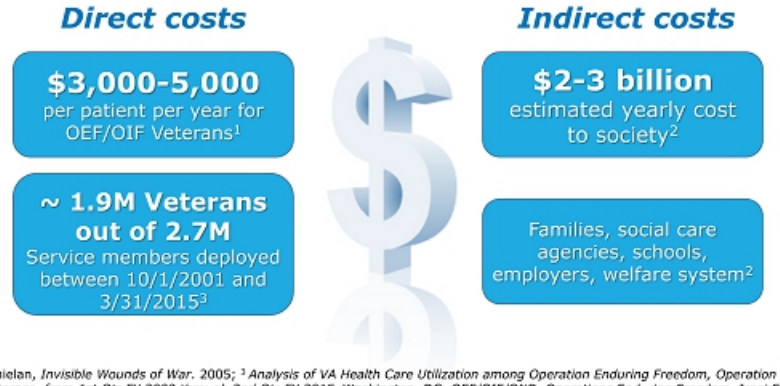
- **Important tolerability issues with SSRIs in this population**

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

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

Growing Economic and Social Burden to Care for Veterans with PTSD

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



[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.

TNX-102 SL: a Potential Bedtime Treatment for PTSD

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

- Phase 2 study (P201/AtEase) showed TNX-102 SL 5.6 mg had a strong signal of treatment effect at Week 12 as measured by CAPS-5[1]
- Phase 3 study (P301/HONOR) provided evidence of effectiveness as early as 4 weeks after treatment but diminished over time due to high placebo response
  - Retrospective analysis showed persistent effectiveness at Week 12 in subgroup with Time Since Trauma ≤9 years from screening
- Both studies can be used as supportive evidence of efficacy and safety for TNX-102 SL NDA submission
- No serious or unexpected adverse events related to TNX-102 SL were reported

Phase 3 study (P302/RECOVERY) initiated in March 2019 and currently enrolling

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

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

TNX-102 SL NDA can be filed without drug abuse and dependency assessment studies

- April 2017 meeting minutes from the March 2017 FDA meeting

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

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

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

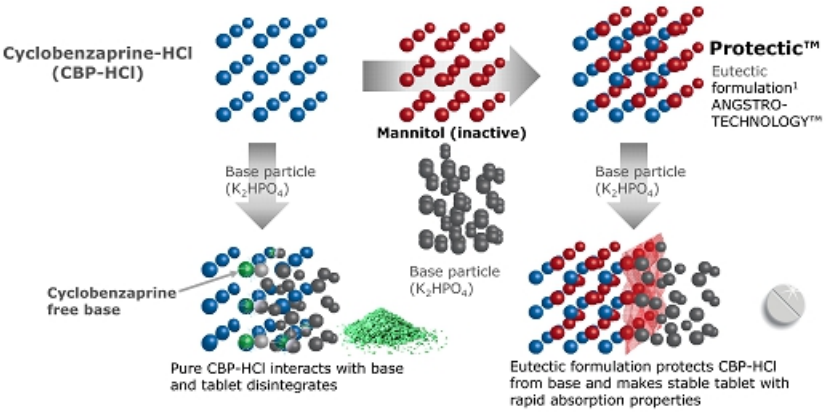
CBP undergoes extensive first-pass hepatic metabolism when orally ingested

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

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

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

Proprietary Cyclobenzaprine Hydrochloride Eutectic Mixture Stabilizes Sublingual Tablet Formulation



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

TNX-102 SL: Hypothesized Novel Mechanism Targets Sleep Quality for Recovery from PTSD

PTSD is a disorder of recovery

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

Memory processing is essential to recovery

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

TNX-102 SL targets sleep quality[3]

- The active ingredient in TNX-102 SL, cyclobenzaprine, interacts with receptors that regulate sleep quality: strongly binds and potently blocks 5-HT_{2A}, α_1-adrenergic and histamine H_1 receptors, permissive to sleep-dependent recovery processes

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

Proposed Mechanism of Action of TNX-102 SL in the Treatment of PTSD:

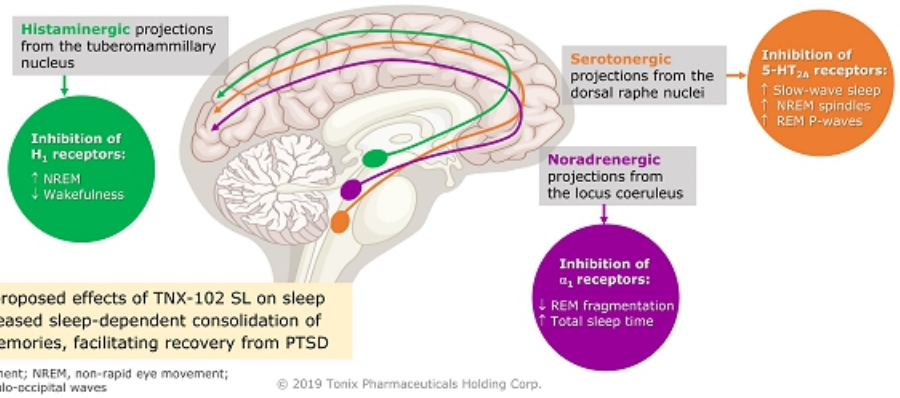
Focus on Nocturnal 5-HT_{2A} Receptor Blockade in REM

- 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.

Proposed Mechanism of Action of TNX-102 SL in the Treatment of PTSD:
The Effects of Nocturnal Neuroreceptor Blockade on Sleep

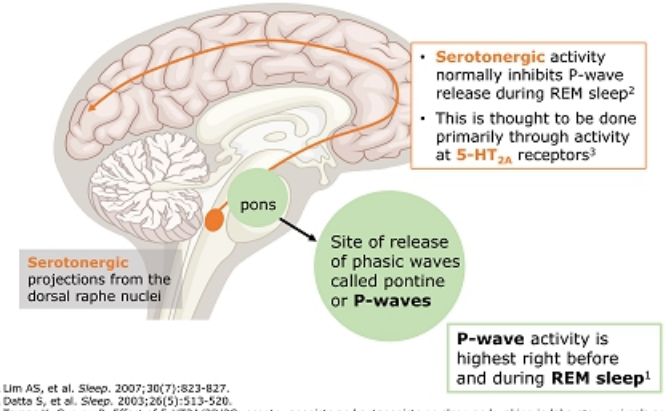
Cyclobenzaprine is a functional antagonist at serotonergic 5-HT_{2A} receptors, noradrenergic α_1 receptors, and histaminergic H_1 receptors



The overall proposed effects of TNX-102 SL 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

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

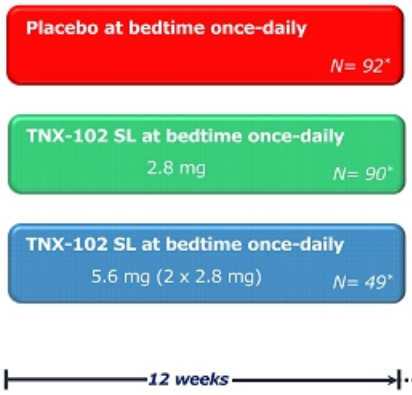


- Increased P-wave activity during REM sleep is critical for fear extinction memory consolidation in rats[4]
- By blocking 5-HT_{2A} receptors, cyclobenzaprine may sustain P-wave activity during REM sleep
- This blockade may lead to better quality of REM sleep with increased fear extinction consolidation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

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

1. Lim AS, et al. *Sleep*. 2007;30(7):823-827.
2. Datta S, et al. *Sleep*. 2003;26(5):513-520.
3. Tamas K, Gyongy 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.

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



- Randomized, double-blind, placebo-controlled trial in military-related PTSD
- Efficacy analysis from 231* patients; 24 U.S. clinical sites
- Enrolled patients with baseline CAPS-5[2] ≥ 29
- Primary Efficacy Analysis:
  - Difference in CAPS-5 score change from baseline between TNX-102 SL 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 population

P201/AtEase Study

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

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

P201/AtEase Study – Summary of Primary and Secondary Analyses (Week 12)

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

BOCF, baseline observation carried forward; CGI-I, Clinical Global Impression - Improvement scale; LOCF, last observation carried forward; MMRM, mixed model repeated measures; PGIC, Patient Global Impression of Change
^Primary analysis p-value not significant comparing Tonmya 2.8 mg versus placebo
*p<0.05

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

General study characteristics:

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

TNX-102 SL 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 (TNX-102 SL 5.6 mg vs. placebo)

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

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

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

P301/HONOR Study- Primary Analysis in mITT Population

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

MMRM with Multiple Imputation

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

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

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

CI = Confidence Interval

MCFB = Mean Change From Baseline

Differences Between P201/AtEase and P301/HONOR Studies Design

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

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

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

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

P201/AtEase and P301/HONOR Demographics and Characteristics

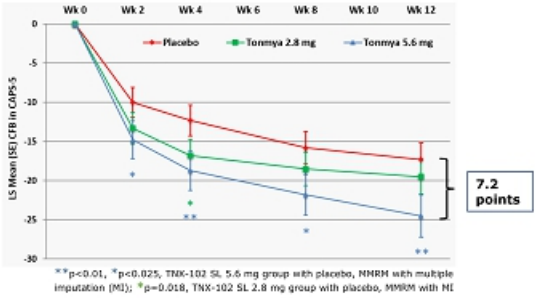
Variable	P201			P301	
	Placebo N=92	TNX 2.8 mg N=90	TNX 5.6 mg N=49	Placebo N=127	TNX 5.6 mg N=125
Females, %	6.50%	6.70%	8.20%	13.40%	8.00%
Age, yrs. (SD)	32.0	34.5	34.8	35.5	35.9
Body Mass Index, kg/m^2	28.9	29.0	29.0	29.3	29.9
Employment (current), %	58.7%	62.2%	67.3%	63.0%	55.2%
Unable to work due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

The striking difference between P201 and P301 was time since trauma

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

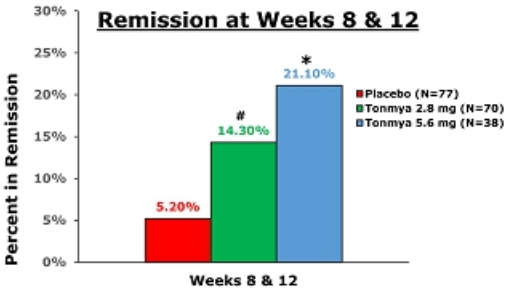
TNX-102 SL Phase 2 Dose-Effect in Military-Related PTSD[1]

PTSD Symptoms (CAPS-5[2] Score)



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

Remission at Weeks 8 & 12



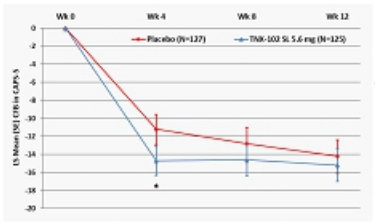
Remission = Loss of Diagnosis and CAPS-5 < 11
Asterisk and hashmark represent pairwise comparisons between TNX-102 SL and Placebo; #p=0.08, Odds Ratio 3.01 (0.89, 10.18)
*p=0.02, Odds Ratio 4.60 (1.27, 16.66); logistic regression

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

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

Phase 3 P301/HONOR Study[1]

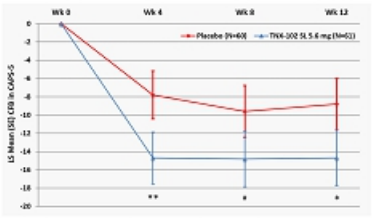
Modified intent to treat (mITT) population



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

~50% mITT Population

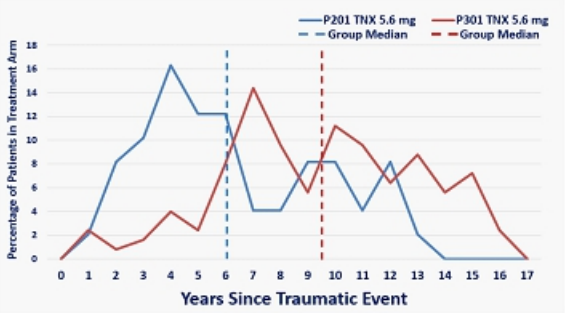
Time Since Trauma (TST) ≤9 yrs



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

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

Retrospective Comparison of Time Since Trauma in P201/AtEase versus P301/HONOR (TNX-102 SL 5.6 mg Groups)



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

- The median time since trauma in P301 was 9.5 years compared to the median time since trauma in P201 of 6.0 years for TNX-102 SL 5.6 mg treated groups

CAPS-5 Mean Change from Baseline Difference from Placebo of TNX-102 SL 5.6 mg in TST Subgroups in P301[1]

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

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

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

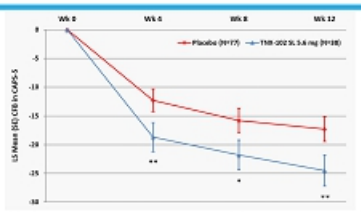
[1]Time Since Trauma in PTSD: Phase 3 Multi-Center, Double-Blind, Placebo-Controlled Trial of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine, in Military-Related PTSD (Study TNX-CY-P301) Presented at CNS Summit in Boca Raton, FL November 1-4, 2018 and abstract published in Innovations in Clinical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

PTSD Treatment Response to TNX-102 SL in Phase 2 and Phase 3 Studies: Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

Change in CAPS-5 over course of treatment with TNX-102 SL

CAPS-5 is a structured interview assessing PTSD severity

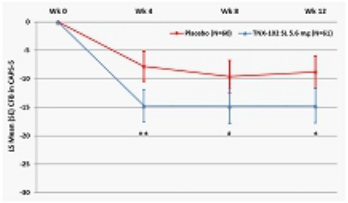
- Required primary endpoint for PTSD drug approval



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

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

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



P301 *TST* ≤9 yr

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

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

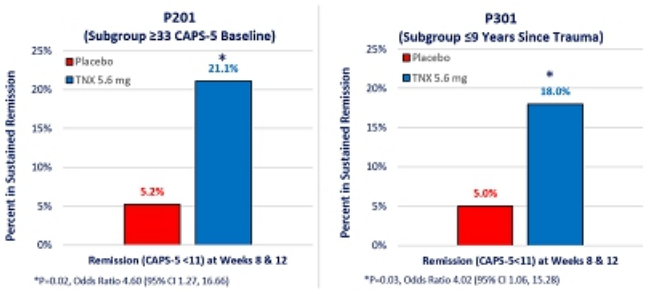
Sustained Remission in Phase 2 and Phase 3 Studies:
Retrospective Analyses of P201 Entry CAPS-5 ≥33 and P301 ≤9 Years Since Trauma Subgroups

Remission is a clinical state that is essentially asymptomatic

In order to confirm remission:

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

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



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

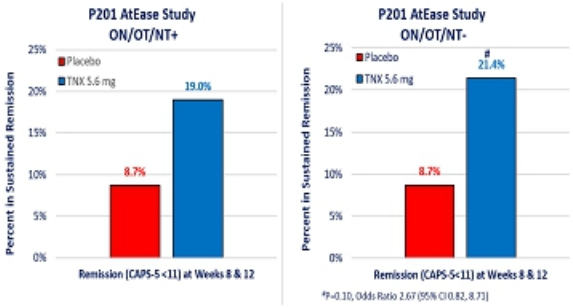
Sustained Remission in P201/AtEase Study Retrospective Analyses of Phase 2 Subgroups with and without Oral AE's (ON/OT/NT)

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

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

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

- Unblinding was unlikely to account for treatment effect



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

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

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

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

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

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

	P201			P301	
Category of Adverse Reaction Preferred Term	Placebo (N=94)	TNX 2.8 mg (N=93)	TNX 5.6 mg (N=50)	Placebo (N=134)	TNX 5.6 mg (N=134)
Systemic Adverse Events*#					
Somnolence	6.4%	11.8%	16.0%	9.0%	15.7%
Dry mouth	10.6%	4.3%	16.0%		
Headache	4.3%	5.4%	12.0%		
Insomnia	8.5%	7.5%	6.0%		
Sedation	1.1%	2.2%	12.0%		
Local Administration Site Reactions*#					
Hypoaesthesia oral	2.1%	38.7%	36.0%	1.5%	37.3%
Paraesthesia oral	3.2%	16.1%	4.0%	0.7%	9.7%
Glossodynia	1.1%	3.2%	6.0%		
Product Taste Abnormal				3.0%	11.9%

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

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

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

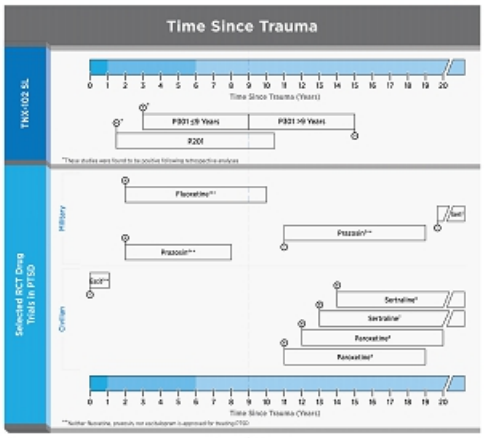
Time Since Trauma – Review of Published Studies

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

- Loss of treatment effect >9 years

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

- SSRIs have a benefit long after trauma



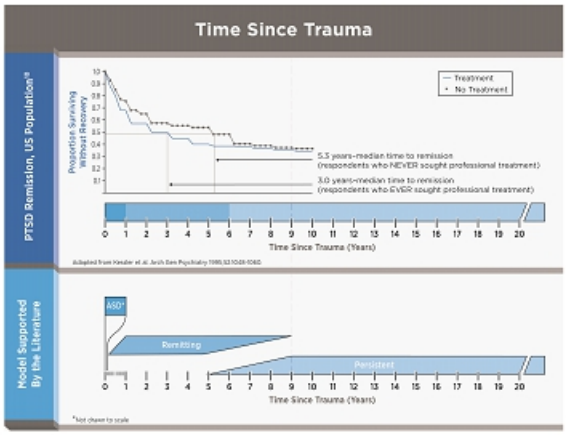
Escit=escitalopram

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

Time Since Trauma – Remitting and Persistent Phases of PTSD

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

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



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

Response to TNX-102 SL for Female Participants in P301/HONOR Study[1]

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

Difference in mean change from baseline in CAPS-5 in females between placebo (N=17) and TNX-102 SL 5.6 mg (N=10) was:

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

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

Predicts therapeutic response to TNX-102 SL 5.6 mg likely in mixed civilian and military PTSD population to be studied in current P302/RECOVERY trial

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

[1] Presented at CNS Summit in Boca Raton, FL November 1-4, 2018; Poster 8A, Friday Nov. 2, 5:00-7:00 PM EDT, Reception and Poster Session, and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12, suppl):S10.
https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

Response to TNX-102 SL for Non-Combat Traumas in P301/HONOR Study in ≤9 Years Time Since Trauma Subgroup[1]

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

To determine the therapeutic effects of TNX-102 SL 5.6 mg in a mixed civilian and military population, difference in MCFB in CAPS-5 was assessed in non-combat traumas in ≤9 years TST subgroup (placebo N=14, TNX-102 SL 5.6 mg N=10):

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

Non-combat traumas treated with TNX-102 SL 5.6 mg showed clinically meaningful separation from placebo at Weeks 4 and 12, suggesting a mixed civilian and military sample within 9 years of index trauma may show a therapeutic response to TNX-102 SL

[1] Presented at CNS Summit in Boca Raton, FL November 1-4, 2018; Poster 8A, Friday Nov. 2, 5:00-7:00 PM EDT, Reception and Poster Session, and abstract published in Innovations in Clinical Neuroscience, November-December 2018;15(11-12, suppl):S10. https://content.equisolve.net/tonixpharma/media/1d0c4055b2863fc74e1ef45f9ddaf42b.pdf

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

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

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

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

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

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

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

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

Results from retrospective analyses lead to improved Phase 3 study design

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

TNX-102 SL for PTSD: New Phase 3 P302/RECOVERY Study – Initiated 1Q 2019

General study characteristics:

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

Primary endpoint:

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

Key Secondary endpoints include:

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

Potential pivotal efficacy study to support NDA approval

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

Late-Stage PTSD Drug Candidates

TNX-102 SL

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

MDMA-assisted psychotherapy

- Indication – "drug assisted psychotherapy"
- Showed activity in a Phase 2 study of PTSD; enrolling in Phase 3 study

Other drugs currently (or recently) in Phase 2 development

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

Commercialization Options

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

Tonix has participated in numerous partnering meetings

Commercial Considerations:

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

TNX-102 SL – Multi-Functional Mechanism Involves Antagonism at 3 Neuronal Receptors

Active ingredient, cyclobenzaprine, interacts with 3 receptors

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

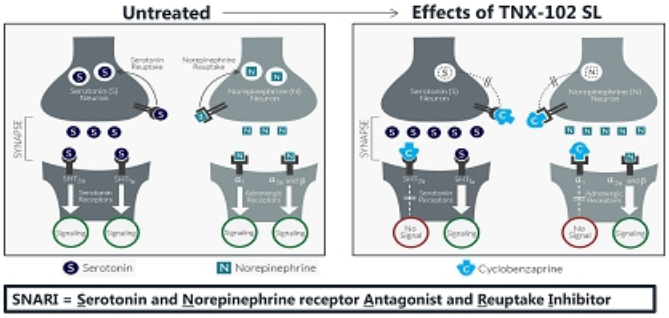
Multi-functional activity suggests potential for other indications

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

Cyclobenzaprine Effects on Nerve Cell Signaling

Cyclobenzaprine is a multi-functional drug - SNARI

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

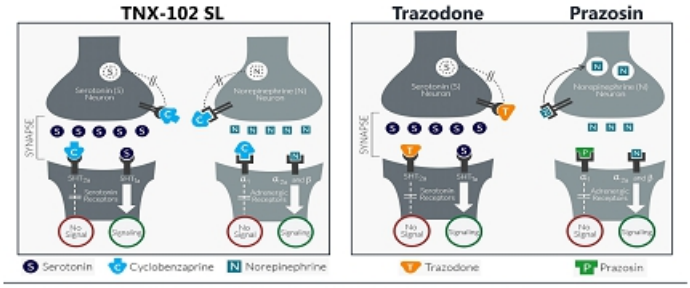


SNARI = Serotonin and Norepinephrine receptor Antagonist and Reuptake Inhibitor

Comparison of TNX-102 SL with Drugs Used Off-Label in PTSD

Trazodone (disordered sleep), prazosin (night terrors)

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



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

Opportunities to Expand to Other Indications

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

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

Psychiatric Disorders

- Stress Disorders (PTSD)
- Mood Disorders
- Anxiety Disorders

Psychiatric Symptoms of Neurological Disorders

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

Chronic Pain States

- Chronic wide-spread pain (fibromyalgia)
- Osteoarthritis

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

- Homeostatic role of sleep quality *in several disorders*

TNX-102 SL – Bedtime Treatment for Multiple Potential Indications

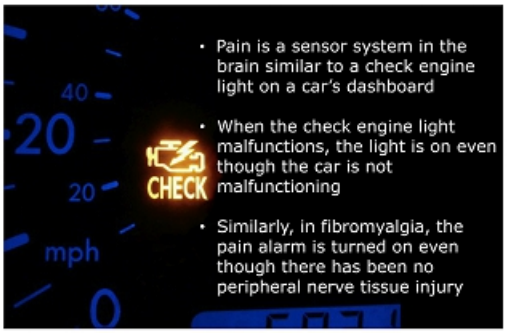
Management of Fibromyalgia (FM) – chronic pain condition

- TNX-102 SL 2.8 mg (half the dose being developed for PTSD) studied in Phase 2/3 trials– 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)
- Consistent improvement in sleep quality demonstrated
- TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) will be studied in new Phase 3 study to support product registration (April 2019 FDA meeting minutes)

Agitation in Alzheimer's Disease

- Received Phase 2/potential pivotal efficacy study protocol comments from FDA in October 2018

TNX-102 SL: Potential Treatment for Fibromyalgia



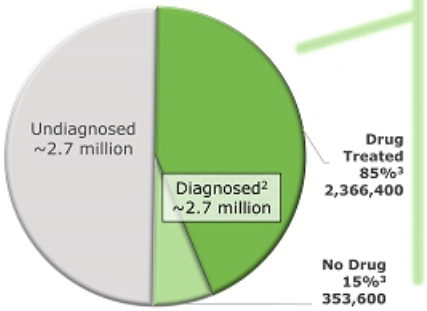
Volkswagen Check Engine (Photograph). (2011, October 14). Wikipedia

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

[1] Philips K & Clauw DJ, Best Pract Res Clin Rheumatol 2011;25:141.
[2] Schaefer et al., Pain Pract, 2015.
[3] Robinson et al, Pain Medicine 2013;14:1400.
[4] White et al, J Occupational Environ Med 2008;50:13.

Fibromyalgia: Market Characteristics

U.S. Prevalence Rate 2-4%[1]
(~5-10 million adults)



Market Characteristics

Prevalence
- One of the more common chronic pain disorders

Diagnosed population
- Large population (~2.7 million) but underdiagnosed relative to prevalence rate
- Majority receive drug treatment

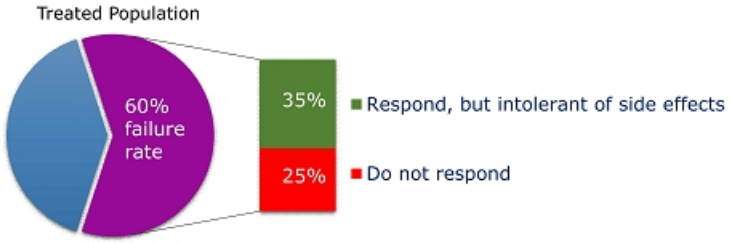
Treatment Pattern
- Polypharmacy the norm - average 2.6 drugs/patient[3]
- Rotation through therapy common: average ~5 drugs/year[3]
- Estimated that >22 million prescriptions are issued for the treatment of fibromyalgia (on- and off-label usage) each year[4,5]

Unmet Need
- Majority of patients do not respond or cannot tolerate therapy[6]

1. American College of Rheumatology (www.ACRPatientInfo.org accessed May 7, 2019) – prevalence rate of 2-4% for U.S. adult population (~250 million)
2. Vincent et al., 2013; diagnosed prevalence rate was 1.1% of adult population or 50% of the prevalent population
3. Robinson, et al., 2012; 85% received drug treatment
4. Vincent et al, Arthritis Care Res 2013;65:786
5. Product sales derived from IMS MIDAS; IMS NDTI used to factor usage for fibromyalgia; data accessed April 2015.
6. Market research by Frost & Sullivan, commissioned by Tonix , 2011

Fewer than Half of Those Treated for Fibromyalgia Receive Sustained Benefit from the Three FDA-Approved Drugs[1]

- The treatment objective is to **restore functionality** and **quality of life** by broadly improving symptoms while avoiding significant side effects
- The majority fail therapy due to **lack of a response** or **poor tolerability**[2]



[1] The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[2] Market research by Frost & Sullivan, commissioned by Tonix (2011)

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

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

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

TNX-102 SL for Fibromyalgia: Summary of a completed Phase 3 F301 study

General study characteristics:

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

Efficacy results:

- mITT population: 425 (81.9%) of 519 patients
- The primary analysis was not statistically significant. However, retrospective analysis showed average pain improvement (secondary endpoint) after 12 weeks of treatment showed statistical significance ($P<0.05$, MMRM)
- Significant improvements observed in sleep quality, patient global impression of change and fibromyalgia-specific measures (secondary analyses).

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

Safety results:

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

Conclusion:

- The promising results and highly relevant efficacy findings support further investigation of TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) as a chronic treatment for FM.

Program updates:

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

*April 2019 FDA meeting minutes

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

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

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

- FDA comments on final protocol received October 2018

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

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

[1]Supplemental New Drug Application

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

Sublingual route of administration (no swallowing)

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

Low dose taken daily at bedtime

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

Role of sleep in clearing debris from the brain

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

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

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

Connection between Sleep Disturbance and Agitation

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

Supported by Potential Mechanism of Action

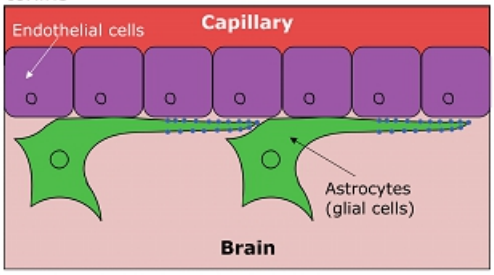
- TNX-102 SL is a multifunctional agent including antagonism of 5-HT_{2A}, α_1-adrenergic and histamine H_1 receptors
- Certain 5-HT_{2A} antagonists have shown clinical efficacy against agitation in dementia including trazodone[4,5], and mirtazapine[6]
- The α_1-adrenergic antagonist prazosin has shown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

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

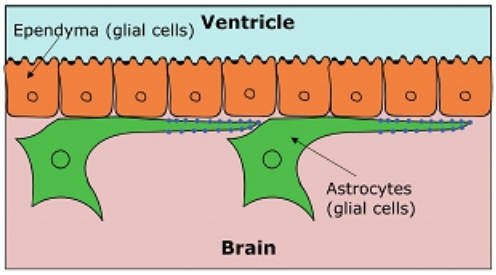
Protective Barriers in the Central and Peripheral Nervous Systems

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

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



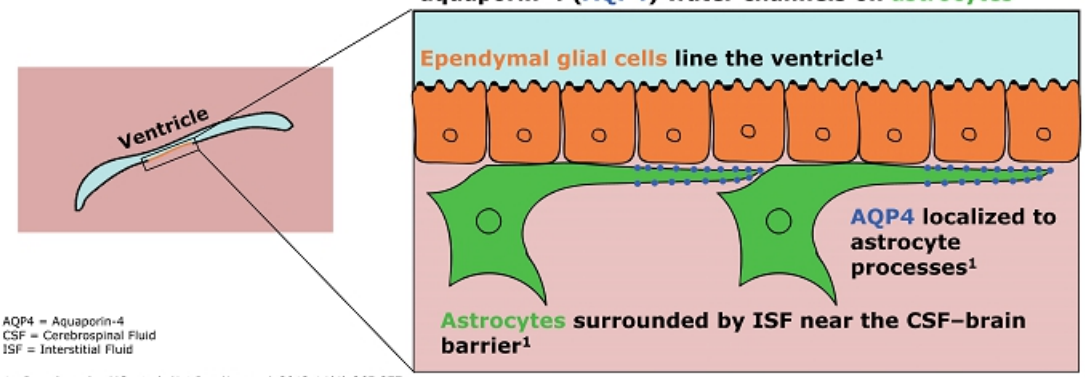
Cerebrospinal Fluid (CSF)–Brain Barrier/Glymphatic System:
extracts toxins from the brain[2]



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

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

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



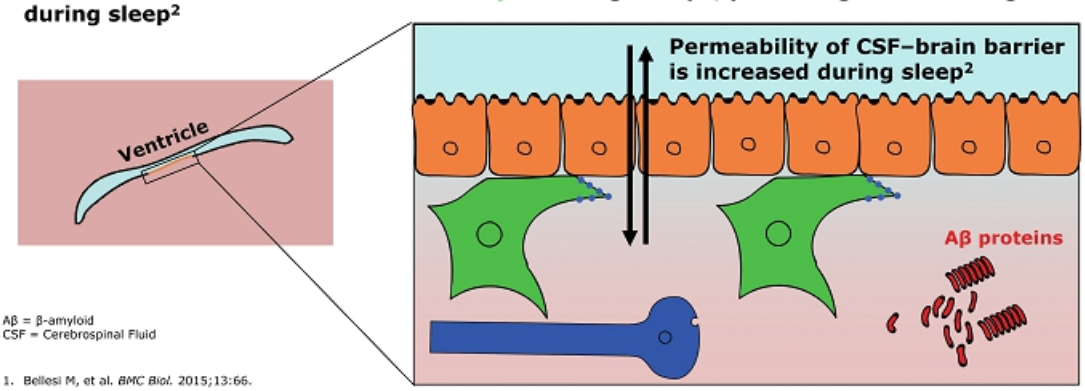
AQP4 = Aquaporin-4
CSF = Cerebrospinal Fluid
ISF = Interstitial Fluid

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

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

Extracellular volume increases during sleep[2]

Astrocytes change shape, promoting fluid exchange[1]



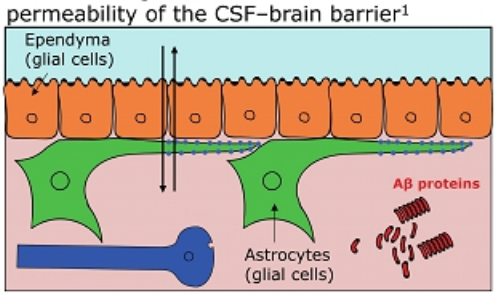
Aβ = β-amyloid
CSF = Cerebrospinal Fluid

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

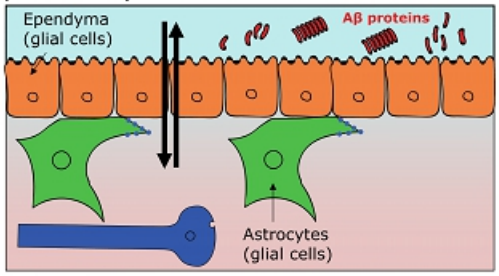
Sleep–Wake Cycles Alter Permeability of the CSF–Brain Barrier

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

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



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



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

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

Competitive landscape

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

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

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

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

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

AUD is a chronic relapsing brain disease

- Characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using

Sleep disturbance is extremely common in alcohol recovery[1]

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

Prevalence

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

Three FDA-approved medications

- Remains an unmet need

Pre-IND meeting with the FDA in October 2019

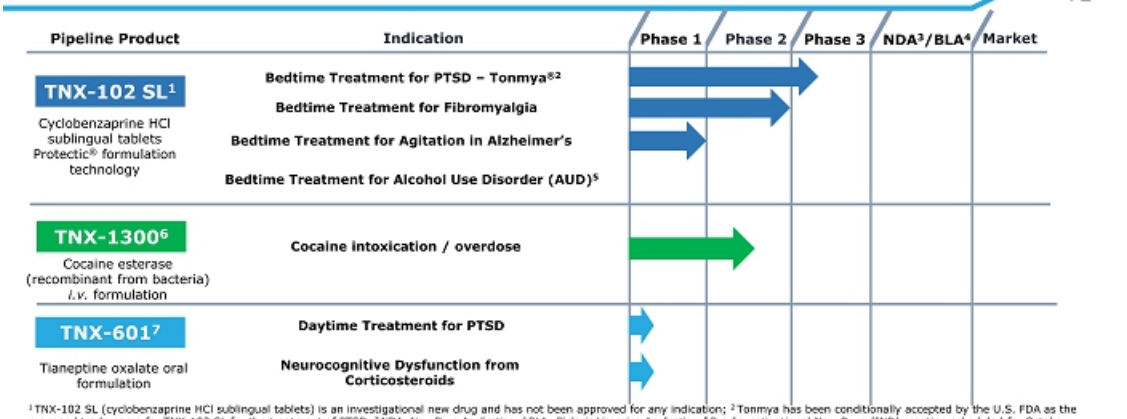
- To discuss a potential 505(b)(2) development plan for TNX-102 SL as a treatment for AUD.
- Potentially a Phase-2 ready IND

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

CNS Candidates in Clinical Development

Psychiatry, Pain and Addiction

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



[1] TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication; [2] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL for the treatment of PTSD. [3] NDA- New Drug Application; [4] BLA –Biologic Licensing Application; [5] Pre-Investigational New Drug (IND) meeting scheduled for October with FDA. Upon receiving FDA clearance of an IND application, TNX-102 SL for AUD will be Phase 2 ready as it is expected to qualify for the 505(b)(2) pathway for approval; [6] TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication; [7] TNX-601 is in the pre-IND stage in the U.S., but a Phase 1 study for formulation development is currently being conducted outside of the U.S.

Preclinical Pipeline[1]

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

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

TNX-1300* for the Treatment of Cocaine Intoxication

Recombinant protein that degrades cocaine in the bloodstream[1]

- Double-mutant cocaine esterase

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

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

**TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication.*

[1] Gao D et al, Mol Pharmacol. 2009. 75(2):318-23.
[2] Nasser AF et al, J Addict Dis. 2014;33(4):289-302.

Produced through rDNA technology in non-disease-producing strain of *E. coli.*

- Cocaine Esterase (CocE) was identified in bacteria (*Rhodococcus*) that use cocaine as its sole source of carbon and nitrogen and that grow in soil surrounding coca plants[1]
- The gene encoding CocE was identified and the protein was extensively characterized[1-3]
- CocE catalyzes the breakdown of cocaine into metabolite ecgonine methyl ester and benzoic acid
- Wild-type CocE is unstable at body temperature, so targeted mutations were introduced in the CocE gene and resulted in the *T172R/G173Q Double-Mutant CocE*, which is active for approximately 6 hours at body temperature[4]

[1] Bresler MM et al, Appl Environ Microbiol. 2000. 66(3):904-8.
[2] Larsen NA et al, Nat Struct Biol. 2002. 9(1):17-21.
[3] Turner JM et al, Biochemistry. 2002. 41(41):12297-307.
[4] Gao D et al, Mol Pharmacol. 2009. 75(2):318-23.

About Cocaine and Cocaine Intoxication

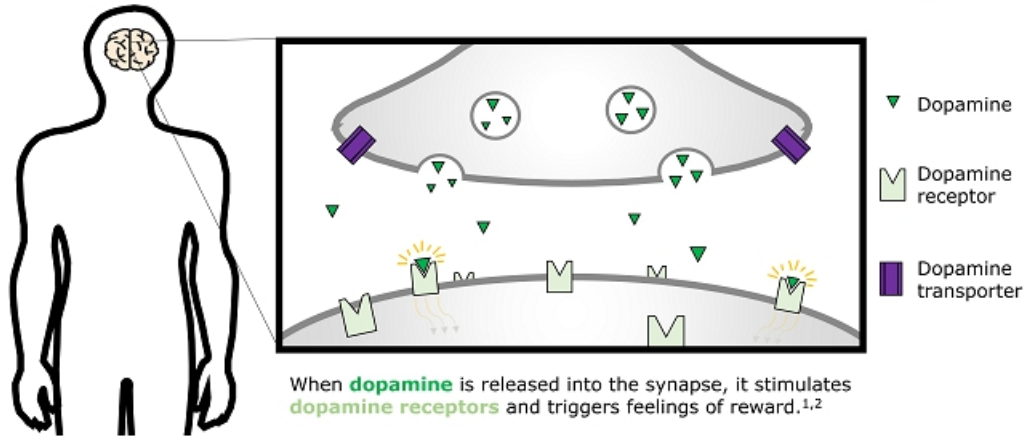
Cocaine: an illegal recreational drug taken for its pleasurable effects and associated euphoria.

- Cocaine blocks the reuptake of the neurotransmitter dopamine (DA) in the CNS
  - Results in accumulation of DA within the synapse and amplifies DA signaling
  - Creates positive feeling but with intense use of cocaine, results in cocaine craving
  - High potential for abuse/addiction (dependence), and *risk of cocaine intoxication.*

Cocaine intoxication: deleterious effects on the body, especially cardiovascular system.

- Common symptoms include tachyarrhythmias and elevated blood pressure, either of which can be life-threatening.
- Known or suspected cocaine intoxication cases are sent immediately to the emergency department, preferably by ambulance in case cardiac arrest occurs during transit.

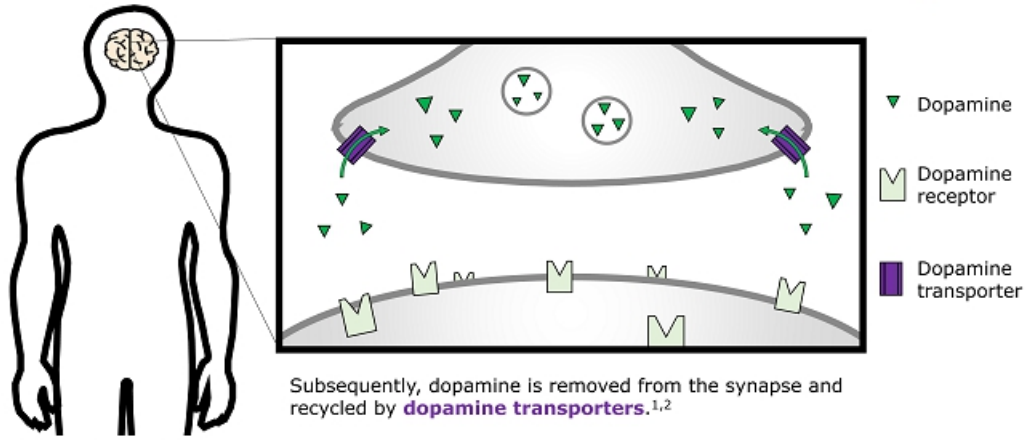
Cocaine Mechanism of Action (MOA)



When **dopamine** is released into the synapse, it stimulates **dopamine receptors** and triggers feelings of reward.[1,2]

1. Benowitz NL. *Pharmacol Toxicol.* 1993.
2. Stahl SM. 4th ed. New York, NY: Cambridge University Press; 2013.

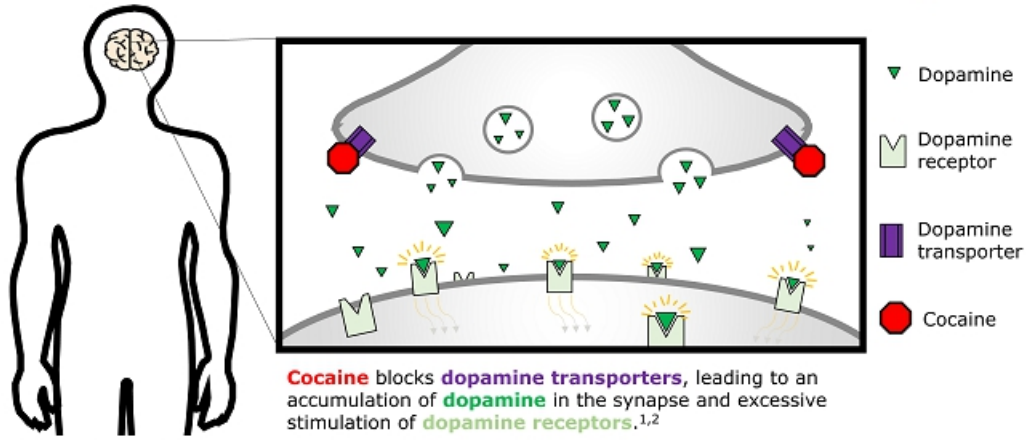
Cocaine MOA



Subsequently, dopamine is removed from the synapse and recycled by **dopamine transporters.**[1,2]

1. Benowitz NL. *Pharmacol Toxicol.* 1993.
2. Stahl SM. 4th ed. New York, NY: Cambridge University Press; 2013.

Cocaine MOA

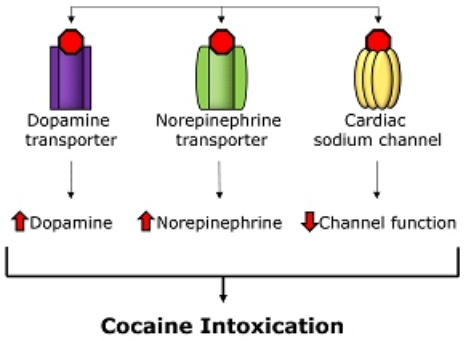


Cocaine blocks **dopamine transporters**, leading to an accumulation of **dopamine** in the synapse and excessive stimulation of **dopamine receptors**.[1,2]

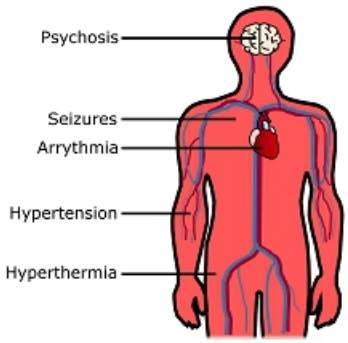
1. Benowitz NL. *Pharmacol Toxicol.* 1993.
2. Stahl SM. 4th ed. New York, NY: Cambridge University Press; 2013.

Cocaine Intoxication is the Result of Cocaine's Activity at Multiple Targets

In addition to dopamine transporters, cocaine also blocks other targets[1]



The effects of cocaine intoxication include[1]:

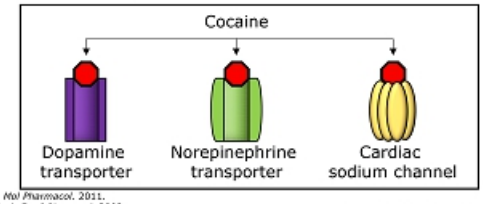


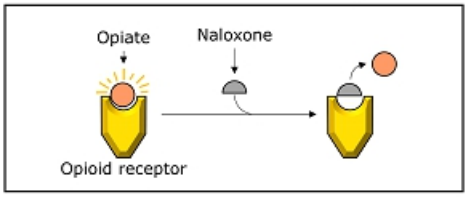
1. Brim et al. *Mol Pharmacol.* 2011.

Pharmacotherapies for Cocaine Intoxication Have Not Been Effective

Treatments for opiates not effective for cocaine:

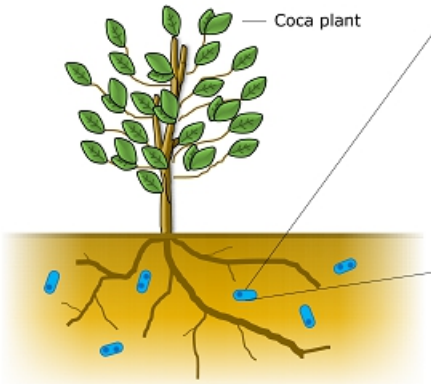
	Cocaine	Opiates
MOA of Toxicity	Complex; mediated by multiple targets with distinct biological functions[1]	Simple; mediated by opioid receptors[2]
Pharmacology	Antagonist[1]	Agonists[2]
Pharmacotherapy	**No FDA-approved medication exists[1]**	Naloxone[2]



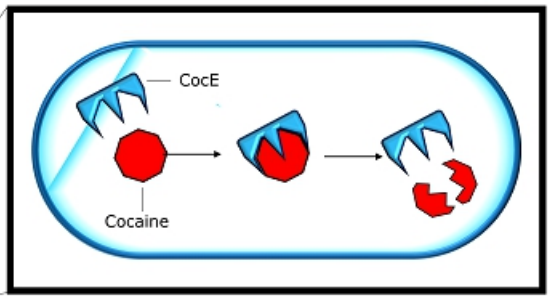


1. Brim et al. *Mol Pharmacol.* 2011.
2. Melichar et al. *Eur J Pharmacol.* 2003.
3. Narasimhan et al. *Future Medicinal Chemistry.* 2012.

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



Cocaine is derived from the coca plant[1]



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

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

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

Pharmacotherapies for Cocaine Intoxication Have Not Been Effective

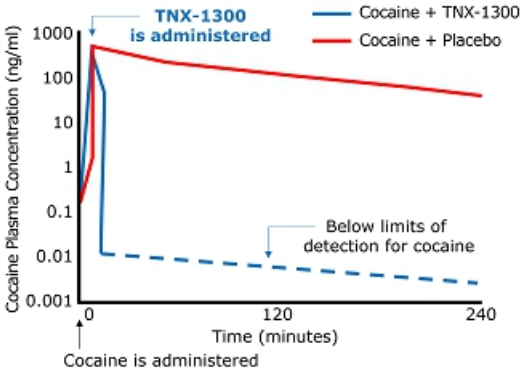
- While simple pharmacological agents such as naloxone (Narcan®) are effective for the treatment of opiate intoxication[1], a similar approach to treat cocaine intoxication is hampered by cocaine's complex mechanism of action, or MOA[2]
- Another key difference between opiates and cocaine is that opiates are agonists at opiate receptors[1], while cocaine acts as an antagonist at its key targets.[2] Compounds that compete with an inhibitor such as cocaine are likely to be inhibitors themselves.[3]
- Despite years of research, pharmacotherapies designed to prevent cocaine from binding to its target molecules have not been effective[2,3]

References

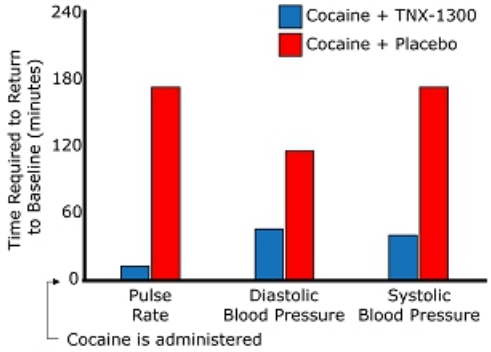
1. Melichar JK, Nutt DJ, Malizia AL. Naloxone displacement at opioid receptor sites measured in vivo in the human brain. *European Journal of Pharmacology*. 2003; 459(2-3):217-219.
2. Brim RL, Noon KR, Collins GT, Nichols J, Narasimhan D, Sunahara RK, Woods JH. The ability of bacterial cocaine esterase to hydrolyze cocaine metabolites and their simultaneous quantification using high-performance liquid chromatography-tandem mass spectrometry. *Molecular Pharmacology*. 2011; 80:1119-1127.
3. Narasimhan D, Woods JH, Sunahara RK. Bacterial cocaine esterase: a protein-based therapy for cocaine overdose and addiction. *Future Medicinal Chemistry*. 2012; 4(2):137-150.

TNX-1300 (CocE) Accelerates Recovery From Cocaine Intoxication in Humans

TNX-1300 cleaves cocaine in humans and removes it from the blood circulation[1] (N=29)



TNX-1300 accelerates recovery from cocaine intoxication without inducing serious side effects[1]



1. Nasser A et al. *J Addict Dis.* 2014.

Note: Figures are for illustrative purposes

The Prevalence of Cocaine Usage and Overdose (U.S.)

Cocaine Usage in the U.S.

5.07 million individuals estimated to have used cocaine in past year[1]

- 2.2 million "current" (i.e. users in the past month) of cocaine (2017)[2]
- 966,000 had cocaine use disorder in past year (2017)[2]

Prevalence of Cocaine Overdose

Based on Drug Abuse Warning Network (DAWN) last compiled in 2011[3,4]

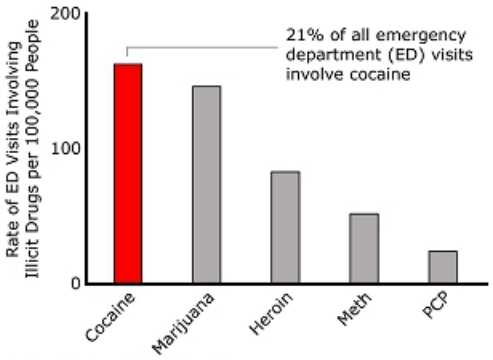
505,224 emergency department visits for cocaine (2011)	
270,677 (53%) treated and released	Less likely to be treated aggressively
167,570 (33%) were admitted to the same hospital	More likely to be treated
60,609 (14%) visits involving drug detox services	Treated to reverse toxicity

[1] Annual Surveillance Report of Drug-Related Risks and Outcomes, United States CDC National Center for Injury Prevention and Control, 2018
[2] Substance Abuse and Mental Health Services Administration. (2018). Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSDUH Series H-53).

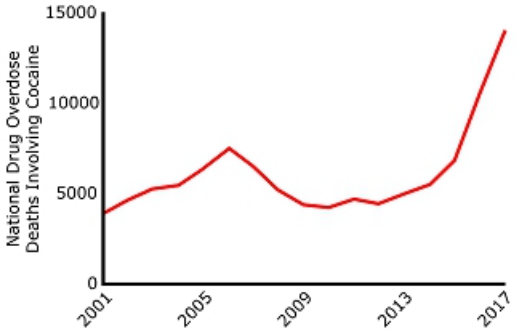
[3] Substance Mental Health Services Administration, Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.
[4] Drug Abuse Warning Network, 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits. Rockville, MD: Center for Behavioral Health Statistics and Quality, SAMHSA, 2013.

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

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



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



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

Note: Figures are for illustrative purposes

Treatment for Cocaine Intoxication

Current Standard of Care

- Patients present with acute agitation, hyperthermia, tachycardia, arrhythmias, and hypertension
- Potential life-threatening sequalae of myocardial infarction, cerebrovascular accident, rhabdomyolysis, respiratory failure, and seizures
- Patients are currently managed only by supportive care for the adverse effects of cocaine intoxication on the cardiovascular and central nervous systems

Potential Benefit of TNX-1300

- By reversing the cause of cocaine intoxication (rather than treating the symptoms), TNX-1300 may offer significant advantages to the current standard of care for cocaine intoxication.
  - Rapid diminution in circulating cocaine
  - Significantly reduce time and resources required for other detox services
  - Reduces the risk of morbidity and mortality

Value of TNX-1300 to Tonix

Features of the Acquired Asset:

- Full rights to the IP and to develop and commercialize TNX-1300 worldwide
- An inventory of investigational drug product
- Clinical trial results from previous Phase 2 study in which TNX-1300 at 100 mg or 200 mg i.v. doses was well tolerated and interrupted cocaine effects after cocaine 50 mg i.v. challenge

Development Plan:

- Re-qualify the drug substance for Good Manufacturing Practice (GMP) purposes
- Conduct non-clinical studies in reproductive toxicology
- Initiate a Phase 2 study in Emergency Room cocaine intoxication

Exclusivity:

- Expected patent protection through 2029
- As a biologic and new molecular entity, TNX-1300 is eligible for 12 years of U.S. market exclusivity upon approval by the FDA.

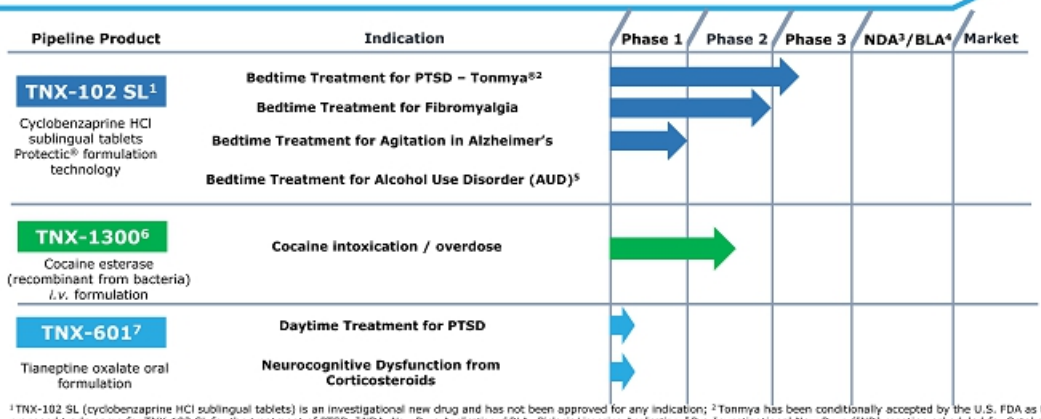
Pipeline Diversification:

- Brings Tonix into an additional therapeutic area: Addiction Medicine

CNS Candidates in Clinical Development

Psychiatry, Pain and Addiction

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



[1] TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication; [2] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL for the treatment of PTSD. [3] NDA- New Drug Application; [4] BLA –Biologic Licensing Application; [5] Pre-Investigational New Drug (IND) meeting scheduled for October with FDA. Upon receiving FDA clearance of an IND application, TNX-102 SL for AUD will be Phase 2 ready as it is expected to qualify for the 505(b)(2) pathway for approval; [6] TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication; [7] TNX-601 is in the pre-IND stage in the U.S., but a Phase 1 study for formulation development is currently being conducted outside of the U.S.

Preclinical Pipeline[1]

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

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

TNX-601 (Tianeptine Oxalate): A Potential Daytime Treatment 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 internal expertise in PTSD (clinical and regulatory experience, market analysis, etc.)**
- ✓ **Mechanism of Action (MOA) is different from TNX-102 SL**

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

Patents and patent applications directed to tianeptine oxalate

- Issued patent directed to methods of treating cognitive impairment associated with corticosteroid treatment

Clinical evidence for treating PTSD for tianeptine sodium

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

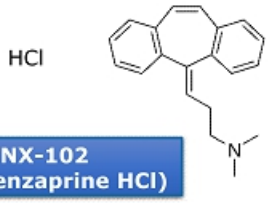
[1] Frančišković T, et al. Psychiatr Danub. 2011 Sep;23(3):257-63. PMID: 21963693
[2] Rumyantseva GM and, Stepanov AL. Neurosci Behav Physiol. 2008 Jan;38(1):55-61. PMID: 18097761
[3] Aleksandrovskiĭ IA, et al. Zh Nevrol Psikhiatr Im S S Korsakova. 2005;105(11):24-9. PMID: 16329631 [Russian]
[4] Onder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

Structural Comparison: TNX-102 and TNX-601

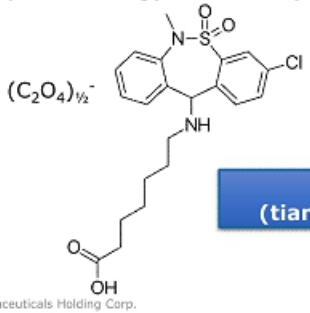
Cyclobenzaprine and tianeptine share structural similarities with classic tricyclic antidepressants (TCAs) and to each other, but each has unique pharmacological properties

- 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-1600[1] (Triple Reuptake Inhibitor): A Potential Daytime Treatment 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 internal expertise in PTSD (clinical and regulatory experience, market analysis, etc.)**
- ✓ **Mechanism of Action (MOA) is different from TNX-102 SL or TNX-601**

TNX-1600 is a New Chemical Entity, triple-reuptake inhibitor

- Inhibits reuptake of serotonin, norepinephrine and dopamine

Patents and patent applications

- Issued patent directed to composition of matter
- Worldwide exclusive license from Wayne State University

Preclinical evidence for treating PTSD in animal model

- Pre-clinical studies have shown TNX-1600 to be active in an animal model of PTSD[2]

[1]TNX-1600, f.k.a. D-578 or (2S,4R,5R)-5-(((2-aminobenzo[d]thiazol-6-yl)methyl)amino)-2-(bis(4-fluorophenyl)methyl)tetrahydro-2H-pyran-4-ol is an inhibitor of reuptake of three monoamine neurotransmitters (serotonin, norepinephrine and dopamine)
[2]Dutta, AK, et al., Eur J. Pharmacol. 2019 862:172632

TNX-1500 (monoclonal antibody anti-CD154): A Potential Treatment for Autoimmune Conditions and Organ Transplant Rejection

Pre-IND Candidate

Targeted as a 1st line monotherapy for autoimmunity and add-on therapy for preventing and treating organ transplant rejection

✓ **Mechanism of Action (MOA) is distinct**

- TNX-1500 blocks T cell helper function

New Molecular Entity, biologic

- US Patient Protection and Affordable Care Act provides 12 years of exclusivity for biologics

Patent applications directed to composition of matter

- Expected patent protection through 2039

Targeting a Condition with Significant Unmet Need

Clinical evidence for anti-CD154 mAbs in Systemic Lupus (SLE) and allogeneic kidney transplant

- Several studies have shown TNX-1500 to be active in the treatment of human SLE[1-3] and transplant[4,5]

[1] Huang W, et al. *Arthritis Rheum.* 46(6):1554–62 (2002)
[2] Boumpas DT, et al, *Arthritis Rheum.* 48:719–27. (2003)
[3] Grammer AC, et al. *J Clin Invest.* 112:1506–20. (2003)
[4] Kawai T, et al. Nat Med. 2000;6:114. (2000);
[5] Koyama I, et al., *Transplantation.* 77(3):460-2. (2004)

About CD40L (CD154)

Transiently expressed T cell surface molecule also known as CD40-ligand[1-4]
- Predominantly expressed by T cells
- Interacts with CD40 on B cells and macrophages

Mediates T cell helper function[1-4]
- Activates B cells for humoral (antibody-mediated) immune response
- Activates macrophages and dendritic cell
- Provides T cell help to activated CD8+ T cells

X-linked Hyper-IgM Syndrome – defective CD40L gene[5-6]
- Lack of T helper function
- Serum antibodies: only IgM, and no IgG or IgE because T cells are required for B cell isotype switching
- If maintained on gamma globulin are otherwise healthy

Member of the TNFα superfamily[4]
- TNFα and RANKL are other family members –drug targets for approved products

[1]Lederman, S., et al. *J. Exp. Med.* 175:1091-1101. 1992. PMID: 1348081.
[2]Lederman, S., et al;. *J. Immunol.* 149:3817-3826. 1992. PMID: 1281189.
[3]Lederman, S., et al. *J. Immunol.* 152:2163. 1994. PMID: 7907632.
[4]Covey, L.R., et al. *Mol. Immunol.* 31:471-484. 1994. PMID: 7514269.
[5]Ramesh, N., et al. 1993. *Inter Immunology* 5:769-773. PMID: 8103673.
[6]Callard, R.E., et al., *J. Immunol.* 153:3295. 1994. PMID: 7916370.

TNFα Superfamily

CD154 is a member of the Tumor Necrosis Factor (TNFα) Super Family[1]

- No mAb against CD154 has been licensed anywhere in the world

Other TNFα Super Family members have proven to be targets for antagonist (blocking) mAbs[2]

- anti-TNFα mAbs for the treatment of certain autoimmune conditions
  - infliximab (Remicade®)
  - adalimumab (Humira®)
  - certolizumab pegol (Cimzia®)
  - golimumab (Simponi®)
- TNFα antagonist receptor fusion protein
  - Etanercept (Enbrel®)
- anti-RANKL (CD254) mAb for the treatment of osteoporosis, treatment-induced bone loss, metastases to bone, and giant cell tumor of bone
  - denosumab (Prolia® or Xgeva®)

[1]Covey, L.R., et al. *Mol. Immunol.* 31:471-484. 1994. PMID: 7514269.
[2]Remicade® and Simponi® are trademarks of Janssen; Humira® is a trademark of AbbVie; Cimzia® is a trademark of UCB; Enbrel® is a trademark of Amgen; and Prolia® and Xgeva® are trademarks of Amgen.

TNX-1500 (anti-CD40L (CD154))

Transplantation/Autoimmune treatment development asset

- 3rd generation of monoclonal antibody (mAb) for a class that has had extensive animal and human testing
- Effects on T cell function with lower potential for side effects (e.g. thrombosis via FcγRIIA (CD32A) - dependent pathway)[1]
- Patent protection expected through 2039

Transplantation

- Unique effects on facilitating tolerance
- Potential to facilitate xeno-transplants (genetically engineered mini-swine)[2]

Autoimmune Diseases

- Unique effect at controlling autoimmune conditions [3-5]
- Clinical data on related mAbs for systemic lupus erythematosus (SLE)[3-5]

Allergy

- Blocks immunoglobin E (IgE) production

[1]Company data
[2]Längin M, et al., Nature. 2018 564(7736):430-433
[3]Huang W, et al. *Arthritis Rheum.* 46(6):1554–62 (2002)
[4]Boumpas DT, et al, *Arthritis Rheum.* 48:719–27. (2003)
[5]Grammer AC, et al. *J Clin Invest.* 112:1506–20. (2003)

TNX-1500 – Potential Treatment for Organ Transplant Rejection

Facilitates 'transplant tolerance' in multiple preclinical transplant models

- anti-CD154 therapy has a unique activity in controlling the immune response to organ transplants[1-3]
- Significant need for new treatments with improved activity and tolerability to prevent or treat organ transplant rejection

Human trials of first generation anti-CD154 showed evidence of activity

- Development halted because of increased risk of thrombosis[4-6]

Potential to enable use of genetically modified, or humanized pig organs – "xenotransplantation." [7,8]

- Potential treatment for humans with advanced organ failure or diabetes

[1] Ferrant JL et al., *International Immunol.* (11):1583 (2004)
[2] O'Neill NA, et al. *Transplantation.* 101(9): 2038 (2017)
[3] Zhang T, et al. *Immunotherapy.* 7(8):899 (2015)
[4] Kawai T, et al. Nat Med. 2000;6:114. (2000)
[5] Koyama I, et al., *Transplantation.* 77(3):460-2. (2004)
[6] Law and Grewal *Adv Exp Med Biol.* 647:8-36 (2009)
[7] Längin M, et al. *Nature.* 564(7736):430 (2018)
[8] Pierson RN 3rd. *J Thorac Cardiovasc Surg.* pii: S0022-5223(19)31024-4. (2019)

TNX-1500 – Potential Treatment for Autoimmune Disease

Treats autoimmune conditions in multiple preclinical transplant models

- anti-CD154 therapy has a unique activity in controlling the immune response in autoimmune models[1-3]
- Significant need for new treatments with improved activity and tolerability to prevent or treat autoimmunity

Human trials of first generation anti-CD154 showed activity

- Clinical trials of hu5c8, in systemic lupus erythematosus (SLE) showed evidence of activity[1-3]
- Development halted because of increased risk of thrombosis[1-3]

[1]Huang W, et al. *Arthritis Rheum.* 46(6):1554–62 (2002)
[2]Boumpas DT, et al, *Arthritis Rheum.* 48:719–27. (2003)
[3]Grammer AC, et al. *J Clin Invest.* 112:1506–20. (2003)

Third Generation anti-CD154: Engineered to Potentially Decrease Risk of Thrombosis

First generation anti-CD154 mAbs

- Constant fragment (Fc) domain interacted with FcγRIIA (CD32A), which suggested a mechanism for increased risk of thrombosis[1,2]

Second generation anti-CD154 mAbs

- Dramatically reduced binding to FcγRIIA[3,4], but had other issues, including decreased efficacy[5,6]

TNX-1500 is a third generation anti-CD154 mAb[6-8]

- Designed by protein engineering to target CD154 therapeutically, while decreasing FcγRIIA binding and the potential for thrombosis

[1] Inwald DP et al., *Circ Res.* 92(9):1041-8 (2003))
[2] Robles-Carrillo L et al., *J Immunol.* 185(3):1577-83. (2010))
[3] Shock A. et al., *Arthritis Res Ther.* 17:234 (2015)
[4] Xie et al., *Journal of Immunol.* 192(9):4083 (2014))
[5] Waters J, *Biocentury*; October 26, (2018)
[6] Company data
[7] NCT02273960; *ClinicalTrials.gov*; "Study to Evaluate Safety and Efficacy in Adult Subjects With ITP (ITP)"; results posted April 1, 2019, accessed July 29, 2019)
[8] Ferrant JL et al., *International Immunol.* (11):1583 (2004)

TNX-1700 (rTFF2): A Potential Treatment for Gastric and Pancreatic Cancers

Pre-IND Candidate

Targeting a Condition with Significant Unmet Need

Targeted as a treatment for Cancer

- ✓ **Particularly for gastric and pancreatic cancer**
- ✓ **Mechanism of Action (MOA) is different from checkpoint inhibitors**
- ✓ **Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies**

Patents and patent applications directed to rTFF2

- Issued patent licensed from Columbia University

Inventor: Dr. Timothy Wang, MD

- Chief, Division of Digestive and Liver Diseases at Columbia University and Cancer Research Center and Silberberg Professor of Medicine
- Investigated the molecular mechanisms of gastrointestinal carcinogenesis for decades
- Leadership roles in gastroenterology and cancer biology fields

Pre-clinical evidence for inhibiting growth of cancer cells

- Several studies have shown rTFF2 to be active in the treatment of cancer[1-2]

[1]Dubeykovskaya Z, et al. Nat Commun. 2016 7:1-11
[2]Dubeykovskaya ZA, et al, Cancer Gene Ther. 2019 26(1-2):48-57

TNX-1700 (rTFF2) for Potential Cancer Treatment

- **Oncology development program**
  - Recombinant trefoil family factor 2 (rTFF2) has effects on cancer cells and the tumor microenvironment[1,2]
- **Potential synergy with anti-PD-1/PD-L1 mAbs (Keytruda® and Opdivo®) and/or anti-CTLA-4 (Yervoy®) "Checkpoint Inhibitors"**
  - anti-PD-1 and anti-PDL-1 are breakthrough treatments, but not all patients respond
  - Increasing the response rate to checkpoint inhibitors is an active area of research
  - rTFF2 acts in the tumor microenvironment
- **Novel mechanism for suppressing myeloid-derived suppressor cells, and activating anti-cancer CD8+ T cells**
  - Implications for both cancer prevention and treatment
  - Potential to synergize with other immunotherapy drugs

[1]Dubeykovskaya Z, et al. *Nat Commun*. 2016 7:1-11
[2]Dubeykovskaya ZA, et al, *Cancer Gene Ther*. 2019 26(1-2):48-57

Cancer: Toxic Tumor Microenvironment

- **Tumor microenvironment sabotages immune T cells**
  - Made up of blood vessels, inflammatory cells, and structural proteins
  - Difficult for cancer-killing immune T cells to penetrate
  - T cells detect and destroy cancer cells.
- **Cancer surrounds tumors with a hostile microenvironment**
  - Tumors thrive, while the body's immune forces are not capable of performing their anti-cancer functions
- **Although the tumor microenvironment is known to be highly immunosuppressive, it has not been known precisely how it specifically hampers the function of T cells**

Trefoil Family Factor 2 (rTFF2) and Cancer Biology

- **TFF2 is a small secreted protein**
  - Encoded by the TFF2 gene in humans
  - Expressed in gastrointestinal mucosa where it functions to protect and repair mucosa
  - TFF2 is also expressed at low levels in splenic memory T cells
  - Upregulated in chronic inflammation
  - Activates the chemokine receptor CXCR4 in cancer cells
    - Blocked by AMD3100 (CXCR4 antagonist) or anti-CXCR4 mAb

- **TFF2 is epigenetically silenced in gastric cancer**
  - Postulated to protect against cancer development through multiple mechanisms
  - Has effects on cancer cells and tumor microenvironment
  - Knockout of the TFF2 gene leads to faster tumor growth

Published Research on TNX-1700 (rTFF2) by Dr. Wang at Columbia

- **Either TFF2 overexpression or adenovirus-delivered rTFF2 markedly suppresses tumor growth[1,2]**
  - Curtailed the proliferation and expansion of myeloid progenitors that give rise to myeloid derived suppressor cells (MDSCs)
  - Adenovirus over-expression decreased tumor growth in a wild-type mouse model
  - Knockout of the TFF2 gene leads to faster tumor growth
- **Novel mechanism for suppressing myeloid-derived suppressor cells, and activating anti-cancer CD8+ T cells**
  - Implications for both cancer prevention and treatment
  - Potential to synergize with other immunotherapy drugs
- **Modified version of human TFF2 appears to show greater stability and efficacy[2]**
  - Native TFF2 has a short half-life

[1]Dubeykovskaya Z, et al. *Nat Commun*. 2016 7:1-11
[2]Dubeykovskaya ZA, et al, *Cancer Gene Ther*. 2019 26(1-2):48-57

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

Pre-IND Stage

Potential improvement over current biodefense tools against smallpox

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

Regulatory strategy

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

Targeting a Potential Public Health Issue

Material threat medical countermeasure under 21st Century Cures Act

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

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

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

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

In mice, TNX-801 behaved like attenuated vaccinia virus

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

How is HPXV related to modern vaccines?

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

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

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

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

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

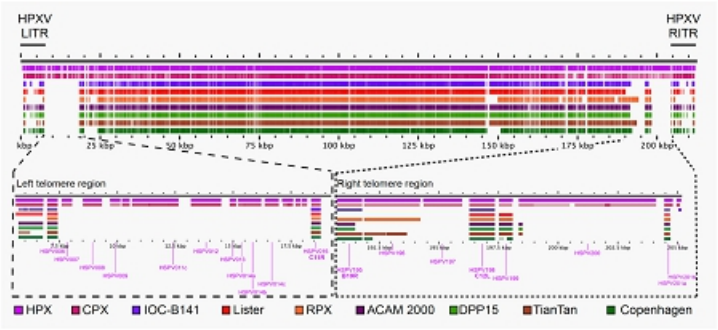
Vaccinia (VACV) strains have demonstrated potential for zoonotic infections and re-infection of humans[2-5]

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

Modern VACV smallpox vaccines are associated with cardiotoxicity[6]

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

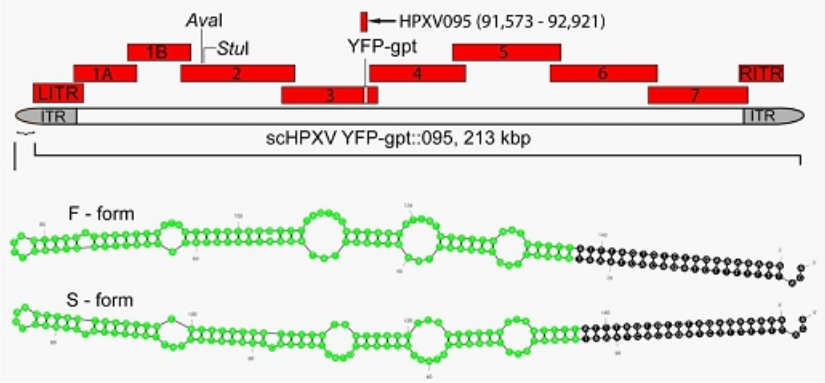
HPXV and its Relationship to Other Orthopoxviruses



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

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

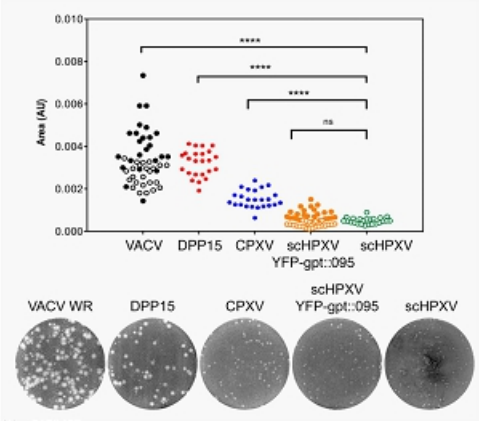
Genome Assembly (212 kbp) by Synthesis of Fragments and Construction of Telomeres



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

Sequence: GenBank entry DQ792504; DNA: GeneArt

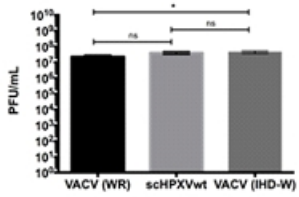
HPXV Produces Small Plaques that are More Like Cowpox Than Vaccinia (VACV)



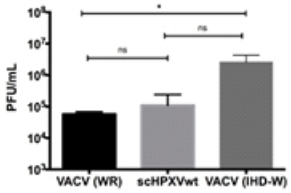
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Production of Cell-Associated and Extracellular Virus

Cell-associated virus

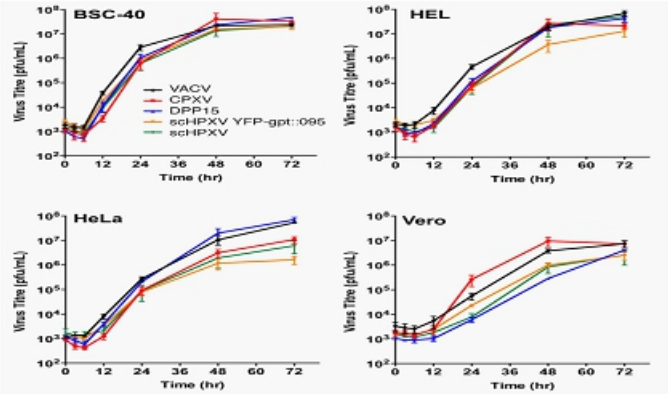


Virus in the media



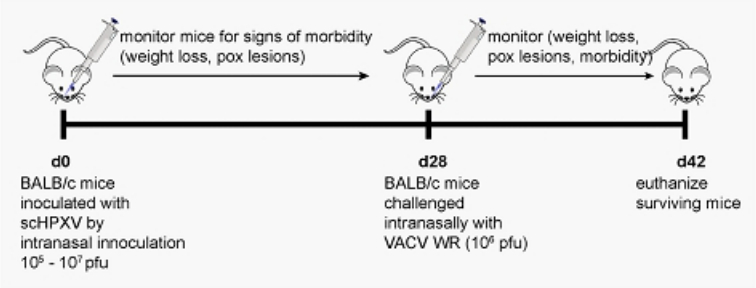
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

HPXV Growth Characteristics



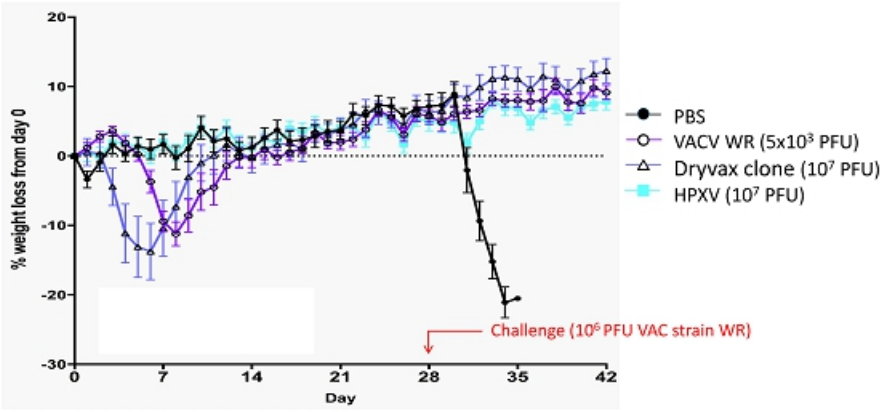
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

Testing Vaccine Protective Activity of HPXV in Mice Model



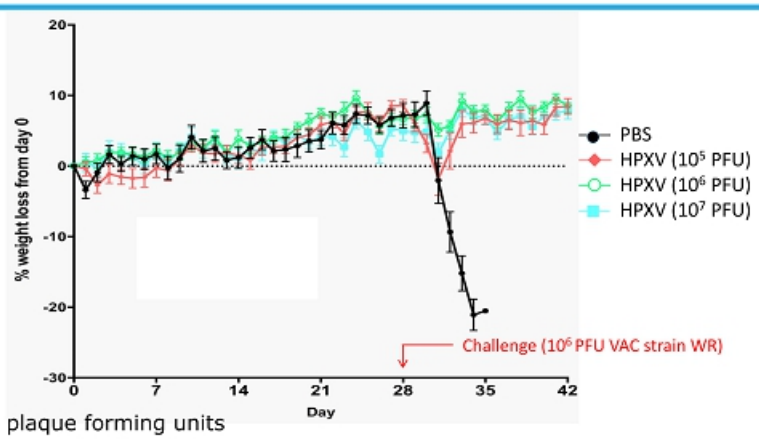
Noyce, RS, Lederman S, Evans DH. PLoS ONE. 2018; 13(1): e0188453
https://doi.org/10.1371/journal.pone.0188453

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



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

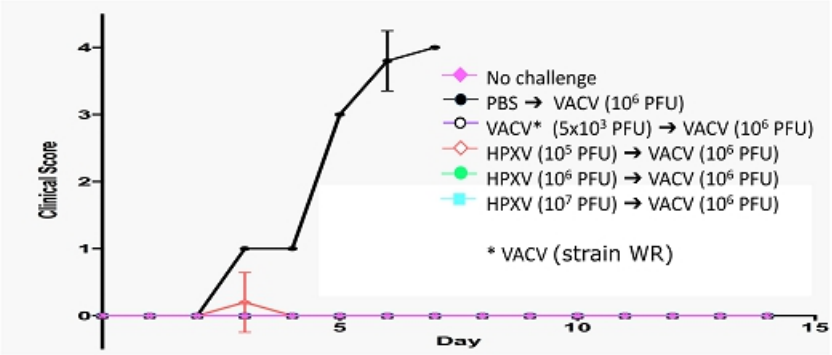
HPXV Vaccine Protection Activity Observed As Low As 10^5 PFU*



*PFU = plaque forming units

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

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



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

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

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

HXPV isolate from the 1976 outbreak later sequenced

Modern smallpox vaccines are associated with cardiotoxicity[1]

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

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

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

Smallpox was eradicated as a result of global public health campaigns

No cases of naturally-occurring smallpox have been reported since 1977

Accidental or intentional transmission of smallpox does not require a natural reservoir

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

Current Needs to Vaccinate Against Smallpox

Ongoing vaccination of U.S. troops

- Troops in the Global Response Force

Threat of smallpox re-introduction

- Strategic National Stockpile & public health policy

Re-emergence of monkey pox[1]

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

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

TNX-801: A Potential Medical Countermeasure

21st Century Cures Act (2016), Section 3086

- Encouraging treatments for agents that present a national security threat

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

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

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

- Priority Review Voucher may be transferred or sold

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

TNX-801 (HPVX)

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

Mechanism of Action

Live virus vaccines stimulate cross-reactive immunity

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

Possible advantages of TNX-801

Potential safety improvement over existing vaccines

- Cardiotoxicity limits widespread smallpox vaccination in at-risk population

Exclusivity

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

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

Evidence of Effectiveness for Smallpox Vaccine

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

- Stimulates interest in the evolution of vaccinia

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

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

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

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

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

ACAM2000[1] – Best Technology of its Time

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

- Some rationale for selection[2]

Growth in serum free Vero cells

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

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

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

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

Rationale for Developing a Potentially Improved New Smallpox Vaccine

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

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

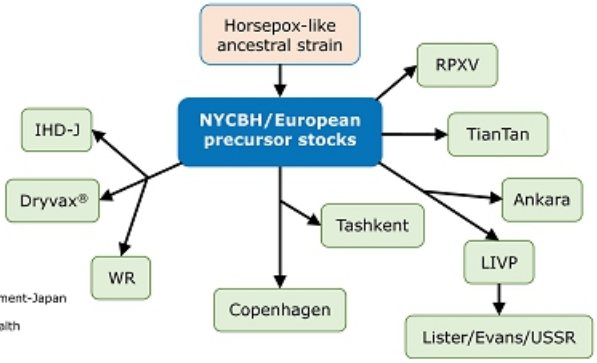
Modern VACV vaccination safety studied in 1081 VACV (Dryvax [62.5%] and ACAM2000 [37.5%]) vaccinees[1]

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

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

Proposed Evolution of Vaccinia Vaccines

Postulated Divergence of Historical Strains of Vaccinia

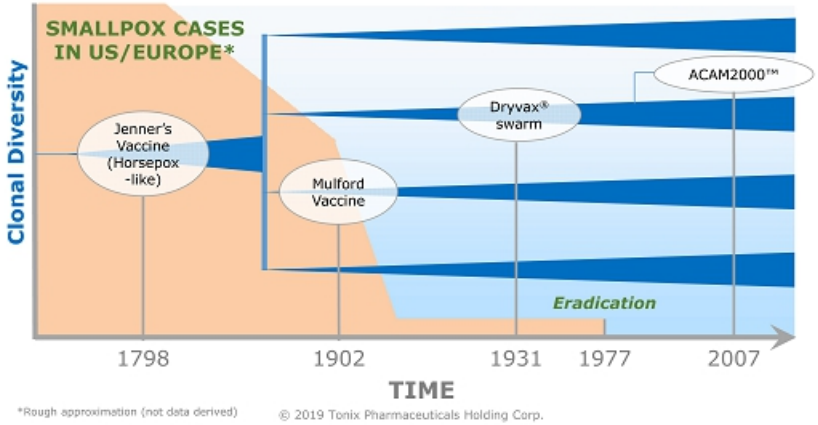


IHD-J=International Health Department-Japan
LIVP=Lister Vaccine Strain
NYCBH=New York City Board of Health
RPXV=Rabbitpox Virus
WR=Western Reserve

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

Proposed Evolution of Vaccinia Vaccines

Relationship to Smallpox Incidence and Eradication



*Rough approximation (not data derived)

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

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

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

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

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

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

Possible Smallpox Prevention and Treatment Strategies

Preventing Vaccine

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

Post-exposure vaccination[1]

- Jenner's vaccine

Priming of the immune system

- Imvamune® (MVA) and DNA vaccines[2]

Pharmacotherapy for infected or exposed individuals

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

Treatment of disseminated viremia in immunocompromised[3]

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

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

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

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

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

Replication correlates positively with immunogenicity

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

Manufacturing and Dosing Requirements

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

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

MVA is hard to scale up for commercial production

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

Antivirals

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

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

Vaccination protects against smallpox – both individuals and populations at risk

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

Vaccination can protect AFTER smallpox infection

- Vaccinia can be administered 1-3 days after infection

Vaccination indirectly protects non-immunized people in a population

- "Wetting the forest" or "herd immunity"

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

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

"The Time is Right"

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

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

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

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

Potential advantages of HPXV- strong immunogenicity with good tolerability

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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Seth Lederman, MD Chairman	**Adeoye "Oye" Olukotun, MD** Squibb, BMS, Mallinckrodt, Esperion
Margaret Smith Bell Standard Life Investments, Putnam Investments, State Street Research	**John Rhodes** Chair, NYS Public Service Commission, CEO, NYS Dept. of Public Service, Booz Allen
Daniel Goodman, MD Psychiatrist, co-founder Psychogenics	**James Treco** First Chicago, Salomon Brothers/Citigroup
Brig. General David Grange (U.S. Army, ret.) Pharm-Olam, PPD, McCormick Foundation	

Milestones – Recently Completed and Upcoming

☑ November 2018	Received FDA minutes confirming agreement on the design of P302/RECOVERY study
☑ March 2019	P302/RECOVERY study initiated
☑ April 2019	Received FDA formal minutes with clear guidance and support for new Phase 3 FM study using TNX-102 SL 5.6 mg
☑ May 2019	In-licensed TNX-1300, product candidate in Phase 2 development for cocaine intoxication
☑ August 2019	In-licensed TNX-1600, product candidate in preclinical development for PTSD
☑ August 2019	Entered into research collaboration to study internally-developed TNX-1500
☑ September 2019	In-licensed TNX-1700, product candidate in preclinical development for gastric and pancreatic cancers
☑ October 2019	Completed long-term exposure studies in participants with PTSD to evaluate tolerability of TNX-102 SL 5.6 mg
☐ October 2019	Meeting with FDA to discuss new program for TNX-102 SL to treat AUD
☐ Second Half 2019	Preliminary human pharmacokinetic and safety data (non-IND study) from selected TNX-601 (tianeptine oxalate) formulation expected
☐ First Half 2020	Topline data from P302/RECOVERY study expected

Pipeline Summary – by Select Therapeutic Areas

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

Pipeline Summary – by Phase of Development

Two Phase 3 Programs in indications affecting millions of Americans

- TNX-102 SL for PTSD: affects 12 million adults in U.S.
- TNX-102 SL for Fibromyalgia: affects between 5-10 million adults in U.S.

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

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

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

TONIX PHARMACEUTICALS

NASDAQ: TNXP

Thank you!

Exhibit 99.02

Investor Presentation

TONIX PHARMACEUTICALS

October 2019

Version P0200 10-16-19 (Doc 0543)

Cautionary Note on Forward-Looking Statements

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

Tonix Pharmaceuticals

Who we are:

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

- Focusing on small molecules and biologics to treat psychiatric, pain and addiction conditions, to improve biodefense through potential medical counter-measures and to prevent and treat organ transplant rejection

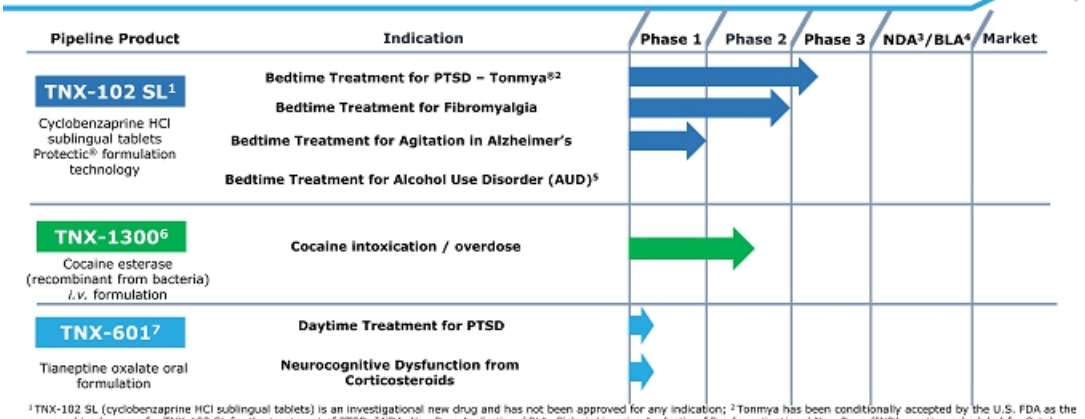
What we do:

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

CNS Candidates in Clinical Development

Psychiatry, Pain and Addiction

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



[1] TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication; [2] Tonmya has been conditionally accepted by the U.S. FDA as the proposed trade name for TNX-102 SL for the treatment of PTSD. [3] NDA- New Drug Application; [4] BLA –Biologic Licensing Application; [5] Pre-Investigational New Drug (IND) meeting scheduled for October with FDA. Upon receiving FDA clearance of an IND application, TNX-102 SL for AUD will be Phase 2 ready as it is expected to qualify for the 505(b)(2) pathway for approval; [6] TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication; [7] TNX-601 is in the pre-IND stage in the U.S., but a Phase 1 study for formulation development is currently being conducted outside of the U.S.

Preclinical Pipeline[1]

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

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

TNX-102 SL Proposed Mechanism: Improving Sleep Quality

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

Therapeutic Area	Target Indication	Status
Psychiatry	Posttraumatic stress disorder (PTSD)	Phase 3
Rheumatology	Fibromyalgia (FM)	Phase 3
Psychiatry / Neurology	Agitation in Alzheimer's Disease (AAD)	Phase 2 ready
Addiction	Alcohol Use Disorder (AUD)	Pre-IND
Chronic pain	TBD	Life-cycle opportunity
Sleep disorders	TBD	Life-cycle opportunity

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

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

Prevalence of PTSD Among Civilians and Veterans

4.7%
Adult population[1]

19-31%
Vietnam veterans[2]

>19%
Iraq/Afghanistan[3]

12 million American adults annually[1]

Women more likely to develop than men[1]

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

Unmet Need for Effective and Safe Therapies for Treatment of PTSD

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

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

PTSD is signature wound of last 25 years of war

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

Potential Therapeutic Advantages of TNX-102 SL

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

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

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

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

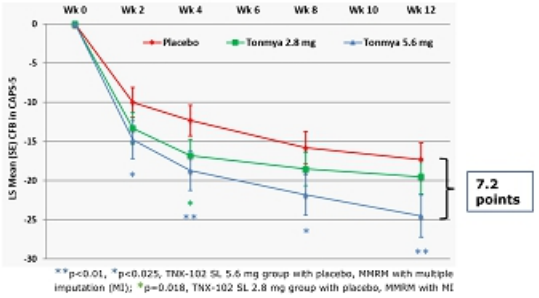
TNX-102 SL is non-addictive

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

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

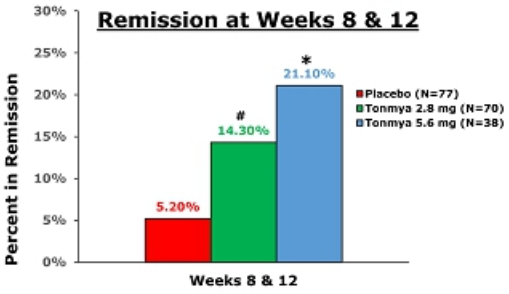
TNX-102 SL Phase 2 Dose-Effect in Military-Related PTSD[1]

PTSD Symptoms (CAPS-5[2] Score)



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

Remission at Weeks 8 & 12



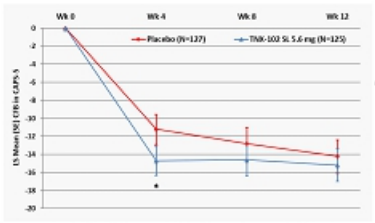
Remission = Loss of Diagnosis and CAPS-5 < 11
Asterisk and hashmark represent pairwise comparisons between TNX-102 SL and Placebo; #p=0.08, Odds Ratio 3.01 (0.89, 10.18)
*p=0.02, Odds Ratio 4.60 (1.27, 16.66); logistic regression

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

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

Phase 3 P301/HONOR Study[1]

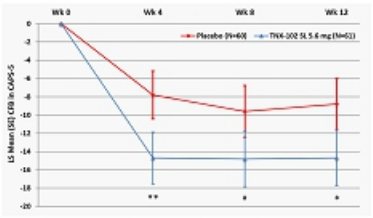
Modified intent to treat (mITT) population



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

~50% mITT Population

Time Since Trauma (TST) ≤9 yrs



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

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

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

	P201			P301	
Category of Adverse Reaction Preferred Term	Placebo (N=94)	TNX 2.8 mg (N=93)	TNX 5.6 mg (N=50)	Placebo (N=134)	TNX 5.6 mg (N=134)
Systemic Adverse Events*#					
Somnolence	6.4%	11.8%	16.0%	9.0%	15.7%
Dry mouth	10.6%	4.3%	16.0%		
Headache	4.3%	5.4%	12.0%		
Insomnia	8.5%	7.5%	6.0%		
Sedation	1.1%	2.2%	12.0%		
Local Administration Site Reactions*#					
Hypoaesthesia oral	2.1%	38.7%	36.0%	1.5%	37.3%
Paraesthesia oral	3.2%	16.1%	4.0%	0.7%	9.7%
Glossodynia	1.1%	3.2%	6.0%		
Product Taste Abnormal				3.0%	11.9%

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

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

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

TNX-102 SL for PTSD: New Phase 3 P302/RECOVERY Study – Initiated 1Q 2019

General study characteristics:

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

Primary endpoint:

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

Key Secondary endpoints include:

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

Potential pivotal efficacy study to support NDA approval

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

Opportunities 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
- Addiction (Alcohol Use Disorder)

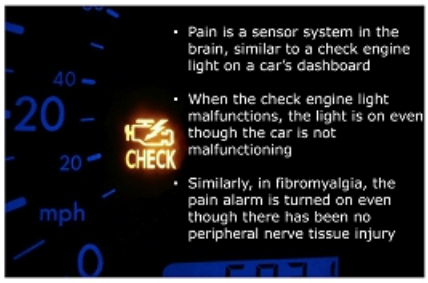
Psychiatric Symptoms of Neurological Disorders
- Agitation in Alzheimer's
- Psychosis in Parkinson's, Alzheimer's and other dementias

Chronic Pain States
- Chronic wide-spread pain (fibromyalgia)
- Osteoarthritis

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: Potential Treatment for Fibromyalgia



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

- Fibromyalgia is considered a neurobiological disorder characterized by[1]: chronic widespread pain, non-restorative sleep, fatigue, diminished cognition
- Believed to result from inappropriate pain signaling in central nervous system in the absence of peripheral injury[1]
- An estimated 5-10 million adults in the U.S. have fibromyalgia[2]
- Causes significant impairment in all areas of life[3]
  - Lower levels of health-related quality of life – reduced daily functioning
  - Interference with work (loss of productivity, disability)
- Fewer than half of those treated for fibromyalgia receive sustained benefit from the three FDA-approved drugs[4]
- Inflicts substantial strain on the healthcare system
  - Average patient has 20 physician office visits per year[5]
  - Annual direct medical costs are twice those of non-fibromyalgia individuals[6]
  - Substantial off-label use of narcotic painkillers and prescription sleep aids[7]

[1] Phillips K & Clauw DJ, Best Pract Res Clin Rheumatol 2011;25:141.
[2] American College of Rheumatology (www.ACRPatientInfo.org accessed May 7, 2019)
[3] Schaefer et al., Pain Pract, 2015.
[4] The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[5] Robinson et al, Pain Medicine 2013;14:1400.
[6] White et al, J Occupational Environ Med 2008;50:13.
[7] Patient Trends: Fibromyalgia", Decision Resources, 2011.

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

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

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

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

- Agitation is commonly diurnal ("sundowning")

Prevalence

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

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

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

[1]Rose, K.et al. (2015). *American Journal of Alzheimer's Disease & Other Dementias, 30*:78
[2]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/
[5]FDA comments on final protocol received October 2018

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

AUD is a chronic relapsing brain disease

- Characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using

Sleep disturbance is extremely common in alcohol recovery[1]

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

Prevalence

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

Three FDA-approved medications

- Remains an unmet need due to compliance and safety issues

Pre-IND meeting with the FDA in October 2019

- To discuss a potential 505(b)(2) development plan for TNX-102 SL as a treatment for AUD.
- Potentially a Phase-2 ready IND

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

TNX-1300* for the Treatment of Cocaine Intoxication

Recombinant protein that degrades cocaine in the bloodstream[1]

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

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

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

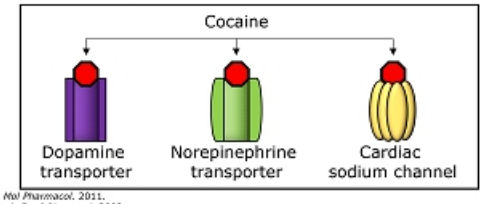
**TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication.*

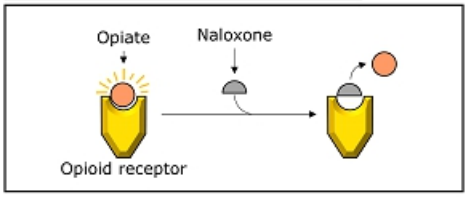
[1] Gao D et al, Mol Pharmacol. 2009. 75(2):318-23.
[2] Bresler MM et al, Appl Environ Microbiol. 2000. 66(3):904-8.
[3] Nasser AF et al, J Addict Dis. 2014;33(4):289-302.

Pharmacotherapies for Cocaine Intoxication Have Not Been Effective

Treatments for opiates not effective for cocaine:

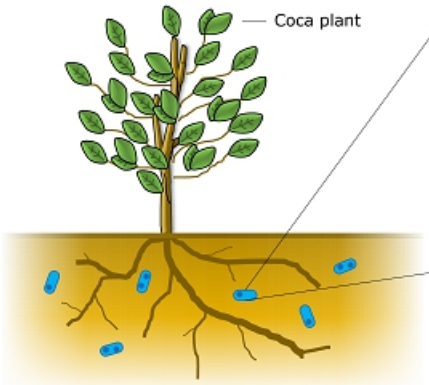
	Cocaine	Opiates
MOA of Toxicity	Complex; mediated by multiple targets with distinct biological functions[1]	Simple; mediated by opioid receptors[2]
Pharmacology	Antagonist[1]	Agonists[2]
Pharmacotherapy	**No FDA-approved medication exists[1]**	Naloxone[2]



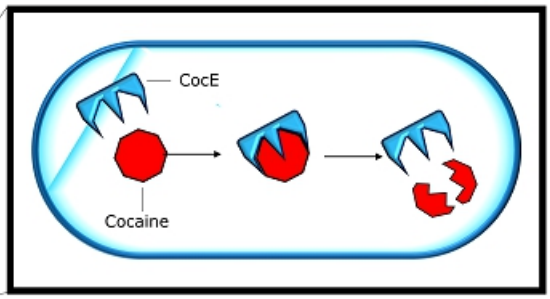


1. Brim et al. *Mol Pharmacol.* 2011.
2. Melichar et al. *Eur J Pharmacol.* 2003.
3. Narasimhan et al. *Future Medicinal Chemistry.* 2012.

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



Cocaine is derived from the coca plant[1]



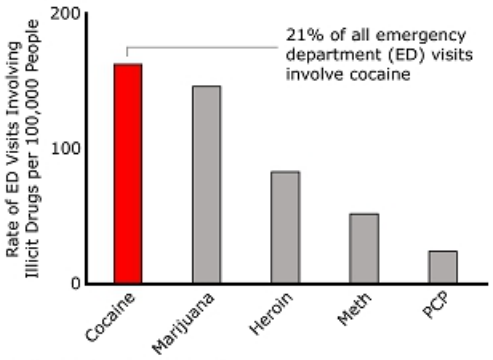
Rhodococcus bacteria living in the roots of the coca plant use CocE to metabolize cocaine[1]

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

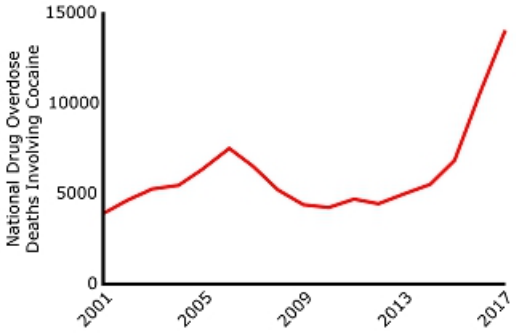
1. Narasimhan D et al. *Future Med Chem*. 2012.

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

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



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



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

Note: Figures are for illustrative purposes

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

Pre-IND Candidate

Targeting a Condition with Significant Unmet Need

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

- ✓ **Leverages expertise in PTSD (clinical and regulatory experience, market analysis, etc.)**
- ✓ **Mechanism of Action (MOA) is different from TNX-102 SL**

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

Patents and patent applications directed to tianeptine

- Issued patent directed to methods of treating cognitive impairment associated with corticosteroid treatment
- Patent application directed to oxalate salt

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

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 | Seward | pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank | svb Silicon Valley Bank | American Capital

Milestones – Recently Completed and Upcoming

☑ November 2018	Received FDA minutes confirming agreement on the design of P302/RECOVERY study
☑ March 2019	P302/RECOVERY study initiated
☑ April 2019	Received FDA formal minutes with clear guidance and support for new Phase 3 FM study using TNX-102 SL 5.6 mg
☑ May 2019	In-licensed TNX-1300, product candidate in Phase 2 development for cocaine intoxication
☑ August 2019	In-licensed TNX-1600, product candidate in preclinical development for PTSD
☑ August 2019	Entered into research collaboration to study internally-developed TNX-1500
☑ September 2019	In-licensed TNX-1700, product candidate in preclinical development for gastric and pancreatic cancers
☑ October 2019	Completed long-term exposure studies in participants with PTSD to evaluate tolerability of TNX-102 SL 5.6 mg
☐ October 2019	Meeting with FDA to discuss new program for TNX-102 SL to treat AUD
☐ Second Half 2019	Preliminary human pharmacokinetic and safety data (non-IND study) from selected TNX-601 (tianeptine oxalate) formulation expected
☐ First Half 2020	Topline data from P302/RECOVERY study expected

Pipeline Summary – by Select Therapeutic Areas

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

Pipeline Summary – by Phase of Development

Two Phase 3 Programs in indications affecting millions of Americans

- TNX-102 SL for PTSD: affects 12 million adults in U.S.
- TNX-102 SL for Fibromyalgia: affects between 5-10 million adults in U.S.

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

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

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

TONIX PHARMACEUTICALS
NASDAQ: TNXP

Thank you!