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): December 14, 2020

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.)**

26 Main Street, Suite 101, Chatham, New Jersey 07928
(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.

Tonix Pharmaceuticals Holding Corp (the "Company") updated its investor presentation, which is 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. A copy of the presentation is filed as Exhibit 99.01 hereto and incorporated herein by reference.

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

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	**Description.**
99.01	Corporate Presentation by the Company for December 2020

SIGNATURE

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

TONIX PHARMACEUTICALS HOLDING CORP.

Date: December 14, 2020

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

Exhibit 99.01

Investor Presentation
NASDAQ:TNXP

TONIX PHARMACEUTICALS

December 2020

Version P0264 12-14-2020 (Doc 0747)

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, risks related to failure to obtain U.S. Food and Drug Administration clearances or approvals and noncompliance with its regulations; our need for additional financing; delays and uncertainties caused by the global COVID-19 pandemic; substantial competition; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties. 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, 2019, as filed with the Securities and Exchange Commission (the "SEC") on March 24, 2020, 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

- **Clinical-stage biopharmaceutical company**
  - Committed to discovering and developing innovative and proprietary new therapeutics
- **Focus on developing biologics and small molecules**
  - **Central Nervous System (CNS)**
    - Pain, neurology, psychiatry, addiction
  - **Immunology**
    - Vaccines, organ transplantation, oncology, autoimmune diseases

Our Pipeline – CNS Portfolio

	CANDIDATES	INDICATION	STATUS
CNS Portfolio	TNX-102 SL[1]	**Fibromyalgia (FM) - Lead Program**	**Mid-Phase 3 – ongoing**
		PTSD	Phase 3 – ongoing
		Agitation in Alzheimer's	Phase 2 ready
		Alcohol Use Disorder	Phase 2 ready
	TNX-1300[2]	Cocaine Intoxication / Overdose	Phase 2
	TNX-1900[3]	Migraine and craniofacial pain	Clinical – pre-IND[4]
	TNX-601 CR	Depression, PTSD, Neurocognitive Dysfunction from Corticosteroids	Clinical – pre-IND[5]
	TNX-1600[6]	Depression, PTSD and ADHD	Preclinical

[1]TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication.
[2]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; licensed from Columbia University.
[3]Assets purchased from Trigemina; license agreement with Stanford University
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900
[5]TNX-601 CR is in the pre-IND stage in the U.S.; a Phase 1 trial for formulation development was recently completed outside of the U.S.
[6]Assets purchased from TRImaran Pharma; license agreement with Wayne State University

Our Pipeline – Immunology & Biodefense Portfolio

	CANDIDATES	INDICATION	STATUS
Immunology Portfolio	**TNX-1800**	**Covid-19 vaccine – Prioritized Program[1]**	**Preclinical**
	TNX-1810, TNX-1820, TNX-1830	Covid-19 vaccine[1]	Preclinical
	TNX-2300	Covid-19 vaccine[2]	Preclinical
	TNX-2600	Covid-19 vaccine[2]	Preclinical
	TNX-801	Smallpox and monkeypox preventing vaccine[3]	Preclinical
	TNX-1200	Smallpox and monkeypox preventing vaccine[4]	Preclinical
	TNX-1500	Organ Transplant Rejection/Autoimmune Conditions[5]	Preclinical
	TNX-1700	Gastric and pancreatic cancers[6]	Preclinical
	TNX-701	Radioprotection	Preclinical

[1]Live attenuated vaccine based on horsepox virus vector
[2]Live attenuated vaccine based on bovine parainfluenza virus vector; option for license with Kansas State University
[3]Live attenuated vaccine based on horsepox virus
[4]Live vaccine based on vaccinia virus
[5]anti-CD40L humanized monoclonal antibody
[6]recombinant trefoil factor 2 (TFF2) based protein; licensed from Columbia University

Overview of TNX-102 SL*

Protectic® proprietary formulation of cyclobenzaprine that supports sublingual administration

TNX-102 SL is a non-opioid, centrally-acting analgesic that works by improving sleep quality

◇ **Scientific Rationale for Protectic® Formulation** ◇

- Engenders unique pharmacokinetic and pharmacodynamic properties that emphasize sleep properties of cyclobenzaprine while minimizing undesirable properties
- Potential therapeutic value in a constellation of disorders where sleep disturbances are:
  - Co-morbid
  - Involved in the onset, progression and severity of the disease

*TNX-102 SL is in clinical stage of development and not approved for any indication

TNX-102 SL: Differentiation from Oral Formulations

FEATURE	BENEFIT	ADVANTAGE
Cyclobenzaprine	40+ years as oral medication	Established safety record
Formulation: Protectic®	Allows submucosal absorption	Not achievable with oral formulation
Administration: sublingual	Bypasses gut	Avoids first-pass metabolism; reduced formation of "activating" metabolite
Pharmacokinetic profile	Rapid absorption (peak at ~4 hours, low trough levels 8-24 hours)	Desired profile for nighttime action
Dose: low (2.8 to 5.6 mg)	Recruitment of high affinity receptors (5-HT_{2A}, α_1, H_1)	Complimentary trimodal mechanism of action with less risk of off-target interference

TNX-102 SL: Potential Treatment for Fibromyalgia (FM)

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

- Fibromyalgia is considered a central nervous system disorder with symptoms that include: chronic widespread pain, nonrestorative sleep, fatigue, diminished cognition and mood disturbances
- Believed to result from inappropriate pain signaling in central nervous system in the absence of peripheral injury[1]
- An estimated 6-12 million adults in the U.S. have fibromyalgia[2], 90% of whom are women
- Causes significant impairment in all areas of life[3]
  - Lower levels of health-related quality of life – reduced daily functioning
  - Interference with work (loss of productivity, disability)
- Fewer than half of those treated for fibromyalgia receive complete relief from the three FDA-approved drugs[4]
- Substantial off-label use of narcotic painkillers and prescription sleep aids[5]
  - Among those diagnosed, more than one-third have used prescription opioids as a means of treatment[6]

[1] Phillips K & Clauw DJ, Best Pract Res Clin Rheumatol 2011;25:141.
[2] American Chronic Pain Association (www.theacpa.org, 2019)
[3] Schaefer et al., Pain Pract, 2015.
[4] The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[5] Patient Trends: Fibromyalgia", Decision Resources, 2011.
[6] Berger A, Dukes E, Martin S, Edelsberg J, Oster G, Int J Clin Pract. 2007; 61(9):1498–1508.

TNX-102 SL: Results from Completed FM Trials

Completed Trials in FM:

- Phase 2 (F202 BESTFIT) – 205 participants randomized
- Phase 3 (F301 AFFIRM) – 519 participants randomized
- Phase 3 (F304 RELIEF) – 503 participants randomized

Topline Efficacy Results:

- Phase 3 (F304 RELIEF) - achieved statistical significance in the primary efficacy endpoint (5.6mg dose)
- Phase 3 (F301 AFFIRM) - did not achieve statistical significance in primary endpoint but showed activity (2.8mg dose)
- Phase 2 (F202 BESTFIT) - did not achieve statistical significance in primary endpoint but showed activity (2.8mg dose)

Safety:

- Well tolerated; side effects consistent with known side effects of cyclobenzaprine

Phase 3 F304/RELIEF Study: Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia in 39 U.S. sites (full sample size N=503)
- Adaptive Design: one unblinded interim analysis based on 50% of randomized participants

[1]Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

Primary endpoint (Week 14):

- Daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline in the weekly average as measured by the numerical rating scale (NRS), using mixed model repeated measures analysis with multiple imputation (MMRM with MI)

Key Secondary endpoints (Week 14):

- Patient Global Impression of Change responder analysis
- Fibromyalgia Impact Questionnaire - Revised (FIQ-R) Symptom Domain score
- FIQ-R Function Domain score
- PROMIS Sleep Disturbance instrument T-score
- PROMIS Fatigue instrument T-score
- Weekly average of the daily diary assessment of sleep quality

Pivotal efficacy study to support NDA approval

F304/RELIEF Study Topline Data: Statistical Significance Achieved on Pre-specified Primary Efficacy Endpoint (p=0.01)

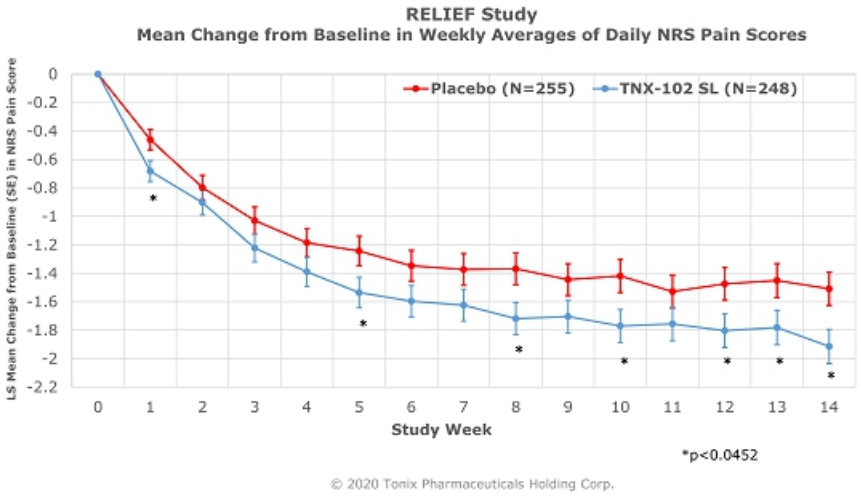
Primary Outcome Measure at Week 14	Placebo (N=255)	TNX-102 SL[2] (N=248)	Treatment Difference	P value
	LS Mean Change from Baseline (SE)	LS Mean Change from Baseline (SE)	Difference in LS Mean Change from Baseline Between TNX-102 SL and Placebo (SE)	
Daily Pain Diary, NRS	-1.5 (0.12)	-1.9 (0.12)	-0.4 (0.16)	**0.010***

Statistical Method: Mixed Model Repeated Measures analysis with Multiple Imputation
*p<0.0452 (requisite p-value hurdle for full study after Interim Analysis)
[1] Same primary endpoint analysis for FDA approvals of Cymbalta® and Lyrica® in fibromyalgia
Abbreviations: LS = least squares; NRS = numeric rating scale; SE = standard error

- Primary efficacy analysis also supported by an exploratory 30% responder analysis of daily diary pain, which indicated 46.8% on TNX-102 SL versus 34.9% on placebo achieved a 30 percent or greater reduction in pain (logistic regression; odds ratio [95% CI]: 1.67 [1.16, 2.40]; p=0.006)
  - 30% responder analysis was the primary analysis in F301 AFFIRM study of TNX-102 SL 2.8 mg
  - Also was the same primary endpoint analysis for FDA approval of Savella® for fibromyalgia

[2] TNX-102 SL is in clinical stage of development and not approved for any indication

F304/RELIEF Study: Primary Efficacy Endpoint Results (continued)



F304/RELIEF Study: Key Secondary Efficacy Endpoints

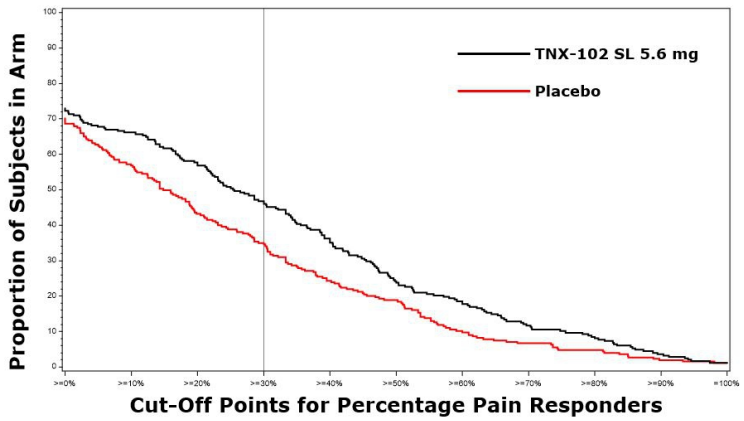
Outcome Measure at Week 14	Intent-to-Treat Analysis[1]	*P*-value
Non-Specific		
Patient Global Impression of Change	Responder Analysis: Proportion "Much Improved" or "Very Much Improved"	0.058
Fibromyalgia Syndrome-Related		
FIQ-R Symptom Domain	Mean Change from Baseline	0.007#
FIQ-R Function Domain	Mean Change from Baseline	0.009#
PROMIS Fatigue	Mean Change from Baseline	0.018#
Daily Sleep Quality Diary, NRS	Mean Change from Baseline	<0.001#
PROMIS Sleep Disturbance	Mean Change from Baseline	<0.001#

nominally significant at p<0.0452
[1] Combined periods (pre- and post-interim analysis); responder analysis is by Logistic Regression (missing = non-responder); the five mean change analyses are by Mixed Model Repeated Measures with Multiple Imputation
Abbreviations: FIQ-R = Fibromyalgia Impact Questionnaire – Revised; NRS = numeric rating scale; PROMIS = Patient-Reported Outcomes Measurement Information System

*TNX-102 SL is in clinical stage of development and not approved for any indication

F304/RELIEF Study: Continuous Responder Analysis (CRA) Graph

- The CRA graph allows one to see the proportion of responders over an entire range of cut-off points
- For example, >=30% improvement in pain is considered clinically meaningful in pain studies
- Looking at that vertical line at >=30% and visualizing a horizontal line to the y-axis tells you the proportion of each arm that achieved that level of pain improvement or better (47% for TNX-102 SL and 35% for placebo)
- It can be seen that TNX-102 SL separates from placebo, always at a higher proportion, up to about >=95% improvement



Adverse Events* (AEs) in F304/RELIEF Study

	TNX-102 SL (N=248)		Placebo (N=255)		Total (N=503)	
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Tongue/mouth numbness	43	17.3	2	0.8	45	8.9
Tongue/mouth pain/discomfort	29	11.7	5	2.0	34	6.8
Taste impairment	16	6.5	1	0.4	17	3.4
Tongue/mouth tingling	14	5.6	1	0.4	15	3.0
Systemic Adverse Events	**N**	**%**	**N**	**%**	**N**	**%**
Somnolence/Sedation	14	5.6	3	1.2	17	3.4

* Table reports only AEs at rate of greater than 5% in either treatment arm

No serious and unexpected AEs in RELIEF related to TNX-102 SL

- Systemic AEs comparable with prior studies and consistent with approved oral cyclobenzaprine product labeling
- Oral AEs similar to prior studies with TNX-102 SL, although tongue/mouth numbness at about half the rate in RELIEF

Safety and Tolerability in F304/RELIEF Study

- No new safety signals in RELIEF at TNX-102 SL 5.6 mg dose
- 82.3% in active arm and 83.5% in placebo arm completed the study
- 8.9% in active arm and 3.9% in placebo arm discontinued due to adverse events
- 7 SAEs in study: 2 in active arm and 5 in placebo arm
  - Of 2 in active arm, one was motor vehicle accident with multiple bone fractures, and other was pneumonia due to infection; both deemed unrelated to TNX-102 SL
- Similar oral administration site reactions as in prior studies with TNX-102 SL
- Overall low rates of systemic side effects, highest being somnolence/sedation at 5.6% in active group, 1.2% in placebo

TNX-102 SL 5.6 mg for Fibromyalgia: 2nd Phase 3 F306/RALLY Study – Enrollment Ongoing

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia in approximately 40 U.S. sites (N=670)
- Adaptive Design: one unblinded interim analysis based on 50% of randomized participants [1]

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)[2] *N= ~335* [3]

Placebo once-daily at bedtime
N= ~335 [3]

14 weeks

[1]Pending submission and agreement from FDA on statistical analysis plan
[2]Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose
[3]Pending submission and agreement from FDA on protocol amendment

Primary endpoint (Week 14):

- Daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline in the weekly average as measured by the numerical rating scale (NRS), using mixed model repeated measures analysis with multiple imputation (MMRM with MI)

Key Secondary endpoints (Week 14) include:

- Patient Global Impression of Change (PGIC): Proportion of patients with a rating of "very much improved" or "much improved"
- Fibromyalgia Impact Questionnaire – Revised (FIQR): Symptoms Domain

Interim results expected in 2nd quarter 2021

Topline results expected in 4th quarter 2021

Potential pivotal efficacy study to support NDA approval

Approved Fibromyalgia Pharmacotherapies

Pfizer

- Drug: Lyrica® or pregabalin (U.S. patent expired in 2018)
- Approved: 2004
- Mechanism: modulates nerve impulses involved in the transmission of pain through selective binding to the alpha2-delta protein of the voltage-gated calcium channels in CNS tissues
- Peak Sales: Approximately $5 billion (including all approved indications)

Lilly

- Drug: Cymbalta® or duloxetine (U.S. patent expired 2014)
- Approved: 2004
- Mechanism: serotonin and norepinephrine reuptake inhibitor (SNRI)
- Peak Sales: Approximately $5 billion (including all approved indications)

Abbvie (developed by Forest Laboratories)

- Drug: Savella® or milnacipran (on patent)
- Approved: 2009
- Mechanism: serotonin and norepinephrine reuptake inhibitor (SNRI)
- Peak Sales: Approximately $130 million (approved for fibromyalgia indication only)

Other Fibromyalgia Pharmacotherapies in Development in the U.S.

Axsome Therapeutics - AXS-14

- Drug: esreboxetine
- Mechanism: Selective norepinephrine reuptake inhibitor
- Developmental Stage: At least mid-Phase 3 (Phase 2 and Phase 3 trial positive*)

Aptinyx - NYX-2925

- Drug: ((2S, 3R)-3-hydroxy-2-((R)-5-isobutyryl-1-oxo-2,5-diazaspiro(3.4)octan-2-yl)butanamide)
- Mechanism: NMDA receptor modulator
- Developmental Stage: Phase 2 study is "active, not recruiting"

Teva - Ajovy®

- Drug: fremanezumab
- Anti-CGRP antibody
- Developmental Stage: Phase 2 proof-of-concept study "recruiting"

*licensed from Pfizer, Jan 2020

TNX-102 SL for Posttraumatic Stress Disorder (PTSD): Three Recent Trials

Phase 2 P201 "AtEase" – Military-related PTSD[1]

- **Reported May 2016 (mITT, N=231)**
- 3 groups: Placebo (n= 92), TNX 2.8 mg (n= 90) and TNX 5.6 mg (n=49)
- Primary endpoint (2.8 mg dose): CAPS-5 CFB, Week 12: MMRM, *P*=0.26 (two-sided)
- Secondary endpoints (5.6 mg dose): CAPS-5 (*P* =0.053), **PGIC (*P*=0.035)** and CGI-I (*P*=0.041)

Phase 3 P301 "HONOR" – Military-related PTSD[2]

- **Discontinued August 2018 (randomized, N=358) due to "futility" at interim analysis (IA)**
- 2 groups at IA: Placebo (n= 125) and TNX 5.6 mg (n= 127)
- Primary endpoint (5.6 mg dose): CAPS-5 CFB, Week 12: MMRM with MI, *P*=0.60 (two-sided)
- Secondary endpoints (5.6 mg dose): **PGIC (*P*=0.020)** and CGI-I (*P* =0.34)

Phase 3 P302 "RECOVERY" – Civilian PTSD[3]

- **Stopped enrollment in Feb 2020 (randomized, N=192) when interim analysis recommended stop for "futility"**
- 2 groups: Placebo (n ~ 96) and TNX 5.6 mg (n ~ 96)
- **Remains blinded**

[1]ClinicalTrials.gov Identifier: NCT02277704
[2]ClinicalTrials.gov Identifier: NCT03062540
[3]ClinicalTrials.gov Identifier: NCT03841773

Abbreviations: CAPS-5 = Clinician-Administered PTSD Scale for DSM-5; CFB = change from baseline; CGI = Clinician Global Impression - Improvement; PGIC = Patient Global Impression of Change; mITT = modified Intent-to-Treat; MMRM = mixed model repeated measures; MI = multiple imputation

Effect of Dose on Adverse Events (AEs) at 5.6 mg in PTSD Studies

Dose-related AEs:

- No serious and unexpected AEs in PTSD at either 2.8 or 5.6 mg doses
- No unique systemic AEs observed for 5.6 mg dose (but generally, a modest increase in frequency)
- Severity and incidence of oral hypoesthesia (oral numbness) are not dose related

		P201			P301	
		Placebo (N=94)	2.8 mg (N=93)	5.6 mg (N=50)	Placebo (N=134)	5.6 mg (N=134)
Systemic Adverse Event * #	Somnolence	6.4%	11.8%	16.0%	9.0%	15.7%
	Dry Mouth	10.6%	4.3%	16.0%		
	Headache	4.3%	5.4%	12.0%		
	Insomnia	8.5%	7.5%	6.0%		
	Sedation	1.1%	2.2%	12.0%		
Local Administration Site Reaction * #	Hypoaesthesia oral	2.1%	38.7%	36.0%	1.5%	37.3%
	Paresthesia 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%

Common Themes from Three Recent PTSD Trials Testing TNX-102 SL

- **Consistent nominal improvement on sleep item on CAPS-5**
  - E6 sleep disturbance item
  - Supported by nominal benefits in PROMIS Sleep Disturbance
  - Evidence of "target engagement", appropriate dosing and pharmacokinetics
- **High placebo response measured by CAPS-5 change from baseline**
  - Studies appear to have provided "enhanced" standard of care
- **Drug separation from placebo at Week 4 was not sustained at Week 12[1]**
  - Continued trend of improvement in placebo groups throughout courses of studies
- **Patient Global Impression of Change (PGIC) consistently improved at Week 12**
  - Patient self-assessment is not tied to disease constructs of CAPS-5/DSM-5
  - Clinician Global Impression of Improvement (CGI-I) also tended to improvement, although was more correlated with CAPS-5 change relative to that seen with PGIC

[1]In P201, 2.8 mg dose was nominally positive at Week 4; in P301, 5.6 mg dose nominally positive at Week 4

Multi-dimensional Analyses

"21st Century Cures Act" addressed use of novel trial designs, simulations and analyses

- Requiring guidance and encouraging increased reliance on novel and adaptive clinical trial designs, including use of modeling and simulation (sec 3021(b)(2))
- Then-FDA Commissioner Gottlieb expressed strong interest in the use of these innovative tools to expedite product development

Practical and ethical considerations motivate efficient extraction of data from trials with the lowest N's

- Excessively large studies, needlessly:
  - Increase the cost of developing drugs and discourage innovation
  - Delay the approval, marketing and availability of effective drugs
  - Prolong the exposure of participants to ineffective drugs
  - Sometimes show statistically significant effects that are not *clinically* meaningful

- "Adequate and well controlled" implies that drug approvals should be based on reasonably sized RCTs that show a statistically significant ($p < 0.05$) probability that drug benefit did NOT occur by chance

Proposed Analysis: Randomization Honoring Non-Parametric Combination of Tests (RHNPCOT)[1]

Honors the actual randomization method of the study
- Uses modern analyses and simulations which are advocated by 21st Century Cures Act

Preserves information from 20 dimensional CAPS-5
- Unlike "total CAPS-5" which collapses data into one dimension

Measure of benefit from all of the CAPS-5 items
- Not a "trimmed" CAPS-5 with fewer items
- No *a posteriori* selection, elimination or weighting of measurements

Assesses PTSD improvement at the Syndromal Level – not Symptom Level
- Not pseudo-specific

Efficient use of data with smaller numbers of study participants
- Ethical (not exposing volunteers unnecessarily) and practical (allows for reasonably sized studies)
- Provides benefit of statistical methods that weren't practical before computers

Concordant with Patient Global Impression of Change (PGIC)
- Patient reported yardstick of benefit – not connected to theoretical constructs of nosology
- PGIC is clinically meaningful

[1] https://www.stat.berkeley.edu/~stark/Seminars/npc-tonix-20.slides.pdf

Future Plans: TNX-102 SL for PTSD

Pharmacogenomics on study participants

- P302 had high percentage of participant DNA collected
- P301 has a subset of participant DNA available
- Exome sequencing to focus on:
  - Drug metabolizing enzymes
  - Neurotransmitter receptors and transporters
  - Genes related to sleep quality
  - Genes related to fear extinction memory processing

Plan to propose new analysis for primary endpoint in next PTSD studies

- Statistical analysis plan to use RHNPCOT for primary analysis

Phase 3 Study in US

- Protocol in development

Phase 3 Study on Kenyan Police

- Protocol in development with Moi University – expected start date 3Q 2021

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 United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020 • European Patent Office (EPO) issued European Patent No. 2968992 in December 2019 (validated in 37 countries). Opposition filed in October 2020 by Hexal AG • China National Intellectual Property Administration issued Chinese Patent No. ZL 201480024011.1 in April 2019 •Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018, Patent No. 6614724 in November 2019, and Patent No. 6717902 in June 2020 •10 granted patents (Indonesia, Saudi Arabia, New Zealand, Australia, Mexico, Taiwan, Israel, South Africa) •31 patent applications pending (4 being allowed in U.S., China, Israel, 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, Patent No. I642429 in December 2018 and Patent No. I683660 in February 2020 • Australian Patent Office issued Australian Patent No. 2013274003 in October 2018 and Patent No. 2018241128 in September 2020 • JPO issued Japanese Patent No. 6259452 in December 2017 • 20 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 No. 9918948 in March 2018 • European Patent Office (EPO) issued European Patent No. 2501234B1 in September 2017 (validated in 37 countries). In response to an opposition filed in June 2018, EPO's Opposition Division maintained the patent in unamended form in October 2019. Opponent has appealed • 1 patent application pending

Opportunities to Expand TNX-102 SL 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

Psychiatric Disorders

- Stress Disorders (PTSD)
- Mood Disorders (Depression)
- 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)

- Sleep quality plays a homeostatic role *in several disorders*

TNX-1800[1]: a COVID-19 Vaccine Candidate

- **Utilizes Tonix's proprietary horsepox virus as a vector**
  - Encodes a protein from SARS-CoV-2, the cause of COVID-19
  - Developed in collaboration with University of Alberta, Canada
- **Animal testing with Southern Research Institute**
  - Non-human primate immune response positive results reported in 4Q20
  - Small animal and non-human primate CoV-2 challenge testing data expected in 1Q21
- **Manufacturing agreement with FUJIFILM Diosynth**
  - Development for Good Manufacturing Practice (GMP) manufacturing for human trials
  - GMP[2] clinical supply expected to be ready for human trials in 2021[3]

[1]TNX-1800 (horsepox/Cov-2 spike live vaccine) is at the pre-IND stage of development
[2] Good Manufacturing Practice = GMP
[3] We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones

COVID-19 Vaccine Landscape

- **We expect more than one vaccine will be approved by FDA**
  - Different vaccines for different individuals
- **More than 150 vaccines in development**
  - Diversity of approaches is important since protective immunity is not yet understood
  - Technologies range from never tested before to 220 years old
  - Uncertainty exists around efficacy, durability and importantly, safety
- **Live attenuated vector systems in development include:**
  - Tonix (horsepox), Tonix (bovine parainfluenza), Merck (measles[1]- and VSV[2]-based), Zydus Cadila (measles-based)

[1]Measles-based vaccine, acquisition of Themis, collaboration with Institute Pasteur
[2]VSV = vesicular stomatitis virus; collaboration with IAVI = International AIDS Vaccine Initiative

Live, Attenuated Virus Vaccines for Other Infectious Diseases[1]

- **Long term, durable immunity**
  - Expected to stimulate T cells and provide years to decades of protection
- **Single administration, scalable manufacturing**
  - Low dose is amplified by replication, mRNA and protein synthesis at vaccination site
- **Block forward transmission (infectivity)**
  - Key to conferring herd immunity and protecting immunocompromised

[1]For example, the eradication of smallpox, containment of measles, mumps, and rubella

TNX-1800 Vaccination of Non-Human Primates Elicited Anti-SARS-CoV-2 Neutralizing Antibodies and Skin Reaction or "Take" in All Eight Animals

STUDY DESIGN:

- Compares TNX-1800 (modified horsepox virus encoding CoV-2 spike protein) to TNX-801 (horsepox virus, live vaccine) at two doses in non-human primates. A control group received a placebo.
- Each of these five groups (TNX-1800 high and low dose; TNX-801 high and low dose and placebo) includes four animals.

NEUTRALIZING ANTI-CoV-2 ANTIBODIES:

- At Day 14 after a single vaccination, all eight of the TNX-1800 vaccinated animals made anti-CoV-2 neutralizing antibodies (≥1:40 titer).
- None of the eight TNX-801 vaccinated control animals, or any of the four animals in the placebo group, made anti-CoV-2 neutralizing antibodies (≤1:10 titer).
- Level of neutralizing anti-CoV-2 antibody production was similar between the low and high dose TNX-1800 groups ((1 x 10^6 Plaque Forming Units [PFU]) and 3 x 10^6 PFU, respectively.

SKIN *TAKE* BIOMARKER:

- All 16 animals vaccinated with either dose of TNX-1800 or the control TNX-801 manifested a "take", or cutaneous response, signaling that the horsepox vector elicited a strong T cell immune response.

TNX-1800 Vaccination of Non-Human Primates Findings, Conclusions and Next Phase

TOLERABILITY:

- TNX-1800 and TNX-801 were well tolerated at both doses.

DOSE:

- Supports the expectation that TNX-1800 at the low dose of 1 x 10^6 PFU is an appropriate dose for a one-shot vaccine in humans.
- Indicates that 100 doses per vial is the target format for commercialization, which is suited to manufacturing and distribution at large scale.

CONCLUSIONS:

- Data show that TNX-1800 induces a strong immune response to CoV-2 in non-human primates.
- Data confirm that "take" is a biomarker of a strong immunological response to TNX-1800's vector, horsepox virus vaccine, and also indicate that "take" is predictive of a neutralizing antibody response to TNX-1800's cargo COVID-19 antigen, which is the CoV-2 spike protein.

NEXT PHASE:

- In the second phase of the study, the TNX-1800 vaccinated and control animals will be challenged with CoV-2. Results are expected in the first quarter of 2021.

TNX-1800[1]: Engineered for Long-term Immunity

- **Based on "vaccinia" vaccine developed more than 200 years ago by Dr. Edward Jenner to prevent smallpox**
  - TNX-1800 has 99.7% colinear identity with circa 1860 smallpox vaccine[2]
  - Eradicated smallpox (only viral disease ever eradicated)
  - Elicits durable (many decades) T cell immunity
  - Single dose protection without adjuvants
  - Manufacturable at scale
  - Minimal "cold chain" supply issues
  - Glass-sparing packaging owing to small unit dose

- **Genetic analysis of early vaccines indicates that Tonix's "horsepox" is closely related to Edward Jenner's "vaccinia"**
  - Modern "vaccinia" evolved during the 220 years it was propagated by primitive methods – for over 120 years before "viruses" were identified

[1]TNX-1800 (horsepox/Cov-2 spike live vaccine) is at the pre-IND stage of development
[2]Brinkmann A et al, Genome Biology (2020) 21:286 https://doi.org/10.1186/s13059-020-02202-0

Why Use a Horsepox Platform for a Vaccine?

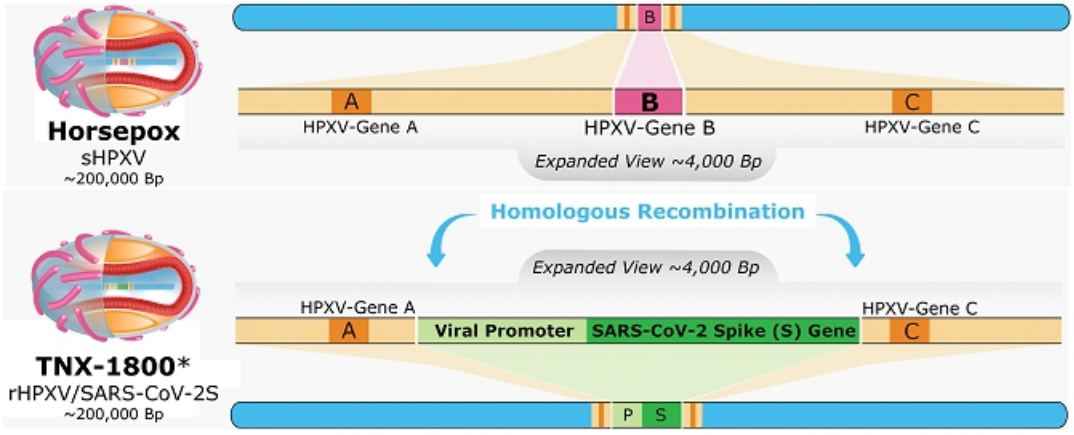
Horsepox can be engineered to express foreign genes

- Lack of persistence or genomic integration in the host
- Strong immunogenicity as a vaccine
- Readily manufacture at scale
- Live, attenuated vaccine – direct antigen presentation

Potential advantages of horsepox over vaccinia

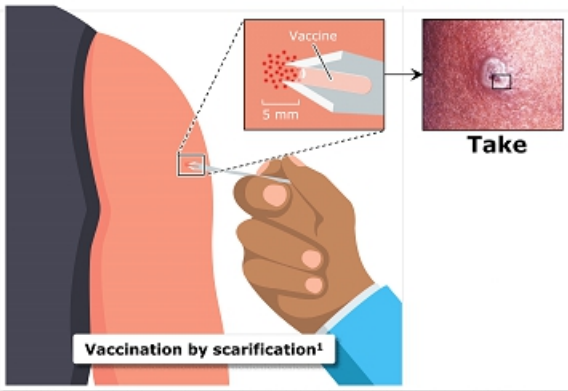
- Maintains strong immunogenicity with potentially improved tolerability
- Relative to non-replicating vaccinia, horsepox's replication in human cells provides direct antigen presentation, which is expected to trigger a T cell immune response, by Class I Major Histocompatibility Complex (MHC) Antigens
- Horsepox may behave differently than vaccinia as a vector, in part because of its different repertoire of genes that modulate immune responses and host range

TNX-1800 is Based on a Horsepox Virus (HPXV) Vector Designed to Express SARS-CoV-2 S Protein



*TNX-1800 is at the pre-IND stage of development

Vaccinia Induces a Skin Reaction Called "Take" – Described by Dr. Edward Jenner

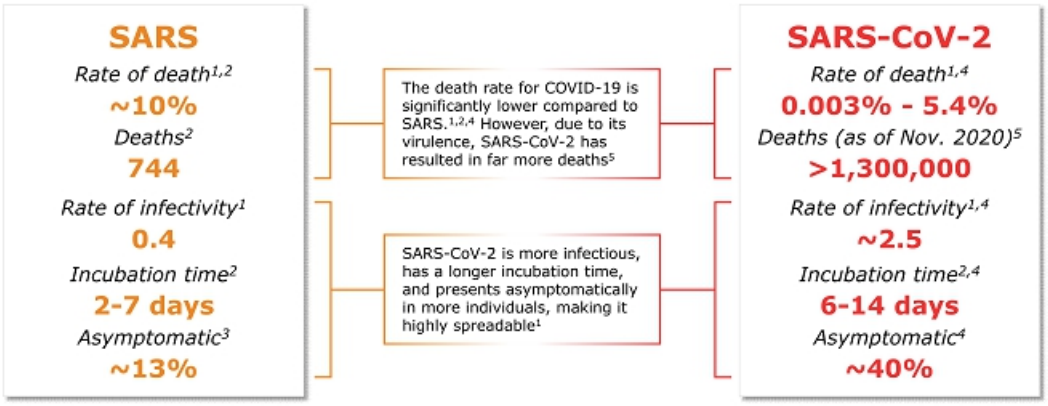


- **Biomarker of protection**
  - Smallpox was eradicated using this marker
  - Revaccination indicated for recipients without "take"
- **Measure of T cell immunity**
  - No need for blood draws or complex laboratory studies
  - No other functional T cell assay is approved or in clinical use for vaccination

*Example of major cutaneous reaction, or "take," resulting from a replication-competent live-virus vaccine delivered via scarification, indicating successful vaccination[1-3]

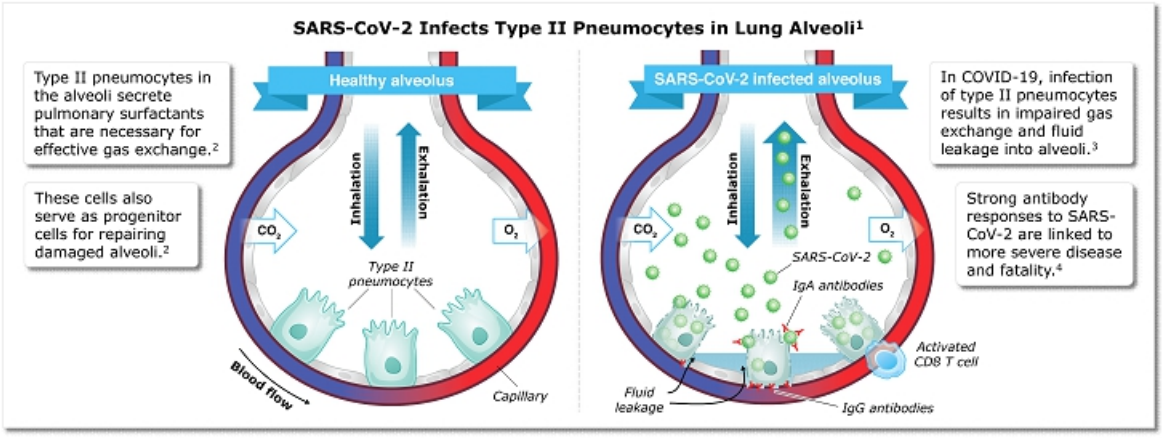
1.Fulginiti VA, et al. *Clin Infect Dis.* 2003;37(2):241-250.
2.Liu L, et al. *Nature Med.* 2010;16(2):224-228.
3.Centers for Disease Control and Prevention. Accessed April 15, 2020. https://phil.cdc.gov/Details.aspx?pid=3276

Unique Challenges of SARS-CoV-2



1. Ceccarelli M, et al. *Eur Rev Med Pharmacol Sci.* 2020;24:2781-2783.
2. Rabaan AA, et al. *Le Infezioni in Medicina.* 2020;28(2):174-184.
3. Wilder-Smith A, et al. *Emerg Infect Dis.* 2020;11(7):1142-1145.
4. Centers for Disease Control and Prevention. Accessed November 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html
5. Johns Hopkins University. Accessed November, 2020. https://coronavirus.jhu.edu/map.html

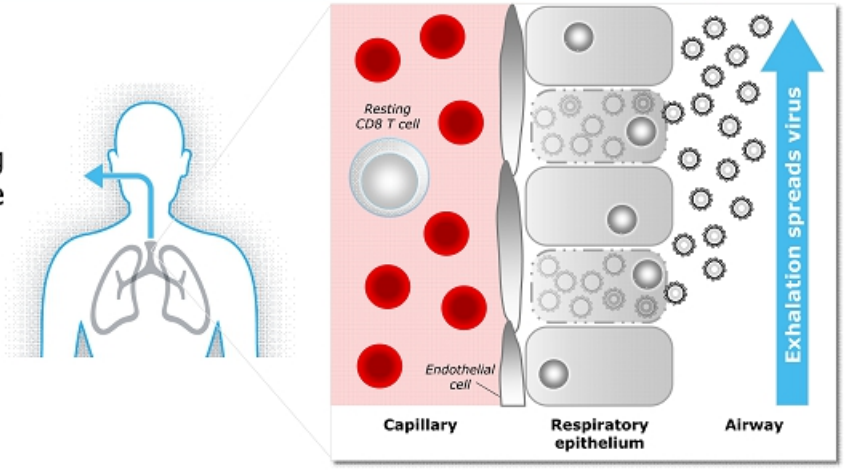
Infection of Type II Pneumocytes Can Lead to Lethal Respiratory Illness



1. Knudsen L, et al. *Histochem Cell Biol.* 2018;150(6):661-676.
2. Mason RJ. *Am J Physiol Lung Cell Mol Physiol.* 2020;319(1):L115-L120.
3. Xu Z, et al. *Lancet Respir Med.* 2020;8(4):420-422.
4. Lee WS, et al. *Nat Microbiol.* 2020;5:1185-1191.

SARS-CoV-2 Hijacks the Respiratory System to Spread Contagious Virus

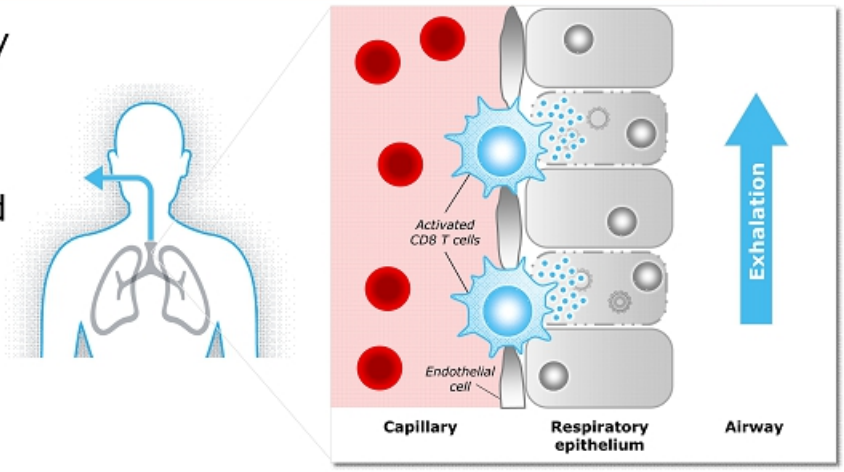
- Virus factories release virions by continuous budding
- Breathing, speaking or coughing has the potential to release virions into the air and transmit infection to others



Bar-On YM, et al. eLife. 2020;9:e57309.

CoV-2 Specific T Cells Kill the Virus Factories

- Natural immunity or vaccine protection has the potential to decrease forward transmission
- T cells specifically kill virally infected cells



Ber-Dn YM, et al. eLife. 2020;9:e57309.

Contrasting T cell and Antibody Immunity

- **T cell immunity**
  - ***Durable or long-lived (many years)***
  - Recognize fragments of pathogens on the surfaces of infected cells
  - Cannot recognize pathogens directly
  - Potential to clear viral infections (by killing infected cells)
  - Potential to block forward transmission (contagion) by infected people

- **Antibody immunity**
  - ***Temporary or short-lived (typically 3-6 months)***
  - Recognize pathogens directly
  - Potential to block viral entry (by recognizing pathogens)
  - Can only recognize virally infected cells that express viral surface proteins

TNX-1800 Upcoming Milestones

Southern Research studies will address two key questions:

1. Will vaccination of animals elicit an immune response to the S protein?
   - 4th Quarter 2020 - Non-human primate immune response positive results reported
2. Will immune response protect animals against a challenge with SARS-CoV-2 virus?
   - 1st Quarter 2021 – Non-human primate and small animal results expected[1]

Detailed analysis of primates planned, including:

- Major cutaneous reaction or "take" in primates
- In vitro stimulation of T cells
- Neutralizing antibodies

[1] We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones

2nd SARS-CoV-2 Vaccine Platform: Bovine Parainfluenza (BPI) Virus

Collaboration with Kansas State University to develop a vaccine candidate for the prevention of COVID-19

- Utilizes a novel live attenuated vaccine vector platform and the CD40-ligand to stimulate T cell immunity
- TNX-2300[1] and TNX-2600[1] drive expression of CoV-2 spike and CD40-L

Live attenuated vaccines based on bovine parainfluenza virus[2-6]

- Previously has been shown to be an effective antigen delivery vector in humans, notably well tolerated in infants and children
- Vector is well suited for mucosal immunization using a nasal atomizer, but it can also be delivered parenterally

Data from small animals to measure efficacy in challenge studies using SARS-COV-2 are expected in the second quarter of 2021

[1]Pre-IND stage of development; [2]Halle, AA *et al. J Gen. Virology* (2003) 84:2153–2162; [3]Halle, AA *et al. J Virology* (2000) 74 (24): 11626–11635; [4]Karron RA *et al. J Inf Dis* (1995) 171: 1107-14; [5]Karron RA *et al. Vaccine* (2012) 30: 3975– 3981; [6]Schmidt AC *et al. J Virology* (2001) 75(10): 4594–4603

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 a bacterium (*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

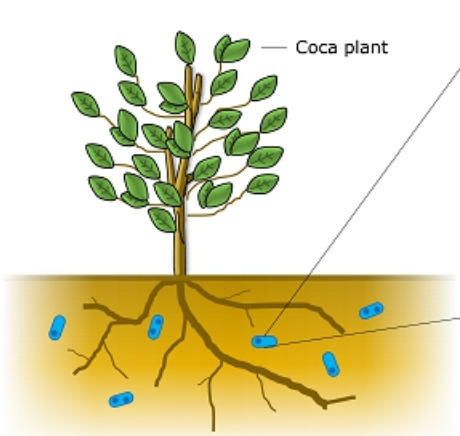
Phase 2 study completed by Reckitt Benckiser (TNX-1300 was formerly RBP-8000)[3]

- 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)

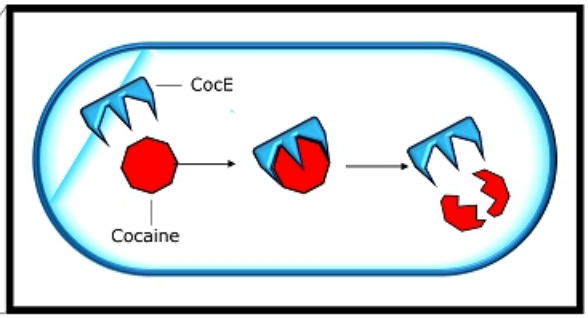
**TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication.*

[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.

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.

TNX-1300 Development Plan

- **Targeting to initiate a Phase 2 open-label, randomized pilot study of TNX-1300 in the first quarter of 2021**
- **Emergency department (ED) setting with patients coming in for treatment of cocaine and/or polysubstance intoxication**
- **Objectives**
  - Primary: To evaluate the safety of TNX-1300 in the ED setting
  - Secondary:
    - To evaluate TNX-1300 in the management of cardiovascular (CV) and other signs and symptoms associated with cocaine intoxication compared to usual care (UC) alone
    - To demonstrate reduction of plasma cocaine, cocaethylene, and ecgonine methyl ester levels after TNX-1300 administration and compare cocaine and cocaethylene levels of TNX-1300 group to those in UC alone

TNX-1900 for the Treatment of Migraine and Craniofacial Pain – Overview

Novel intranasal oxytocin formulation being developed as a prophylactic treatment for chronic migraine

- Based on a propriety formulation of oxytocin*, a naturally occurring human hormone that acts as a neurotransmitter in the brain

Clinical and preliminary research has shown that low oxytocin levels in the body can lead to increase in headache frequency, and that increased oxytocin levels can relieve headaches

- Certain other chronic pain conditions are also associated with decreased oxytocin levels

Oxytocin when delivered via the nasal route, results in enhanced binding of oxytocin to receptors on neurons in the trigeminal system, inhibiting transmission of pain signals

Intranasal oxytocin has been shown in animals that it can also block CGRP release, a pathway known to be critical to the pathogenesis of migraine attacks.

*Oxytocin is approved by the U.S. Food and Drug Administration (FDA) as Pitocin®, an intravenous infusion or intramuscular injection drug, for use in pregnant women to induce labor. An intranasal form of oxytocin was marketed by Novartis to assist in nursing as Syntocinon®, but the product was withdrawn and the New Drug Application (NDA) has been discontinued.

TNX-1900 for the Treatment of Migraine – Prevalence

One billion individuals worldwide suffer from migraines (~14% of population)[1]

Migraine is the second leading cause of years lived with disability[1]

In U.S., the estimated cost of all migraine headaches was $78 billion in 2014[2]

- Approximately 30% of those costs ($23 billion) were direct medical costs

Chronic migraine (≥ 15 headaches / month) effects about 1-2% of individuals[3]

- 75-150 million individuals worldwide
- 3-7 million in the U.S.

CGRP antibodies are the only migraine specific prophylaxis drugs approved in decades

- Requires parenteral administration (systemic effects on peripheral CGRP pathways)
- Long term safety concerns with prolonged systemic blockade of CGRP receptor[4]

[1] GBD 2016 Headache Collaborators, Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Neurol 2018; 17: 954–76
[2] Gooch, C. L., et al., The Burden of Neurological Disease in the United States: A Summary Report and Call to Action. Ann Neurol. 2017; 81:479-484
[3] Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[4] Robbins, At Stake: The Possible Long-Term Side Effects of CGRP Antagonists, https://www.practicalpainmanagement.com/pain/headache/stake-possible-long-term-side-effects-cgrp-antagonists, accessed November 8, 2020.

TNX-1900 for the Treatment of Migraine – Mechanism of Action

Preclinical research showed that nasally applied TNX-1900 selectively inhibits the activity of trigeminal pain-sensing nerve cells and blocks the release of CGRP

- TNX-1900 is believed to interrupt pain signals at the trigeminal ganglia by suppressing electrical impulses, a potentially different activity than drugs that just block CGRP

Migraine attacks are caused, in part, by the release of CGRP from pain-sensing nerve cells that are part of the trigeminal system

- The CGRP binds to receptors on other nerve cells and starts a cascade of events that eventually results in a severe headache. This, in turn, reduces various kinds of trigeminal nerve associated pain and prevents CGRP from acting at receptors in the central nervous system that are involved in migraine.

We believe targeted delivery of oxytocin could translate into selective blockade of CGRP release in the trigeminal ganglion and not throughout the body, which could be a potential safety advantage over systemic CGRP inhibition

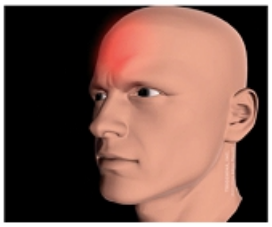
- In addition, daily dosing is more quickly reversible, in contrast to monthly or quarterly dosing, giving physicians and their patients greater control

TNX-1900 for the Treatment of Migraine – Mechanism of Action (continued)

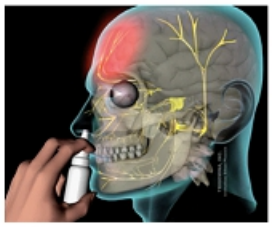
CGRP: NEUROTRANSMITTER THAT HAS BEEN VALIDATED AS KEY MIGRAINE TARGET

TNX-1900 believed to partially block release of CGRP in the trigeminal nerve

Proprietary Nasal to Brain Delivery



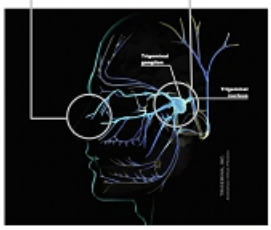
HEAD PAIN



PATIENT USES TNX-1900

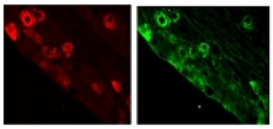
Permeates nasal mucosa

Transported to trigeminal system and brain



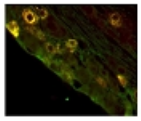
TARGETED DELIVERY

Oxytocin Receptors Co-Localize with CGRP in most Trigeminal Ganglia Neurons



Oxytocin Receptors CGRP

Overlay of Oxytocin Receptors and CGRP Staining



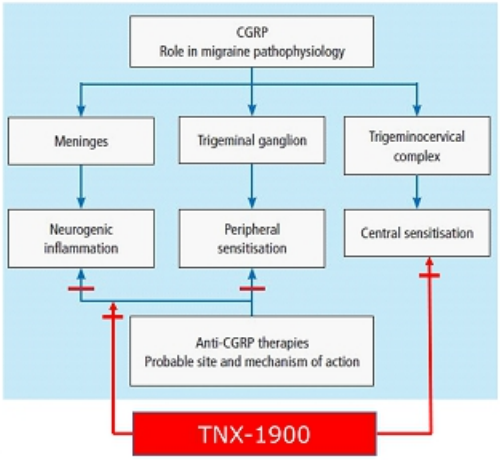
Abbrev. CGRP, calcitonin gene-related peptide

TNX-1900: Mechanism of Action (continued)

In animal models, intranasal oxytocin concentrates in the trigeminal system

Inhibits trigeminal neuronal firing, and decreases CGRP (and PACP) release onto meningeal vasculature and within the brainstem

- **Believed to have effects on:**
  - Neurogenic inflammation
  - Peripheral sensitization, where CGRP otherwise promotes neuronal-glial signaling of pain to trigeminal ganglion
  - Central sensitization, in which CGRP otherwise causes sensitization of NMDA receptor, reducing threshold for glutamate – creating allodynia
- **Anti-CGRP antibodies may only work on inflammation and peripheral sensitization**
  - Due to poor blood brain barrier penetration



Abbrev. CGRP, calcitonin gene-related peptide; PACP, pituitary adenylate cyclase-activating peptide
Figure adapted from Krishnaswamy R et al. Anti-CGRP monoclonal antibodies: breakthrough in migraine therapeutics. Progress in Neurology and Psychiatry. Vol 23.03, July-Sept, 2019.

TNX-1900 for the Treatment of Migraine – Development Status

In June 2020, Tonix acquired a proprietary formulation of nasal oxytocin solution for intranasal delivery from Trigemina

Also acquired migraine and pain treatment technologies of Trigemina, Inc. and assumed license for some of technologies from Stanford University

A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

Completed by Trigemina prior to acquisition

Tonix intends to submit an IND application for this program to the FDA in the first quarter of 2021

Targeting start of a Phase 2 study of TNX-1900 for the prophylactic treatment of chronic migraine in the U.S. in the second quarter of 2021

- Primary endpoint expected to be mean change in number of migraine headache days from the last 28 days of baseline to the last 28 days of treatment in each treatment group

Pipeline[1] Summary – by Select Therapeutic Areas

Public Health

- **TNX-1800, TNX-1810, TNX-1820 & TNX-1830 (live modified horsepox vaccine) for preventing COVID-19**
  Preclinical
- **TNX-2300 and TNX-2600 (live bovine parainfluenza vaccine) for preventing COVID-19**
  Preclinical

Biodefense

- **TNX-801 (live horsepox vaccine) for preventing smallpox and monkeypox**
  Preclinical
- **TNX-1200 (live vaccinia vaccine) for preventing smallpox and monkeypox**
  Preclinical
- **TNX-701 (oral radioprotective agent) for radioprotection**
  Preclinical

Transplantation/ Autoimmunity

- **TNX-1500 (anti-CD40-Ligand) for preventing rejection of solid organ transplants**
  Preclinical
- **TNX-1500 (anti-CD40-Ligand) for treating autoimmune disease**
  Preclinical

Oncology

- **TNX-1700 (rTFF2[2]) for treatment of gastric and pancreatic cancer**
  Preclinical

[1] Experimental new medicines and biologics, not approved for any indication
[2] Recombinant Trefoil Family Factor 2 – licensed from Columbia University

Pipeline[1] Summary – by Select Therapeutic Areas (continued)

Pain

- **TNX-102 SL (sublingual cyclobenzaprine) for fibromyalgia**
  Phase 3/RELIEF
  Phase 3/RALLY
- **TNX-1900 (intranasal oxytocin) for craniofacial pain**
  Clinical – pre-IND stage

Psychiatry

- **TNX-102 SL (sublingual cyclobenzaprine) for PTSD**
  Phase 3/RECOVERY
- **TNX-102 SL (sublingual cyclobenzaprine) for agitation in Alzheimer's**
  Phase 2 ready
  FDA Fast Track designation
- **TNX-601 CR (tianeptine oxalate and naloxone) for depression and PTSD**
  Clinical - Pre-IND stage
- **TNX-1600 (triple reuptake inhibitor[2]) for PTSD, Depression and ADHD[3]**
  Preclinical

Addiction Medicine

- **TNX-1300 (cocaine esterase) for cocaine intoxication**
  Phase 2
  FDA Breakthrough Therapy designation
- **TNX-102 SL (sublingual cyclobenzaprine) for alcohol use disorder**
  Phase 2 ready

Neurology

- **TNX-1900 (intranasal oxytocin) for migraine**
  Clinical – pre-IND stage

[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) – licensed from Wayne State University
[3] ADHD = attention deficit hyperactivity disorder

Milestones – Recently Completed and Upcoming[1]

☑ September 2020	Interim analysis of TNX-102 SL Phase 3 F304/RELIEF study in fibromyalgia completed
☑ 4th Quarter 2020	Non-human primate immune response positive results reported
☑ 4th Quarter 2020	Positive topline data from TNX-102 SL Phase 3 F304/RELIEF study in fibromyalgia reported
❑ **2021**	**Initiation of Phase 1 safety study of TNX-1800 for COVID-19 expected**
❑ **1st Quarter 2021**	**Small animal & non-human primate efficacy data from TNX-1800 in COVID-19 models expected**
❑ **1st Quarter 2021**	**Initiation of Phase 2 open-label safety study of TNX-1300 in ED setting for cocaine intoxication**
❑ **1st Quarter 2021**	**Submission of IND application for TNX-1900 for the treatment of migraine**
❑ **2nd Quarter 2021**	**Initiation of Phase 2 study of TNX-1900 for the treatment of migraine**
❑ **2nd Quarter 2021**	**Small animal efficacy data from TNX-2300 in COVID-19 models expected**
❑ **2nd Quarter 2021**	**Interim analysis of TNX-102 SL Phase 3 F306/RALLY study in fibromyalgia expected**
❑ **4th Quarter 2021**	**Topline data from TNX-102 SL Phase 3 F306/RALLY study in fibromyalgia expected**

[1] We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones.

Management Team

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TONIX PHARMACEUTICALS

Thank You!