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): February 19, 2021

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: (862) 904-8182

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 February 2021

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: February 19, 2021

By: /s/ Bradley Saenger

Bradley Saenger
Chief Financial Officer

Exhibit 99.01

Investor Presentation
NASDAQ:TNXP

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TONIX PHARMACEUTICALS

February 2021

Version P0274 2-19-2021 (Doc 0787)

Cautionary Note on Forward-Looking Statements

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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

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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)**
  - Lead: fibromyalgia program in mid-Phase 3
  - Pipeline: Pain, neurology, psychiatry, addiction
- **Immunology**
  - Lead: COVID-19 vaccine in non-human primate testing
  - Pipeline: 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-Related Sleep Disturbance[2]	Phase 3 ready
		Agitation in Alzheimer's	Phase 2 ready
		Alcohol Use Disorder	Phase 2 ready
	TNX-1300[3]	Cocaine Intoxication / Overdose	Phase 2
	TNX-1900[4]	Migraine and craniofacial pain	Clinical – pre-IND[5]
	TNX-601 CR	Depression, PTSD, Neurocognitive Dysfunction from Corticosteroids	Clinical – pre-IND[6]
	TNX-1600[7]	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]PTSD-Related Sleep Disturbance is a proposed new indication pending discussion with FDA
[3]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.
[4]Acquired from Trigemina; license agreement with Stanford University
[5]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900
[6]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.
[7]Acquired 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-2100	SARS-CoV-2 skin test for T cell immunity[2]	Pre-IND
	TNX-2300	Covid-19 vaccine[3]	Preclinical
	TNX-2600	Covid-19 vaccine[3]	Preclinical
	TNX-801	Smallpox and monkeypox preventing vaccine[4]	Preclinical
	TNX-1200	Smallpox and monkeypox preventing vaccine[5]	Preclinical
	TNX-1500	Organ Transplant Rejection/Autoimmune Conditions[6]	Preclinical
	TNX-1700	Gastric and pancreatic cancers[7]	Preclinical
	TNX-701	Radioprotection	Preclinical

[1]Live attenuated vaccine based on horsepox virus vector
[2]*In vivo* diagnostic: SARS-CoV-2 peptide epitope mixtures for intradermal administration to measure delayed-type hypersensitivity to SARS-CoV-2
[3]Live attenuated vaccine based on bovine parainfluenza virus vector; option for license with Kansas State University
[4]Live attenuated vaccine based on horsepox virus
[5]Live vaccine based on vaccinia virus
[6]anti-CD40L humanized monoclonal antibody
[7]recombinant trefoil factor 2 (TFF2) based protein; licensed from Columbia University

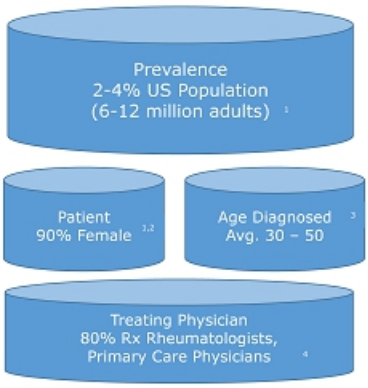
TNX-102-SL[1]: New Potential Treatment for the Management of Fibromyalgia

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

Background on Fibromyalgia

Fibromyalgia:

Chronic condition that causes widespread pain all over the body, sleep problems, fatigue, and often emotional and mental distress



[1] American Chronic Pain Association (www.theacpa.org. 2019)
[2] Wallitt, B., Nahin, R.L., Katz, R.S., Bergman, M.J., Wolfe, F. (2015). The Prevalence and Characteristics of Fibromyalgia in the 2012 National Health Interview Survey. *PLoS One*; 10(9): e0138024.
[3] Lawrence, R.C., Felson, T., Helmick, C.G., et al. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. *Arthritis Rheum*. 2008;58(1):26-35.
[4] Patient Trends: Fibromyalgia", Decision Resources, 2011.

Current Pharmacotherapy for Fibromyalgia

Limitations of Current Therapies

Fewer than half of those treated for fibromyalgia receive relief from the three FDA-approved drugs[1]

- Lack of overall response leading to discontinuation
- Inadequate response for some symptoms leading to the need for augmentation
- Lack of tolerability leading to discontinuation or reduction in dose (underdosing)

Current Treatment Patterns As A Result of Limitations

Switch Rates/Rotation/Discontinuation

- Over 50% of patient starting an FDA approved therapy for FM switch or discontinue therapy after 12 months[2]

Polypharmacy

- Average patient is using 2.6 drugs for treating their fibromyalgia, 50% of patients take 3 or more medications concomitantly[3]

Opioid Usage

- While prescription opioid usage has declined (from 40% in 2010 to 29% in 2017[4]), it remains high

Market Dissatisfaction

Only 43% of patients indicated that they are satisfied with their medication for FM[5]

[1] Frost and Sullivan, 2010
[2] Liu et al., 2016
[3] Robinson et al., 2012; prospective observational study with 1,700 participants with fibromyalgia.
[4] Sarmento et al., J Opioid Manag 2019; 15(6):460-77 – prescription opioid usage among diagnosed FM patients at one site
[5] Robinson et al., 2013; prospective observational study with 1,700 participants with fibromyalgia

Fibromyalgia Unmet Need and Ideal Treatment Profile

Unmet Medical Need:

Current treatment patterns indicate that new, more effective, and better-tolerated treatments are necessary for management of FM[1]

Ideal Treatment Profile:

Works by a different mechanism of action

Single therapy that addresses the core FM symptoms

- Pain
- Sleep
- Fatigue

Well tolerated with low discontinuation

- Low systemic tolerability
- No weight gain or impact on sexual function

Non-opioid

Suitable for chronic use

Reduces disability and improves daily living (global function)

[1] Yang, et al, 2016

TNX-102 SL 5.6 mg: Results from Completed Positive Phase 3 RELIEF Study

Completed Positive Trial in FM:

- Topline results announced in December 2020
- 503 participants randomized across 39 sites in U.S.
- 95% of participants were women

Topline Efficacy Results:

- Achieved statistical significance in the pre-specified primary efficacy endpoint of reducing daily pain (p=0.01)
- Activity shown in key secondary endpoints measuring improvements in sleep and fatigue

Safety:

- Well tolerated; side effects consistent with known side effects of cyclobenzaprine; no new safety signals observed

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, histaminergic H_1, and muscarinic M_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

Positive 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

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)[1] *N= 248*

Placebo once-daily at bedtime
N= 255

14 weeks

[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)

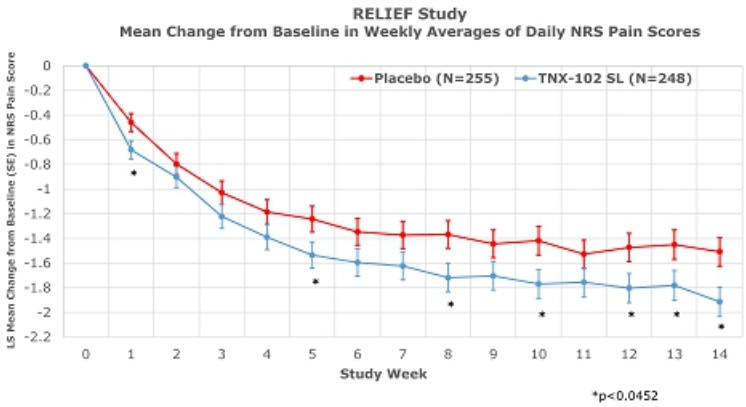
Primary Outcome Measure at Week 14	Placebo (N=255)	TNX-102 SL[2] (N=248)	Treatment Difference	P value
	LS Mean Change from Baseline (SE)	LS Mean Change from Baseline (SE)	Difference in LS Mean Change from Baseline Between TNX-102 SL and Placebo (SE)	
Daily Pain Diary, NRS	-1.5 (0.12)	-1.9 (0.12)	-0.4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

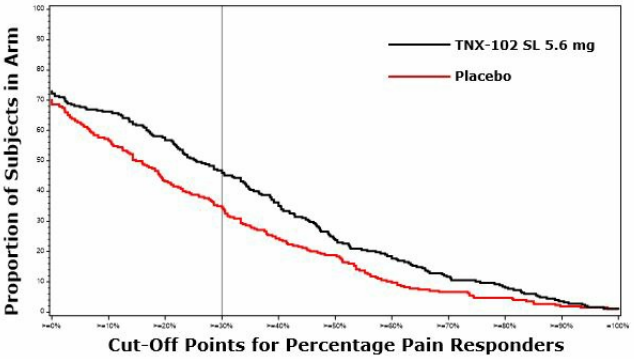
Outcome Measure at Week 14	Intent-to-Treat Analysis[1]	*P*-value
Non-Specific		
Patient Global Impression of Change	Responder Analysis: Proportion "Much Improved" or "Very Much Improved"	0.058
Fibromyalgia Syndrome-Related		
FIQ-R Symptom Domain	Mean Change from Baseline	0.007#
FIQ-R Function Domain	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

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[1]:

- Daily diary sleep quality NRS score change
- Fibromyalgia Impact Questionnaire – Revised (FIQR): Symptoms Domain change
- PROMIS Fatigue instrument change

Interim results expected in 3rd quarter 2021

Topline results expected in 4th quarter 2021

Potential pivotal efficacy study to support NDA approval

[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
PROMIS = Patient-Reported Outcomes Measurement Information System

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"

Virios Therapeutics – IMC-1

- Drug: Combination of famciclovir and celecoxib
- Anti-viral (herpes simplex) and COX-2 inhibitor non-steroidal anti-inflammatory drug (NSAID)
- Developmental Stage: Phase 2a completed

*licensed from Pfizer, Jan 2020

TNX-102 SL[1]: PTSD-related Sleep Disturbance[2]

[1]TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication.
[2] Refined indication of PTSD-related sleep disturbance pending agreement from FDA.

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)

Impact of PTSD:

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

PTSD is a risk factor for:

- Depression, alcohol and substance abuse, absenteeism/ unemployment, homelessness, violent acts, suicidal thoughts and suicide

PTSD: Prevalence and Demographics

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]

- Vast majority of PTSD is civilian PTSD
- Among diagnosed civilians with PTSD, the population tends to be about 2/3 female[4]
  - Women more likely to develop than men[2]:

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

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

- Ongoing vulnerability to memory intrusions and trauma triggers if there is deficient 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, histamine H_1, and muscarinic M_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

TNX-102 SL for PTSD: Completed Phase 3 P302/RECOVERY, Study Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study with baseline CAPS-5[1] ≥ 33 in approximately 29 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 included (N=192)

Primary endpoint:

- CAPS-5[1] mean change from baseline at Week 12 (TNX-102 SL 5.6 mg vs. placebo)

Secondary endpoints include:

- Change from baseline Clinical Global Impression – Severity scale
- Change from baseline Sheehan Disability Scale total score
- PROMIS Sleep Disturbance instrument T-score change from baseline
- Patient Global Impression of Change

Interim analysis: results reported in 1Q 2020 which resulted in stop for futility recommendation; enrollment was stopped and participants who were already enrolled completed the study

Topline data: reported 4Q2020, statistical significance not achieved for primary endpoint; activity observed in secondary endpoints

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

P302/RECOVERY Topline Results
Trial Efficacy Endpoints

	TNX-102 SL (N=80)		Placebo (N=83)		TNX-102 SL v. Placebo				
Week 12 Outcome Measure	LS Mean	SE	LS Mean	SE	LSMD	SE	95% CI	p-value*	ES
CAPS-5 CFB – Primary Endpoint	-20.7	1.97	-18.5	1.9	-2.2	2.3	-6.7, 2.3	0.343	0.15
CGI-S score CFB	-2	0.18	-1.5	0.17	-0.5	0.22	-0.9, -0.1	0.024	0.36
PGIC score	2.3	0.16	2.8	0.16	-0.5	0.19	-0.9, -0.1	0.007	0.43
PROMIS SD T-score CFB	-13	1.57	-9.4	1.51	-3.5	1.82	-7.1, 0.1	0.055	0.30
CAPS-5 item E6/SD CFB	-1.3	0.19	-0.9	0.19	-0.4	0.23	-0.8, 0.1	0.086	0.28

Abbreviations: CAPS-5 = Clinician-Administered PTSD Scale; CFB = change from baseline; CGI-S = Clinical Global Impression – Severity; CI = confidence interval; ES = effect size; LS = least squares; LSMD = least squares mean difference; N = number; PGIC = Patient Global Impression of Change; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = sleep disturbance; SE = standard error
*All secondary p-values are descriptive

P302/RECOVERY Topline Results
Safety Endpoints

Change in Weight, Blood Pressure, Heart Rate between Baseline and Last Assessment

	TNX-102 SL (N=80)		Placebo (N=84)	
Change in Outcome Measure	Mean	95% CI	Mean	95% CI
Weight (kg)	0.03	-0.48, 0.54	0.58	-0.01, 1.16
Systolic blood pressure (mmHg)	1.8	-0.8, 4.5	1.3	-1.4, 4.0
Diastolic blood pressure (mmHg)	1.5	-0.5, 3.5	-0.2	-2.3, 1.9
Heart rate (beats per minute)	1.8	-1.0, 4.5	1.5	-1.1, 4.0

Abbreviations: CI = confidence interval; N = number

- Greater weight increase in placebo by 0.58 kg than TNX-102 SL by 0.03 kg
- No clinically meaningful increases in systolic or diastolic blood pressure by TNX-102 SL
- No clinically meaningful increase in heart rate by TNX-102 SL

P302/RECOVERY Topline Results
Effects of TNX-102 SL on Female Sexual Function

	TNX-102 SL (N=65)		Placebo (N=64)		TNX-102 SL v. Placebo				
Wk 12 Outcome Measure	LS Mean	SE	LS Mean	SE	LSMD	SE	95% CI	p-value**	ES
CSFQ-14 CFB* (female)	4.6	0.84	2.4	0.86	2.2	1.21	-0.2, 4.6	0.07	0.32

Abbreviations: CSFQ-14 = Changes in Sexual Functioning Questionnaire short form: CI = confidence interval; ES = effect size; LS = least squares; LSMD = least squares mean difference; N = number; SE = standard error; Wk = week.
*higher score on CSFQ-14 indicates better sexual functioning
** p-value is descriptive

- Trend for improvement in female sexual function in TNX-102 SL group after 12 weeks of treatment – underpowered sample size but effect size of 0.32
  - Of importance given impairment in sexual function common with SSRIs
- Too few male subjects in TNX-102 SL group (N=15) and placebo group (N=19) for meaningful statistical comparison

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

Phase 3 P302 "RECOVERY" – Civilian PTSD (79% female)[1]

- **Reported Topline in December 2020 (mITT, N = 163)**
- 2 groups: Placebo (n = 83) and TNX 5.6 mg (n = 80)
- Primary endpoint (5.6 mg dose): CAPS-5 CFB, Week 12: MMRM, *P*=0.34 (two-sided)
- Secondary endpoints (5.6 mg dose): CGI-S* (*P*=0.024) and **PGIC* (*P*=0.007)**
- Stopped enrollment in Feb 2020 (randomized, N=192) when interim analysis recommended stop for "futility"

Phase 3 P301 "HONOR" – Military-related PTSD (89% male)[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 2 P201 "AtEase" – Military-related PTSD (93% male)[3]

- **Reported Topline in 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)**

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

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

Adverse Event Profile of TNX-102 SL 5.6 mg in Phase 3 Trials in Both Civilian (P302) and Military-Related (P301) PTSD

- No serious and unexpected AEs in PTSD at the 5.6 mg dose
- No systemic AE at ≥ 5% observed for 5.6 mg dose that was common to both studies
- Incidence of oral hypoaesthesia (numbness) and oral paraesthesia (tingling) similar in both studies

		P301 (Military)		P302 (Civilian)	
		Placebo (N=134)	5.6 mg (N=134)	Placebo (N=91)	5.6 mg (N=96)
Systemic Adverse Event * #	Somnolence	9.0%	15.7%		
	Dry Mouth			3.3%	8.3%
	URTI			4.4%	5.2%
Local Administration Site Reaction * #	Hypoaesthesia oral	1.5%	37.3%	1.1%	29.2%
	Paraesthesia oral	0.7%	9.7%	1.1%	7.3%
	Tongue discomfort			0.0%	5.2%
	Product Taste Abnormal	3.0%	11.9%		

URI = upper respiratory tract infection

#Only adverse events (AEs) are listed that are at a rate of ≥ 5% in the TNX-102 SL-treated groups

*No values in a row for either study means the AE in the active group in that study was at a rate of <5%

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

- **Consistent nominal improvement or trend at Week 12 for sleep measurements**
  - Supported by nominal benefits in PROMIS Sleep Disturbance and E6 sleep disturbance item in CAPS-5 analysis
  - Evidence of "target engagement", appropriate pharmacokinetics for nighttime dosing
- **Consistent nominal improvement or trend at Week 12 for Patient Global Impression of Change (PGIC) and Clinician Global Impression (CGI-I and CGI-S)**
  - For PGIC, participants themselves rate how they feel; for CGI, clinicians rate the overall improvement; neither measurement is tied to any theoretical construct of disease recovery such as the assumptions inherent in the CAPS-5 items
  - High placebo responses not seen in global patient- and clinician-reported measures (i.e., PGIC, CGI)
- **High placebo response measured by CAPS-5 change from baseline**
  - Studies appear to have provided "enhanced" standard of care
- **Consistent drug separation from placebo on CAPS-5 at Week 4[1] not sustained at Week 12**
  - Continued trend of improvement in placebo groups throughout courses of studies
- **Low systemic side effects and good tolerability across the three trials**

[1]In P201, 2.8 mg dose showed effect size at Week 4 of 0.38; in P301, 5.6 mg effect size at Week 4 of 0.30; in P302, 5.6 mg effect size at Week 4 of 0.29)

Sleep Disturbance Recognized as Clinically Valid Approach to Address PTSD

VA Study on Sleep in PTSD currently recruiting non-registrational 4-arm study of trazodone, eszopiclone, gabapentin and placebo on VA PTSD patients[1]

- **Insomnia Severity Index (ISI) is the primary endpoint**
- The PTSD subscale of the Pittsburgh Sleep Quality Index (PSQI) is a secondary endpoint
- CAPS-5 administered by centralized raters is a secondary endpoint
- Targeting 1,334 patients

Trazodone has a similar proposed Mechanism of Action to TNX-102 SL[1]

- Both are antagonists of 5-HT_{2A}
- Both are taken at bedtime[2]

[1]ClinicalTrials.gov Identifier: NCT03668041
[2]Bedtime use of trazodone is experimental and off-label, approved dosing for depression is *three times daily*

Future Plans: TNX-102 SL for PTSD

Plan to propose new indication: "PTSD-related sleep disturbance"

- Sleep disturbance is a core symptom of PTSD
- TNX-102 SL works by improving sleep quality which, as a result, improves sleep-dependent emotional memory processing necessary to recovery from PTSD; demonstrated by activity in secondary endpoints measuring sleep disturbance across three registration quality trials (~800 randomized participants) that correlated with patient rated global improvement on PGIC
- New indication would require acceptance by FDA

Phase 3 Study of PTSD in Kenyan Police

- Placebo response in CNS studies is growing faster in the U.S. than in other countries[1,2]
- Protocol in development with Moi University – expected start date 3Q 2021

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 ratings; genes related to fear extinction memory processing as evidenced by reduction in trauma-reminder triggered psychological or physical reactions; genes related to response on PGIC

[1]Gopalakrishnan, M et al. J Clin Psychiatry. 2020; 81(2):19r12960
[2]Laughren, TP J Clin Psychiatry. 2020; 81(2):19com13110

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

[1]TNX-1800 (horsepox/Cov-2 spike live vaccine) is at the pre-IND stage of development

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
  - 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 2nd half of 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

Concerns With Current COVID-19 Vaccines with Emergency Use Authorization (EUA)

- **Durability of protection**
  - Are vaccinated people protected one year later?
  - Durable protection is associated with T cell response
- **Protection against death/ventilator support**
  - Protection against severe disease and death would be strong motivations for many to be vaccinated
- **Protection against forward transmission**
  - Highly contagious nature of CoV-2 is a major problem driving pandemic
- **Safety of vaccine**
  - Risk:benefit for different age groups may vary – e.g. adults below 30 have low risk of disease
- **No biomarker of protection**
  - No test to establish protection from vaccination
- **Cost and accessibility**
  - High production cost and issues with cold-chain distribution

Warp-Speed COVID-19 Vaccines: Live Virus Vaccines Take Longer to Develop

- **mRNA**
  - Moderna (mRNA-1273, LNP[1]-encapsulated CoV-2 Spike ["Spike"] mRNA) EUA[2]
  - Pfizer & BioNTech (LNP-encapsulated Spike mRNA) EUA
- **Subunit**
  - Sanofi/GSK (recombinant Spike protein with adjuvant[3]) In Phase 3
  - Novavax (NVX-CoV2373, recombinant Spike protein with adjuvant[4]) In Phase 3
- **Non-replicating virus**
  - J&J (Ad26.COV2-S, Ad26 encoding Spike) +Phase 3 reported (Jan 2021)
  - Astra-Zeneca/Oxford (AZD1222, ChAdOx-1 encoding Spike) In Phase 3 (EUA in UK and India)
- **Live attenuated virus**
  - Merck (TMV-083, modified measles[5]-encoding Spike) Terminated Jan '21 - Phase 1[6]
  - Merck (V591, pseudo-typed VSV[7]-encoding Spike) Terminated Jan '21 - Phase 1[6]

[1]Lipid Nanoparticle = "LNP"
[2]Emergency Use Authorization = "EUA"
[3]GSK adjuvant AS03 contains squalene, DL-α-tocopherol and polysorbate
[4]Novavax adjuvant Matrix-M1 contains saponin extracted from the Quillaja saponaria Molina tree

[5]Measles-based vaccine, acquisition of Themis, collaboration with Institute Pasteur
[6]Merck Discontinues Development of SARS-CoV-2/COVID-19 Vaccine Candidates; Continues Development of Two Investigational Therapeutic Candidates - Merck.com
[7]VSV = vesicular stomatitis virus; collaboration with IAVI = International AIDS Vaccine Initiative

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 (mRNA) to 220 years old
  - Uncertainty exists around efficacy, durability and importantly, safety
- **Live attenuated vector systems in development include:**
  - Tonix (horsepox), Tonix (bovine parainfluenza), Zydus Cadila (measles-based)

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 (1×10^6 Plaque Forming Units [PFU]) and 3×10^6 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 1×10^6 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?

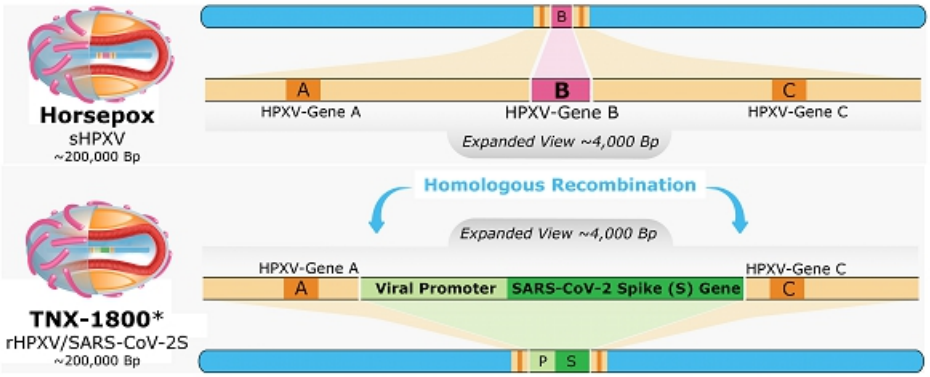
Horsepox can be engineered to express foreign genes

- 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

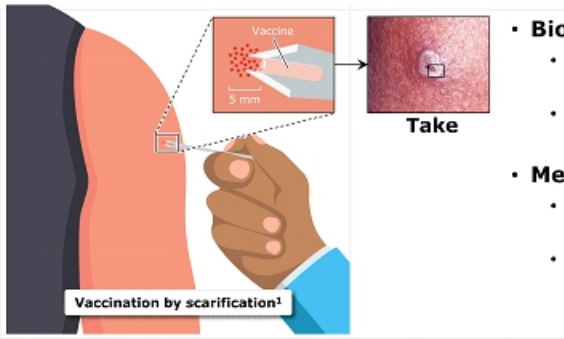
- Maintains strong immunogenicity with potentially improved tolerability
- Relative to non-replicating vaccinia, horsepox's replication in human cells provides direct antigen presentation, which is expected to trigger a T cell immune response, by Class I Major Histocompatibility Complex (MHC) Antigens
- 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



Take

- **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]

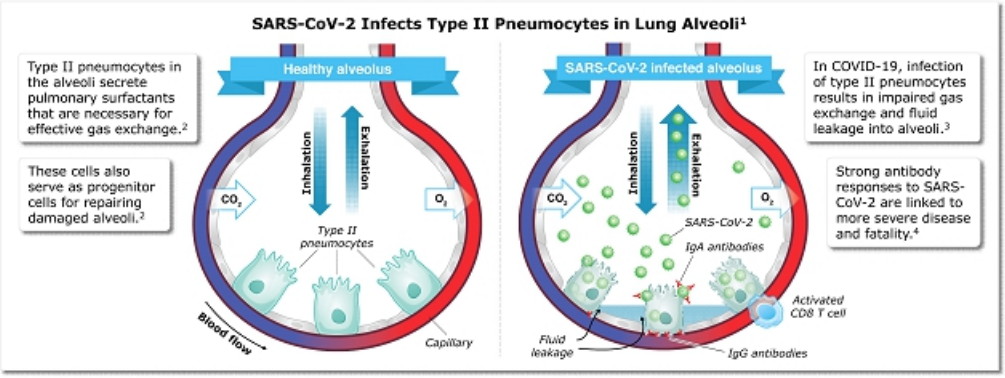
1.Fulginiti VA, et al. *Clin Infect Dis.* 2003;37(2):241-250.
2.Liu L, et al. *Nature Med.* 2010;16(2):224-228.
3.Centers for Disease Control and Prevention. Accessed April 15, 2020. https://phil.cdc.gov/Details.aspx?pid=3276

Unique Challenges of SARS-CoV-2

SARS		SARS-CoV-2
Rate of death[1,2] **~10%**	The death rate for COVID-19 is significantly lower compared to SARS.[1,2,4] However, due to its virulence, SARS-CoV-2 has resulted in far more deaths[5]	*Rate of death*[1,4] **0.003% - 5.4%**
Deaths[2] **744**		*Deaths (as of Nov. 2020)*[5] **>1,300,000**
Rate of infectivity[1] **0.4**	SARS-CoV-2 is more infectious, has a longer incubation time, and presents asymptomatically in more individuals, making it highly spreadable[1]	*Rate of infectivity*[1,4] **~2.5**
Incubation time[2] **2-7 days**		*Incubation time*[2,4] **6-14 days**
Asymptomatic[3] **~13%**		*Asymptomatic*[4] **~40%**

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. *J Travel Med.* 2020;27(2):taaa020.
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

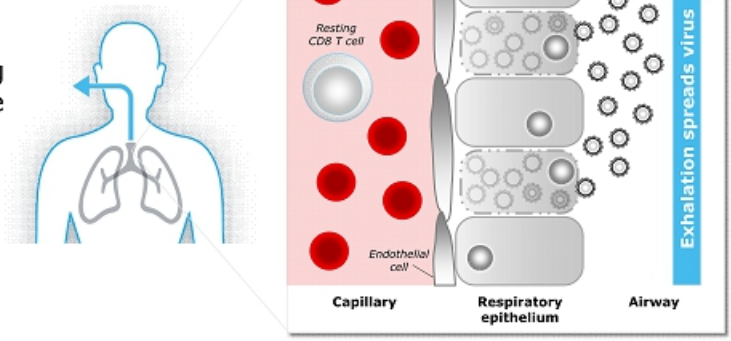
Infection of Type II Pneumocytes Can Lead to Lethal Respiratory Illness



1. Knudsen L, et al. *Histochem Cell Biol.* 2018;150(6):661-676.
2. Massa RE. *Am J Physiol Lung Cell Mol Physiol.* 2020;319(1):L119-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

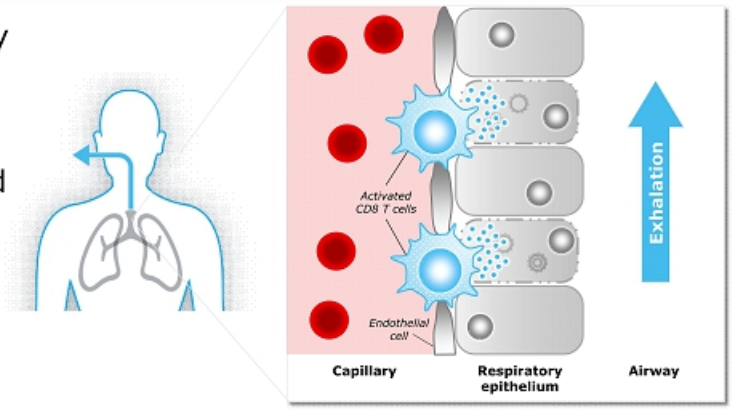
- Virus factories release virions by continuous budding
- Breathing, speaking or coughing has the potential to release virions into the air and transmit infection to others



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



Bar-On 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: Potential Development and Uses

- **Potential to protect against CoV-2 Variants**
  - T cell epitopes are short stretches of peptides (~8-14 aa fragments) that so far seem to be conserved between variants
  - Clinical trials will test potential protection against CoV-2 variants
    - For example, the "British" (B.1.1.7), "Brazilian" (P.1) and "South African" (B.1.351) strains have emerged
    - B.1.351 may elude the protection conferred by certain vaccines against other strains
- **Pre- and Post-pandemic vaccine**
  - Development will begin with clinical trials in adults
  - Subsequent development will focus on children
    - Analogous to the historical use of horsepox and vaccinia as childhood immunizations to prevent (and ultimately eradicate) smallpox
  - Potential to block forward transmission (contagion) by infected people
  - Trial participants will be stratified by pre-existing antibody and T cell immunity
    - TNX-2100[1] skin test (slide 56) may be used to stratify for T cell immunity

[1]TNX-2100 (SARS-CoV-2 epitope peptide mixtures for intradermal administration) is at the pre-IND stage of development

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-2100[1]: Diagnostic Product Candidate to Test for SARS-CoV-2 T Cell Immunity

[1]TNX-2100 is in the pre-investigational new drug (IND) stage of development and has not been approved for any indication.

TNX-2100[1]: Potential Skin Test to Measure SARS-CoV-2 Exposure and T Cell Immunity

TNX-2100 (SARS-CoV-2 epitope peptide mixtures for intradermal administration)

- Based on mixtures of synthetic peptides for intradermal administration
- Designed to elicit delayed-type hypersensitivity (DTH) in individuals who have been exposed to SARS-CoV-2 or who have been successfully vaccinated
- Potential to measure the presence and strength of functional *in vivo* T cell immunity

Potentially scalable test for widespread use

- Current tests[2] for T cell immunity to SARS-CoV-2 require specialized laboratories and are not amenable to standardization

[1]TNX-2100 is in the pre-IND stage of development and has not been approved for any indication.
[2]Intracellular cytokine staining (ICS) measured by flow cytometry after *in vitro* stimulation of purified peripheral blood mononuclear cells

TNX-2100: Potential Uses and Development Plans

TNX-2100 has the potential to serve as:

- a biomarker for cellular immunity and protective immunity
- a method to stratify participants in COVID-19 vaccine trials by immune status
- an endpoint in COVID-19 vaccine trials
- a biomarker of durability of vaccine protection

FDA feedback on pre-IND meeting questions received in February 2021

- Peptides have been manufactured under current good manufacturing process or cGMP

Development plans

- Second quarter 2021: Plan to submit IND
- Second half 2021: Plan to initiate clinical testing pending approval of IND

TNX-1300[1]: New Potential Treatment for Cocaine Intoxication

[1]TNX-1300 is an investigational new biologic and has not been approved for any indication.

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

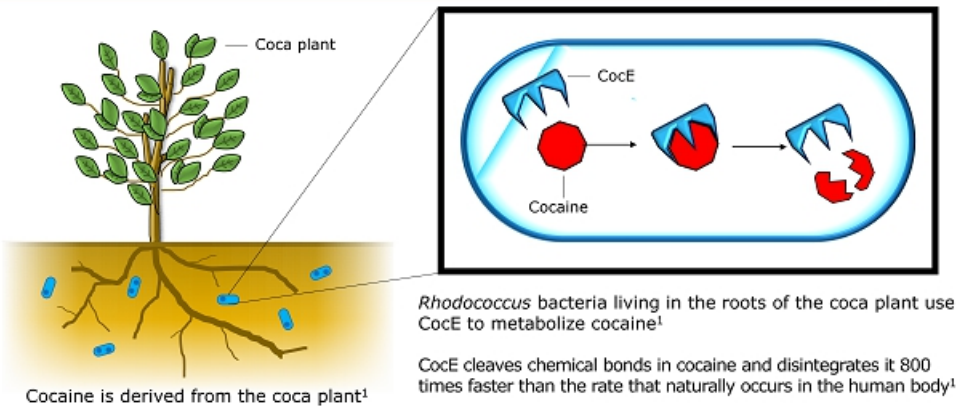
Phase 2 study completed by Reckitt Benckiser (TNX-1300 was formerly RBP-8000)[3]

- 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[1]: New Potential Treatment for Migraine and Craniofacial Pain

[1]TNX-1900 is at the pre-IND stage of development. A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900.

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

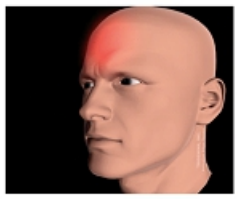
- In addition, daily dosing is more quickly reversible, in contrast to monthly or quarterly dosing, giving physicians and their patients greater control

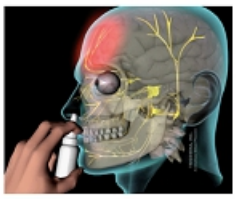
TNX-1900 for the Treatment of Migraine – Mechanism of Action (continued)

CGRP: NEUROTRANSMITTER THAT HAS BEEN VALIDATED AS KEY MIGRAINE TARGET

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

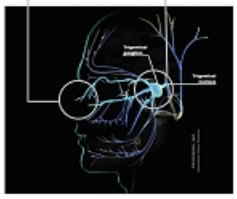
Proprietary Nasal to Brain Delivery



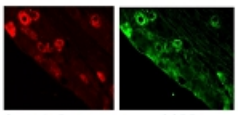


Permeates nasal mucosa

Transported to trigeminal system and brain

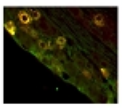


Oxytocin Receptors Co-Localize with CGRP in most Trigeminal Ganglia Neurons



Oxytocin Receptors CGRP

Overlay of Oxytocin Receptors and CGRP Staining



HEAD PAIN | PATIENT USES TNX-1900 | TARGETED DELIVERY

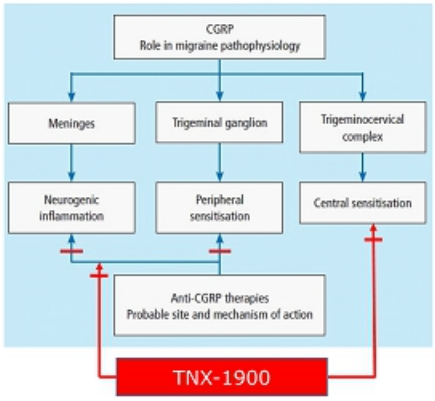
Abbrev. CGRP, calcitonin gene-related peptide

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 plans to submit an IND application for this program to the FDA in the second 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

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 Sleep Disturbance**
  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

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

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
- **TNX-2100 (DTH skin test) for detecting exposure and T cell immunity to SARS-CoV-2**
  Pre-IND

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

Milestones – Recently Completed and Upcoming[1]

☑ 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
❑ **1st Quarter 2021**	**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**
❑ **2nd Quarter 2021**	**Submission of IND application for TNX-1900 for the treatment of migraine**
❑ **2nd Quarter 2021**	**Submission of IND application for TNX-2100 for SARS-CoV-2 skin test**
❑ **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**
❑ **3rd 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**
❑ **2nd Half 2021**	**Initiation of Phase 1 safety study of TNX-1800 for COVID-19 expected**
❑ **2nd Half 2021**	**Initiation of clinical trials for TNX-2100 SARS-CoV-2 skin test expected**

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

Management Team

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Jessica Morris
Chief Operating Officer

TONIX PHARMACEUTICALS

Thank You!