

**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): June 1, 2023

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

**Nevada
(State or Other Jurisdiction
of Incorporation)**

**001-36019
(Commission
File Number)**

**26-1434750
(IRS Employer
Identification No.)**

26 Main Street, 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 Capital 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.
	<u>99.01</u>	Corporate Presentation by the Company for June 2023
	104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: June 1, 2023

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



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, the risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. 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, 2022, as filed with the Securities and Exchange Commission (the “SEC”) on March 13, 2023, 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.

Who We Are



OUR MISSION

Tonix Pharmaceuticals is committed to improving population health by **inventing and developing** innovative therapies and vaccines, through **broad in-house capabilities and creative collaborations**, to help address important unmet needs.



OUR VISION

Tonix strives to be a leader in providing **novel drug therapies and vaccines** to **improve population health around the world**.



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Investment Highlights



DIVERSE PIPELINE

Tonix's core focus is on **central nervous system** disorders, but we also target unmet needs across multiple therapeutic areas including **immunology, infectious disease** and **rare disease**.



IN-HOUSE CAPABILITIES

Investment in domestic, **in-house, R&D and manufacturing** to accelerate development timelines and improve the ability to respond to pandemics.



STRATEGIC PARTNERSHIPS

Partnering strategically with other **biotech companies, world-class academic and non-profit research organizations** to bring innovative therapeutics to market faster.



FINANCIAL POSITION

Tonix had approximately **\$72 M in cash and cash equivalents** as of 3/31/23. Tonix has no debt.



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Pipeline: Key Clinical Programs

Candidates*	Indication	Status/Next Milestone
TNX-102 SL ¹	Fibromyalgia (FM) Long COVID (PASC ²)	Mid-Phase 3 - >50% enrolled Phase 2 enrollment complete
TNX-1300 ³	Cocaine Intoxication - <i>FDA Breakthrough Designation</i>	Mid-Phase 2, Targeted 3Q 2023 Start
TNX-1900 ⁴	Prevention of Chronic Migraine	Phase 2 - enrolling ⁵
TNX-601 ER	Depression	Phase 2 - enrolling ⁶
TNX-2900 ⁷	Prader-Willi Syndrome - <i>FDA Orphan Drug Designation</i>	Phase 2 ready
TNX-1500 ⁸	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1, Targeted 3Q 2023 Start
TNX-801 ⁹	Smallpox and mpox vaccine	Phase 1, Targeted 1Q 2024 Start

*All of Tonix's product candidates are investigational new drugs or biologics and none has been approved for any indication.

¹TNX-102 SL (cyclobenzaprine HCl sublingual tablets) also has active INDs for Agitation in Alzheimer's Disease (AAD), Alcohol Use Disorder (AUD), and Posttraumatic Stress Disorder (PTSD). All indications are Phase 2 ready.

²Post-Acute Sequelae of COVID-19.

³TNX-1300 (double-mutant cocaine esterase) is licensed from Columbia University.

⁴Acquired from Trigemina; license agreement with Stanford University; Planned investigator-initiated Binge Eating Disorder (BED) study is expected start 2Q 2023.

⁵A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

⁶Phase 1 trial for formulation development was completed outside of the U.S.; Other potential indications include PTSD and neurocognitive dysfunction from steroids

⁷Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)

⁸anti-CD40L humanized monoclonal antibody – IND cleared

⁹Live attenuated vaccine based on horsepoxvirus

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**CNS:
KEY CANDIDATES**

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Five Late-Stage CNS Programs to be in the Clinic in 2023¹ Three studies Enrolling Now

Active Studies

- **In Phase 3:**
 - TNX-102 SL for fibromyalgia (>50% enrolled) Potential Pivotal Study
- **In Phase 2:**
 - TNX-102 SL for fibromyalgia-type Long COVID (enrollment complete)
 - TNX-1900 for migraine headache (new mechanism for US patients)
 - TNX-601 ER for major depressive disorder (new mechanism for US patients) Potential Pivotal Study

Entering Phase 2

- **In 3Q 2023:**
 - TNX-1300 for cocaine intoxication (FDA Breakthrough Therapy Designation) Potential Pivotal Study

¹Not approved for any indication

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TNX-102 SL* Cyclobenzaprine (Protectic®) Pipeline in a Product

A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

Potent binding and antagonist activities at the serotonergic-5-HT_{2A}, adrenergic- α ₁, histaminergic-H₁, and muscarinic-M₁ cholinergic receptors to facilitate restorative sleep

Innovative and proprietary PROTECTIC® Rapid drug exposure following nighttime administration

Differentiators:

Relative to Oral Cyclobenzaprine

- Lower daytime exposure
- Avoids first-pass metabolism
- Reduces risk of pharmacological interference from major metabolite

Relative to Standard of Care

- Potential for better tolerability while maintaining efficacy
- Not scheduled with no recognized abuse potential

Patents Issued

*TNX-102 SL has not been approved for any indication.

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Fibromyalgia

Status: Mid-Phase 3

- One positive Phase 3 study (RELIEF) completed
- Second Phase 3 study (RALLY) missed primary endpoint
- Confirmatory Phase 3 study (RESILIENT) is currently enrolling
 - >50% enrolled

Next Steps: Topline results expected 4Q 2023

Fibromyalgia-Type Long COVID

Status: Phase 2

- Phase 2 study (PREVAIL) has completed enrollment of 60 patients

Next Steps: Topline results expected 3Q 2023

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TNX-102 SL*: Fibromyalgia Cyclobenzaprine Protectic® Sublingual Tablets



CNS PORTFOLIO

PROFILE

Fibromyalgia (FM) is a chronic pain disorder resulting from amplified sensory and pain signaling within the CNS

- Affects an estimated 6-12 million adults in the U.S., approximately 90% of whom are women¹
- Symptoms include chronic widespread pain, nonrestorative sleep, fatigue, and cognitive dysfunction
- Patients struggle with daily activities, have impaired quality of life, and frequently are disabled
- Physicians and patients report common dissatisfaction with currently marketed products



When the check engine light malfunctions, the light is on even though the car is not malfunctioning

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia

Additional Indications: Long COVID, PTSD, Agitation in Alzheimer's, Alcohol Use Disorder

Status: One Positive Phase 3 study RELIEF completed²

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT is currently enrolling

Next Steps: Topline results expected 4Q 2023

*TNX-102 SL has not been approved for any indication.

¹American Chronic Pain Association (www.theacpa.org, 2019)

²Lederman et al., (2023) Arthritis Care & Research "Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results From the RELIEF Trial", in press

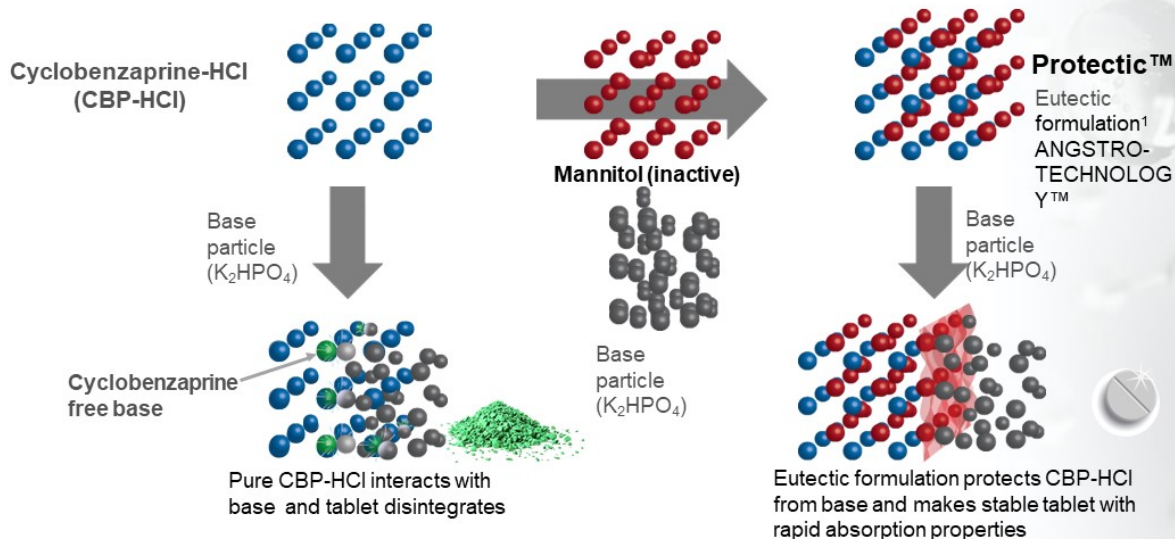
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TNX-102 SL (Sublingual Cyclobenzaprine HCl tablets*)

Proprietary cyclobenzaprine HCl eutectic mixture stabilizes sublingual tablet formulation



¹U.S. Patent issued May 2, 2017

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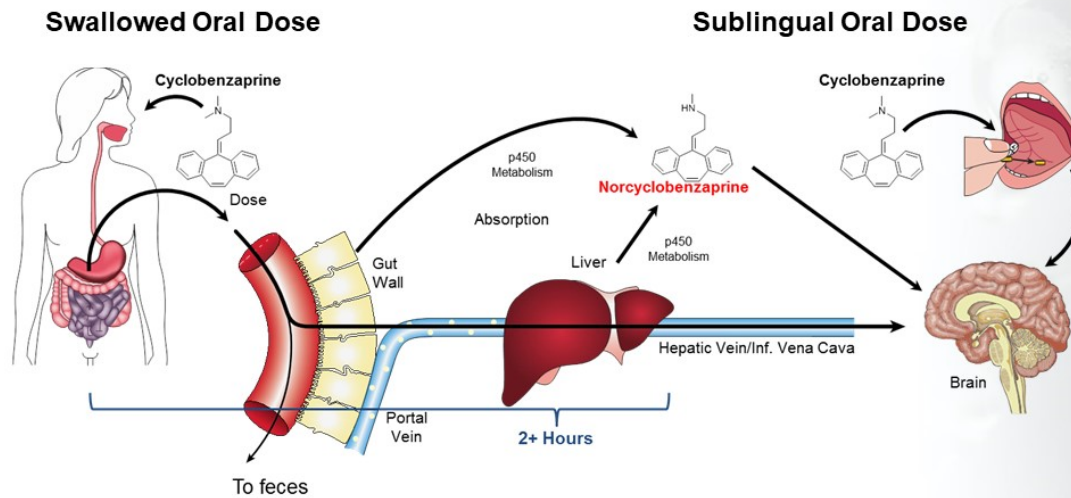
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TNX-102 SL Sublingual Administration*

Transmucosal absorption avoids first pass hepatic metabolism



U.S. Patent issued May 2, 2017

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TNX-102 SL: Phase 3 RESILIENT Study Design



General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia
- U.S. sites only, expected to enroll approximately 470 patients

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
 - Weekly averages of the daily numerical rating scale scores

Key Secondary Endpoints:

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

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

Placebo once-daily at bedtime

14 weeks

*Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

ClinicalTrials.gov Identifier: NCT05273749
A Phase 3 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With Fibromyalgia (RESILIENT)

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TNX-102 SL*: Fibromyalgia-Type Long COVID (PASC) Cyclobenzaprine Protectic® Sublingual Tablets

PROFILE

- Occurs in approximately 13% of recovered COVID-19 patients¹
- As many as 40% of Long COVID patients experience multi-site pain, a hallmark of fibromyalgia^{2,3}
- Symptoms of Long COVID, like multi-site pain, fatigue and insomnia, are the hallmarks of chronic pain syndromes like fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)
- In August 2022, the HHS released the National Research Action Plan on Long COVID⁴ which endorses the connection between Long COVID and chronic fatigue syndrome

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia-Type Long COVID (PASC)

Additional Indications: Fibromyalgia, PTSD, Agitation in Alzheimer's, Alcohol Use Disorder

Status: Phase 2 study PREVAIL has completed enrollment of 60 patients

Next Steps: Topline results expected 3Q 2023

Patents Issued

*TNX-102 SL has not been approved for any indication.

¹September 1, 2022- CDC - <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html>

²Harris, H, et al. Tonix data on file. 2022

³TnNetX Analytics

⁴Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID.

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Fibromyalgia-Type Long COVID

- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained symptoms¹⁻²



Symptoms (multi-site pain, fatigue, sleep disorders and cognitive dysfunction) overlap with the key symptoms of fibromyalgia

Nociplastic pain³: (new term for "Central and Peripheral Sensitization") Pain that arises from altered nociception despite no clear evidence of tissue damage, or for disease or lesion of the somatosensory system causing the pain

¹Bierle et al., 2021. *J Prim Care Community Health*. 12:21501327211030826

²Moghimi et al., 2021. *Curr Neurol Neurosci Rep*. 21(9):44

³Trouvin et al., 2019. *Best Pract Res Clin Rheumatol*. 33(3):101415

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TNX-102 SL: Phase 2 PREVAIL Study Design



CNS PORTFOLIO

Study characteristics:

- Randomized, double-blind, placebo-controlled study of TNX-102 SL in fibromyalgia-type Long COVID
- U.S. sites only, has enrolled approximately 60 patients

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
 - Weekly averages of the daily numerical rating scale scores

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

Placebo once-daily at bedtime

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

ClinicalTrials.gov Identifier: NCT05472090

A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL in Patients With Multi-Site Pain Associated With Post-Acute Sequelae of SARS-CoV-2 Infection (PREVAIL)

14 weeks

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TNX-601 ER*: Depression Tianeptine Hemioxalate Extended-Release Tablets (39.4 mg)



CNS PORTFOLIO

PROFILE

- A novel, oral, extended-release once-daily tablet
- Treatment effect of tianeptine sodium immediate release *t.i.d.* in depression is well-established
- Tianeptine restores neuroplasticity in animal models
- PPAR- β/δ and PPAR- γ agonist

Differentiators:

Relative to tianeptine IR available ex-US:

- Once daily dosing

Relative to traditional antidepressants:

- Unique mechanism of action – beyond neurotransmitter modulation
- Tianeptine sodium IR has similar efficacy but fewer side effects than traditional antidepressants

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder (MDD)

Additional Indications: PTSD, Neurocognitive Disorder From Corticosteroids, Alzheimer's Disease¹

Status: Phase 2 MDD study UPLIFT is currently enrolling

Next Steps: Interim analysis results on first 50% of sample expected 4Q 2023

Patents Issued

*TNX-601 ER has not been approved for any indication.

¹García-Alberca et al., 2022. J Alzheimers Dis. 88(2):707-720

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TNX-601 ER - Phase 2 UPLIFT* Study Design

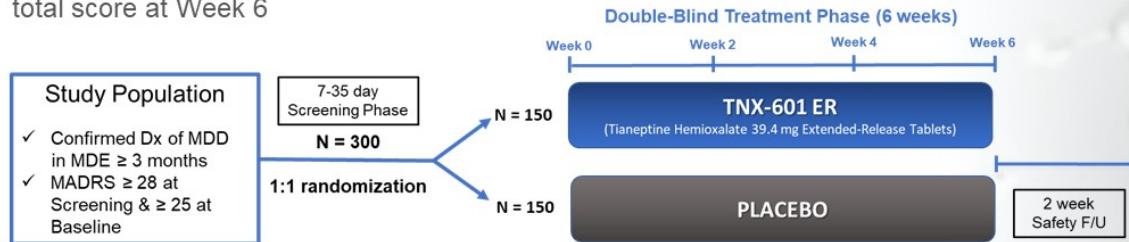
UPLIFT Study

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Major Depressive Disorder to evaluate monotherapy with TNX-601 ER versus placebo
- Parallel design with two arms – treatment with tianeptine hemioxalate 39.4 mg or placebo
- ~30 U.S. sites only, expected to enroll approximately 300 patients
- One unblinded interim analysis based on 50% of randomized participants expected 4Q'23

Primary Endpoint:

- Mean change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at Week 6



*ClinicalTrials.gov Identifier: NCT05686408

Abbreviations: Dx, diagnosis; ER, extended-release; F/U, follow-up; MDD, major depressive disorder; MDE, major depressive episode; N, number

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TNX-601 ER – Racemic Tianeptine – Composed of Two Isomers

Racemic tianeptine:

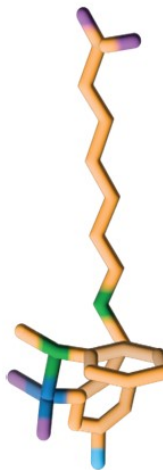
- Approved in Europe and ex-US
- 1:1 mixture of 2 mirror-image isomers^{1,2}
- Weak μ -opioid receptor agonism²
 - Risk of abuse or diversion for euphoric effects³

(S)-Tianeptine: PPAR- β/δ agonist, no opiate liability

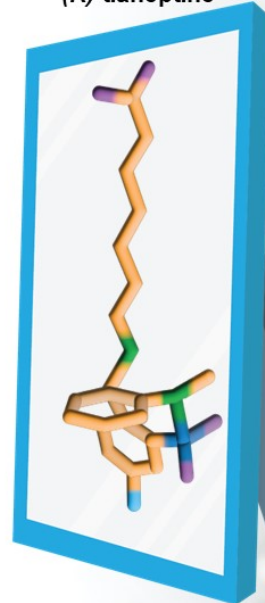
- Both (S)- and (R)-tianeptine are agonists of PPAR- γ
- New mechanism of action for treating depression

	Racemic-Tianeptine	(S)-Tianeptine TNX-4300	(R)-Tianeptine
μ -Opioid Receptor	+	-	+
PPAR- β/δ	+	+	-
PPAR- γ	+	+	+

(S)-tianeptine



(R)-tianeptine



1. Stablon. Summary of product characteristics. Les Laboratoires Servier Industrie; 2014. 2. PubChem. Accessed November 10, 2022. <https://pubchem.ncbi.nlm.nih.gov/compound/Tianeptine> 3. Drug Enforcement Administration. May 2019. Accessed November 11, 2022. https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf

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TNX-4300*: Depression, Alzheimer's & Parkinson's diseases

Estianeptine (Single (S)-isomer of Tianeptine)



PROFILE

- Single isomer, oral treatment
- Proposed mechanism of action from lab studies indicates estianeptine is the active ingredient of TNX-601 ER
 - PPAR- β/δ and PPAR- γ agonist
 - Free of μ -opioid receptor activity
- Estianeptine restores neuroplasticity in tissue culture

Differentiators:

Relative to racemic tianeptine IR or TNX-601 ER:

- Lack of opioid liability

Relative to traditional antidepressants:

- Unique mechanism of action – beyond neurotransmitter modulation
- Racemic tianeptine sodium IR has similar efficacy but fewer side effects than traditional antidepressants

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder (MDD)

Additional Indications: PTSD, Neurocognitive Disorder From Corticosteroids, Alzheimer's Disease¹

Status: Pre-clinical

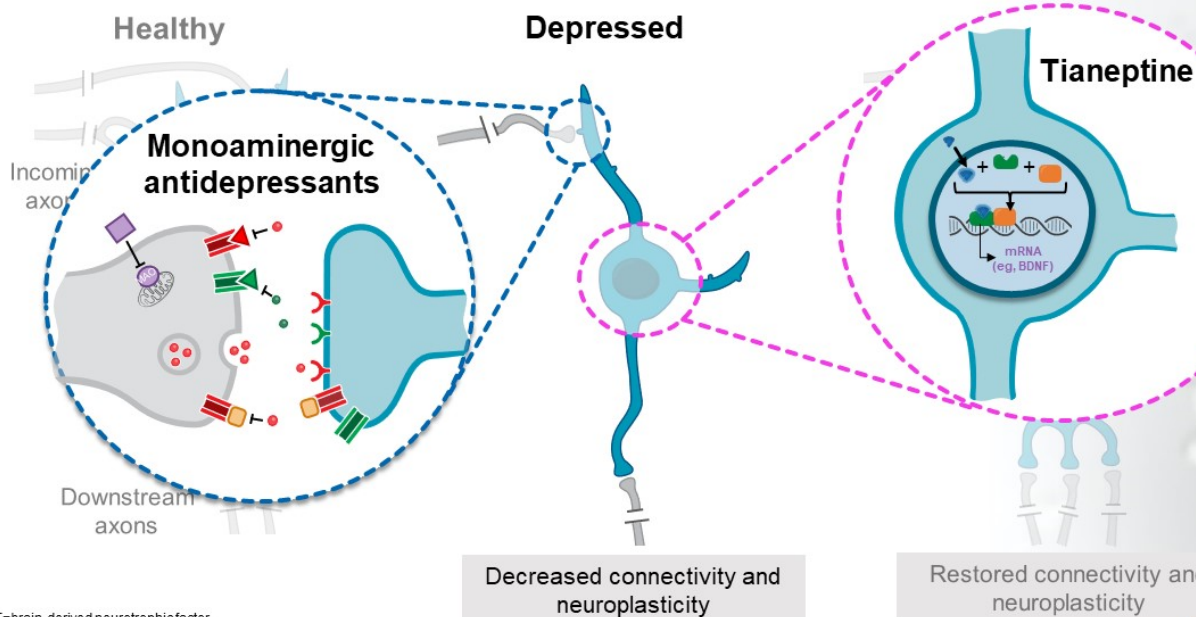
Next Steps: Expect IND can be supported by pre-clinical and clinical data from TNX-601 (racemic tianeptine) development

Patents Issued

*TNX-4300 has not been approved for any indication.

¹García-Alberca et al., 2022. J Alzheimers Dis. 88(2):707-720

While Monoaminergic Antidepressants Work at the Synapse, (S)-Tianeptine "Cuts in Line" to More Directly Affect Neuroplasticity



BDNF=brain-derived neurotrophic factor.

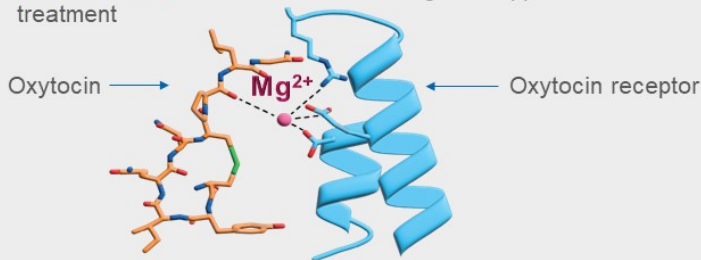


TNX-1900*: Migraine Intranasal Potentiated Oxytocin (OT) with Magnesium

PROFILE

- Intranasal OT has potential utility in treating migraine¹
- Magnesium is known to potentiate the binding of OT to its receptor^{2,3}
- One billion individuals worldwide suffer from migraines

Differentiator: Novel non-CGRP antagonist approach to treatment



Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Chronic Migraine

Additional Indications: Acute Migraine, Craniofacial Pain, Insulin Resistance, Binge Eating Disorder

Status: Phase 2 study PREVENTION is currently enrolling⁴

Next Steps: Topline results expected 4Q 2023

Investigator initiated Phase 2 trial in obesity-associated binge eating disorder 2Q 2023

*TNX-1900 has not been approved for any indication. CGRP = calcitonin gene-related peptide.

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¹Tzabazis et al., 2017, *Headache*, 57 Suppl 2:64-75

²Antoni et al., 1989, *Biochem J*, 257(2):611-4

³Meyerowitz et al., 2022, *Nat Struct Mol Biol*, (3):274-281

⁴A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900



TNX-1900: Phase 2 PREVENTION Study Design



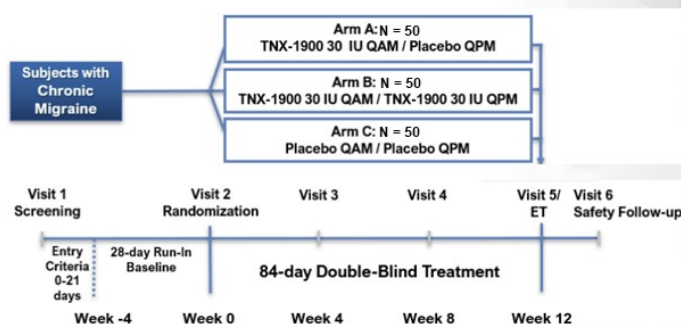
PREVENTION Study

General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms— two treatment regimens and one placebo) in chronic migraine
- U.S. sites only, expected to enroll approximately 150 patients
- Topline results expected 4Q'23

Primary Endpoint:

- Mean change in the number of migraine headache days between the 28-day Run-In phase and the last 28-days of the Treatment phase (TNX-1900 vs. placebo)



ClinicalTrials.gov Identifier: NCT05679908

A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)

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TNX-1300*: Cocaine Intoxication Cocaine Esterase (CocE)

PROFILE

Cocaine is the main cause for drug-related ED visits¹

CocE is a recombinant protein that degrades cocaine in the bloodstream

- Rapidly reverses physiologic effects of cocaine
- Drops plasma exposure by 90% in 2 minutes

Differentiators: Rapidly metabolizes cocaine in the bloodstream; no other product currently on the market for this indication



Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Cocaine Intoxication

Status: Mid-Phase 2

Next Steps: Initiate new Phase 2 trial 3Q 2023

- Single-blind, placebo (+ usual care) controlled, randomized, potentially pivotal study
- Expected to enroll approximately 60 emergency department patients at sites in the US

FDA Breakthrough Therapy Designation

Awarded Cooperative Agreement Grant from National Institute on Drug Abuse (NIDA)

¹Havakuk et al., 2017. J Am Coll Cardiol. 70:101-113

ED = emergency department.

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**RARE DISEASE:
KEY CANDIDATES**

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TNX-2900*: Hyperphagia in Prader-Willi Syndrome Intranasal Potentiated Oxytocin (OT) with Magnesium

PROFILE

Prader-Willi Syndrome is the most common genetic cause of life-threatening childhood obesity

- Rare disease occurring in 1 in 10,000 to 1 in 30,000 births

Differentiator: No approved therapeutic currently on the market for hyperphagia in PWS

Dangers of PWS Hyperphagia:



DEVELOPMENT PROGRAM

Market Entry: Hyperphagia in Prader-Willi Syndrome

Additional Indications: Rare Hyperphagia Conditions

Status: Phase 2 ready

Next Steps: IND submission

FDA Orphan Drug Designation

Patents Issued

*TNX-2900 is in the pre-IND stage of development and has not been approved for any indication.

¹Miller et al., 2011. *Am J Med Genet A*. 155A(5):1040-1049

²Butler et al., 2017. *Genet Med*. 19(6):635-642

³Butler MG. NORD. Updated 2018. Accessed May 25, 2022. <https://rarediseases.org/rare-diseases/prader-will-syndrome/>

⁴Prader-Willi Syndrome Association USA. Accessed May 25, 2022. <https://www.pwsausa.org/what-is-prader-will-syndrome/>

⁵Muscogiuri et al., 2021. *J Endocrinol Invest*. 44(10):2057-2070

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IMMUNOLOGY: KEY CANDIDATES

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TNX-1500*

Next Generation α -CD40 Ligand (CD40L) Antibody

The CD40-CD40L pathway is a pivotal immune system modulator and a well-established and promising treatment target

Differentiators: Expected to deliver efficacy without compromising safety

First Generation: Development halted due to thromboembolic (TE) complications—blood clots—traced to Fc gamma receptor (Fc γ R)

Second Generation: Eliminated the Fc γ R TE complication but potency and half life was reduced, limiting utility

Third Generation (TNX-1500): Re-engineered to better modulate the binding of Fc γ R.



*TNX-1500 has not been approved for any indication. Patents filed.

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Prevention of Allograft Rejection

Status: Phase 1 ready – IND cleared

- Collaborations ongoing with Mass General Hospital on heart and kidney transplantation in non-human primates

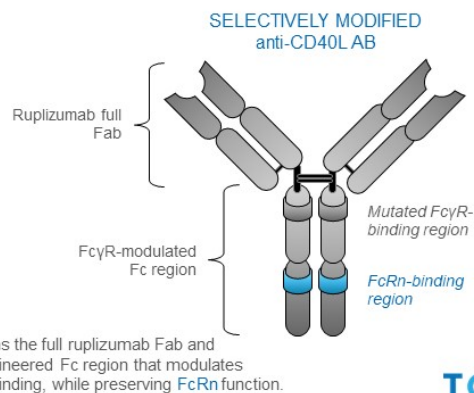
Next Steps: Initiate Phase 1 study 3Q 2023

Autoimmune Diseases

Status: Potential future indications include:

Sjögren's Syndrome, Systemic Lupus Erythematosus

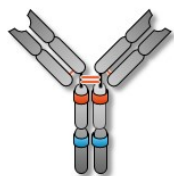
- These indications require large studies, but represent large target markets



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Third-Generation α -CD40L Engineered to Decrease Risk of Thrombosis

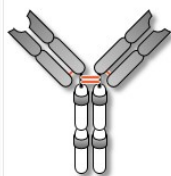
First-generation anti-CD40L mAbs



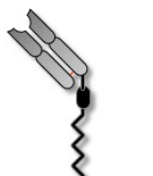
Ruplizumab

Constant fragment (Fc) domain interacted with Fc γ RIIA (CD32A), which suggested a mechanism for the increased risk of thrombosis.^{1,2}

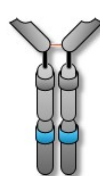
Second-generation anti-CD40L proteins



Aglycosyl Ruplizumab



Dapirolizumab



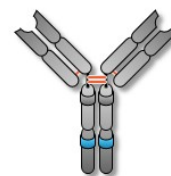
Letolizumab



Dazodalibep

Second-generation anti-CD40L proteins exhibited dramatically reduced binding to Fc γ RIIA³⁻⁶ but had other issues, including decreased efficacy, shortened half-life, or engendering of anti-drug antibodies (ADAs).⁷⁻⁹

Third-generation anti-CD40L mAbs*



TNX-1500

TNX-1500 is engineered to target CD40L therapeutically while reducing Fc γ RIIA binding and thereby lowering the potential for thrombosis.¹⁻⁹

*Sanofi's frexalimab (formerly SAR441344) and Eledon's tegoprubart (formerly AT-1501) also are Fc modified

¹Inwald et al., 2003. *Circ Res*. 92(9):1041-1048

²Robles-Carrillo et al., 2010. *J Immunol*. 185(3):1577-1583

³Shock et al., 2015. *Arthritis Res Ther*. 17(1):234

⁴Xie et al., 2014. *J Immunol*. 192(9):4083-4092

⁵Ferranti et al., 2004. *Int Immunol*. 16(11):1583-1594

⁶Karnell et al., 2019. *Sci Transl Med*. 11(489):eaar6584

⁷ClinicalTrials.gov identifier: NCT02273960. Updated July 16, 2019. Accessed June 1, 2021. <https://clinicaltrials.gov/ct2/show/results/NCT02273960?view=results>

⁸Waters, 2018. *BioCentury*.

⁹Company data

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Other anti-CD40L Monoclonal Antibodies in Development

UCB (Co-developed with Biogen) – Systemic Lupus Erythematosus (SLE)

- Phase 3 Trial Currently Enrolling (NCT04294667)
 - Topline results expected 1H 2024¹
- Dapirolizumab pegol (pegylated Fab)

Horizon (being acquired by Amgen) – Sjögren's Syndrome (SjS)

- Two Positive Phase 2 studies reported^{2,3}
- Dazodalibep (tn03 fusion protein)

Sanofi – Sjögren's Syndrome (SjS), Multiple Sclerosis (MS), Systemic Lupus Erythematosus (SLE)

- Phase 2 Trial Currently Enrolling in SjS (NCT04572841) and SLE (NCT05039840)
- Active Phase 2 Trial in Relapsing MS (NCT04879628)
- SAR441344 (Fc-modified)

Eledon – Amyotrophic Lateral Sclerosis (ALS) and Kidney Transplant

- Phase 2 Trial Completed in ALS (NCT04322149)
- Phase 1/2 Trial Currently Enrolling in Kidney Transplant (NCT05027906)
- Tegoprubart, f.k.a. AT-1501 (Fc-modified)

Lundbeck and AprilBio – Neurology

- Phase 1 Trial Currently Enrolling in Healthy Adults (NCT05136053)
- APB-A1 or Lu AG22515 (HAS fusion protein)

¹<https://www.ucb.com/our-science/pipeline>

²<https://ir.horizontherapeutics.com/news-releases/news-release-details/horizon-therapeutics-plc-announces-phase-2-trial-evaluating>

³<https://ir.horizontherapeutics.com/news-releases/news-release-details/horizon-therapeutics-plc-announces-phase-2-trial-evaluating-0>

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TNX-801*

Recombinant Pox Vaccine (RPV) Platform Using Live Virus Technology

Differentiators:

- **Live virus vaccines are the most established vaccine technology**
 - Starting with Edward Jenner's smallpox vaccine, the first vaccine, which eradicated smallpox
 - Prevents forward transmission
 - Effective in eliciting durable or long-term immunity
- **Economical to manufacture at scale**
 - Low dose because replication amplifies dose in vivo
 - Single shot administration
- **Standard refrigeration required for shipping and storage**

*TNX-801 is in the pre-IND stage of development and has not been approved for any indication. Patents filed.

¹Noyce et al., 2018. *PLoS One*. 13(1): e0188453.



Mpox and Smallpox Vaccine

Status: Preclinical

- TNX-801 is a cloned version of horsepox¹ (without any insert) purified from cell culture

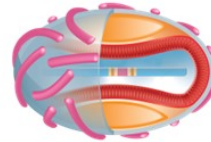
Next Steps: Initiate Phase 1 Trial 1Q 2024

Vaccine for Future Emerging Infectious Diseases

Example: TNX-1850 for COVID-19

Status: Model System

TNX-801*
scHPXV (Horsepox)
212,811 bp



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Live Virus Vaccine Platform: Recombinant Pox Vaccine (RPV) Technology for Emerging Infectious Diseases and Oncolytics

Vaccinia

Horsepox

**ANTIGEN
CODING**

Mpox and Smallpox

COVID-19

Future Pandemics & New
Infectious Diseases

Biodefense

Oncology

RPV VECTOR BELIEVED SIMILAR TO EDWARD JENNER'S VACCINE¹⁻³

*Using Proven Science To Address Challenging Disease States, We Have Created A
Programmable Technology Platform Aimed At Combating Future Threats To Public Health*

¹Shrick, 2017. *N Engl J Med* 377:1491-1492

²Esparza, 2020. *Vaccine*. 38(30): 4773-4779

³Brinkmann, 2020. *Genome Biol*. 21: 286

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INFECTIOUS DISEASE PORTFOLIO



Internal Development & Manufacturing Capabilities

R&D Center (RDC) – Frederick, MD

- **Functions:**
 - Accelerated development of vaccines and antiviral drugs against COVID-19, its variants and other infectious diseases
 - Research advancing CNS and immunology drugs
- **Description:** ~48,000 square feet, BSL-2 with some areas designated BSL-3
- **Status:** Operational



Advanced Development Center (ADC) – North Dartmouth, MA

- **Function:** Development and clinical scale manufacturing of biologics
- **Description:** ~45,000 square feet, BSL-2
- **Status:** Operational



Architectural Rendering

Commercial Manufacturing Center (CMC) – Hamilton, MT

- **Function:** Phase 3 and Commercial scale manufacturing of biologics
- **Description:** ~44-acre green field site, planned BSL-2
- **Status:** Planning for site enabling work in 2023

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**PRECLINICAL
PIPELINE**

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Pipeline: Key Pre-Clinical Programs

Candidates*	Indication	Status/Next Milestone
TNX-1610 ¹	Attention Deficit Hyperactivity Disorder (ADHD)	Preclinical
TNX-1700 ²	Gastric and colorectal cancers	Preclinical
TNX-1850 ³	COVID-19 (horsepox-based live virus vaccine platform)	Preclinical
TNX-2300 ⁴	COVID-19 (bovine parainfluenza virus-based live virus vaccine)	Preclinical
TNX-3700 ⁵	COVID-19 (zinc nanoparticle mRNA technology)	Preclinical
TNX-3900	Filoviruses (broad spectrum antiviral)	Preclinical
TNX-4000	Filoviruses (broad spectrum antiviral)	Preclinical
TNX-4300	Depression (estianeptine)	Preclinical

¹Acquired from TRImaran Pharma; license agreement with Wayne State University

²Recombinant trefoil factor 2 (rTFF2) based protein; licensed from Columbia University

³Live attenuated vaccine based on horsepox virus vector, expressed SARS-CoV-2 spike protein. TNX-1850 is based on the BA.2 variant spike protein.

⁴Live attenuated vaccine based on bovine parainfluenza (BPI) virus

⁵COVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation with CD40L molecular trigger

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TNX-1700*: Gastric and Colorectal Cancers Recombinant Trefoil Factor 2 (rTFF2-HSA) Fusion Protein

Potential New Cancer Treatment

- TNX-1700 (rTFF2-HSA) has effects on cancer by altering the tumor micro-environment
- Mechanism of action: suppresses myeloid-derived suppressor cells and activates anti-cancer CD8+ T cells
- Potential synergy with anti-PD1 or anti-PD-L1 monoclonal antibodies (mAbs)

Preclinical Evidence for Inhibiting Growth of Cancer Cells

- In an MC38 mouse model of colorectal cancer, mTNX-1700 (murine TNX-1700) alone inhibited tumor growth by 50%, and combination therapy with anti-PD1 inhibited tumor growth by 87%¹
- In an advanced mouse model of gastric cancer, mTNX-1700 combination therapy with anti-PD1 inhibited tumor growth by 78%²
- Mechanistically, the combination therapy reduced intratumoral MDSCs, profoundly increased tumor-infiltrating CD8+ T cells, and significantly reduced spontaneous metastasis²

Market Entry: Immuno-oncology, combination therapy with PD1 blockers for gastric and colorectal cancer

Status: Preclinical

Next Steps: Animal studies ongoing

Differentiator: No product yet identified consistently augments PD1 effects on cold tumors

Licensed from Columbia University

- Developing in partnership under sponsored research agreement

Patents Filed

*TNX-1700 is in the pre-IND stage of development and has not been approved for any indication.

¹Daugherty, 2023. AACR Annual Meeting. <https://www.tonixpharma.com/wp-content/uploads/2023/04/MDSC-Targeted-mTFF2-MSA-mTNX-1700-Suppresses-Tumor-Growth-and-Increases-Survival-in-Anti-PD-1-Treated-MC38-and-CT26-wt-Murine-Colorectal-Cancer-Models.pdf>

²Qian, 2023. AACR Annual Meeting. <https://www.tonixpharma.com/wp-content/uploads/2023/04/MDSC-targeted-TFF2-MSA-synergizes-with-PD-1-blockade-therapy-in-advanced-gastric-cancer-models.pdf>

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IMMUNOLOGY PORTFOLIO



Preclinical Infectious Disease Therapeutics in Development

TNX-2300*: Live Virus Vaccine Based on Bovine Parainfluenza (BPI) Virus

Market Entry: COVID-19 Vaccine

Status: Preclinical

Next Steps: Animal studies with Kansas State University (KSU) to test the effect of co-expression of CD40-ligand to stimulate T cell immunity

TNX-3700*: Zinc Nanoparticle (ZNP) Formulation for mRNA Vaccines

Market Entry: Booster for COVID-19 Vaccines

Status: Preclinical

Next Steps: Research at KSU on CoV-2 spike based vaccine in tissue culture and animals; initiate animal studies in 1H 2023

TNX-3900*: Host-Directed Broad-Spectrum Antiviral

Market Entry: Coronaviruses and Filoviruses

Status: Preclinical

Next Steps: Further in-house development

TNX-4000*: Direct-Acting Broad-Spectrum Antiviral

Market Entry: Coronaviruses, Retroviruses, and Filoviruses

Status: Preclinical

Next Steps: Further in-house development

*TNX-2300, TNX-3700, TNX-3900 and TNX-4000 are in the pre-IND stage of development and have not been approved for any indication.

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TONIX TEAM, NETWORK AND FUTURE OUTLOOK

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Key Development Partners



TNX-1500: ALLOGRAFT REJECTION

TNX-1300: COCAINE INTOXICATION
TNX-1700: GASTRIC AND COLORECTAL CANCERS



TNX-1900: MIGRAINE & OTHER INDICATIONS

TNX-801: SMALLPOX AND MONKEYPOX VACCINE
TNX-1850: COVID-19 VACCINE



TNX-2900: PRADER-WILLI SYNDROME

TNX-3700: COVID-19 VACCINE (ZINC NANOPARTICLE mRNA TECHNOLOGY)
TNX-2300: BOVINE PARAINFLUENZA VIRUS



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Management Team



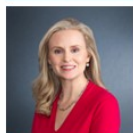
Seth Lederman, MD
Co-Founder, CEO & Chairman



Gregory Sullivan, MD
Chief Medical Officer



Bradley Saenger, CPA
Chief Financial Officer



Jessica Morris
Chief Operating Officer



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Milestones: Recently Completed and Upcoming

- ✓ 2nd Quarter 2022 Phase 3 RESILIENT study start of TNX-102 SL for the management of fibromyalgia
- ✓ 3rd Quarter 2022 Phase 2 PREVAIL study start of TNX-102 SL for the treatment of fibromyalgia-type Long COVID
- ✓ 1st Quarter 2023 Phase 2 PREVENTION study start of TNX-1900 for the treatment of migraine
- ✓ 1st Quarter 2023 Phase 2 UPLIFT study start of TNX-601 ER for major depressive disorder

Expected Data

- 3rd Quarter 2023 Topline results of Phase 2 PREVAIL study of TNX-102 SL for fibromyalgia-type Long COVID
- 4th Quarter 2023 Topline results of Phase 2 PREVENTION study of TNX-1900 for chronic migraine
- 4th Quarter 2023 Interim Analysis results of Phase 2 UPLIFT study of TNX-601 ER for major depressive disorder
- 4th Quarter 2023 Topline results of Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia

Expected Clinical Trial Initiations

- 3rd Quarter 2023 Phase 1 study start of TNX-1500 for prevention of allograft rejection
- 3rd Quarter 2023 Phase 2 study start of TNX-1300 for the treatment of cocaine intoxication
- 1st Quarter 2024 Phase 1 study start of TNX-801 for prevention of mpox and smallpox

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THANK YOU

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