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): April 13, 2023

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, 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.

On April 13, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that it is eliminating the interim analyses in the Phase 3 RESILIENT study of its TNX-102 SL (sublingual cyclobenzaprine tablets) product candidate for fibromyalgia, and the Phase 2 PREVENTION study of its TNX-1900 (intranasal potentiated oxytocin) product candidate for chronic migraine. A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference.

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 99.02 hereto and incorporated herein by reference.

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

Item 8.01. Other Events.

On April 13, 2023, the Company announced that it is eliminating the interim analyses in the registration-enabling, confirmatory Phase 3 RESILIENT study of its TNX-102 SL product candidate for fibromyalgia, and the Phase 2 PREVENTION study of its TNX-1900 product candidate for chronic migraine in order to streamline the trials and to provide topline data for both programs in the fourth quarter of 2023. Target enrollment for the PREVENTION study will be reduced from approximately 300 participants to approximately 150 participants to accommodate the new timing.

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials,

clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press Release of the Company, April 13, 2023
99.02	Corporate Presentation by the Company for April 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: April 13, 2023

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

Exhibit 99.01

Tonix Pharmaceuticals Expedites Fibromyalgia and Chronic Migraine Programs

Streamlining Phase 3 Fibromyalgia and Phase 2 Chronic Migraine Trials by Eliminating Interim Analyses

Topline Results Expected for Both Programs in Fourth Quarter 2023

CHATHAM, N.J., April 13, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, today announced that it is eliminating the interim analyses in its registration-enabling, confirmatory Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia and its Phase 2 PREVENTION study of TNX-1900 for chronic migraine. The modifications to the RESILIENT and PREVENTION studies are designed to streamline the trials and to provide topline data for both programs in 2023. Target enrollment for the core TNX-102 SL fibromyalgia study remains approximately 470 participants while target enrollment for the TNX-1900 chronic migraine study will be reduced from approximately 300 participants to approximately 150 participants, to accommodate the new topline timing.

"In an effort to expedite and deliver on clinical timelines, we are modifying the designs of our confirmatory, registration-enabling Phase 3 trial in fibromyalgia and our Phase 2 trial in chronic migraine," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "By eliminating the interim analyses, we remove the statistical penalties associated with this type of analysis, conserve resources, and can plan on topline results for each of these studies in the fourth quarter of 2023. Fibromyalgia and migraine each affect millions of people, and we remain committed to aligning our operational and scientific efforts on these core CNS programs. We are excited to progress these programs closer to FDA approval, upon achieving positive topline data."

Key Anticipated 2023 Milestones

Updated Guidance

- Eliminating interim analysis of Phase 3 RESILIENT study of TNX-102 SL (sublingual cyclobenzaprine tablets) for fibromyalgia.
- Eliminating interim analysis of Phase 2 PREVENTION study of TNX-1900 (intranasal potentiated oxytocin) for chronic migraine; topline results now expected in the fourth quarter of 2023.

Unchanged Guidance

- Topline results of Phase 3 RESILIENT study of TNX-102 SL (sublingual cyclobenzaprine tablets) for fibromyalgia in the fourth quarter of 2023.
- Topline results of Phase 2 PREVAIL study of TNX-102 SL for fibromyalgia-type Long COVID in the third quarter of 2023.
- Interim analysis results of Phase 2 UPLIFT study of TNX-601 ER (tianeptine hemioxalate extended-release tablets) for major depressive disorder in the fourth quarter of 2023.

- Initiate enrollment in a potentially pivotal Phase 2 study of TNX-1300 (recombinant double-mutant cocaine esterase for injection) for the treatment of cocaine intoxication in the second quarter of 2023.
- Initiate enrollment in a Phase 1 study of TNX-1500 (anti-CD40L monoclonal antibody) for the prophylaxis of rejection in kidney transplantation in the second quarter of 2023.
- Initiate enrollment in a Phase 1 study of TNX-801 (live virus vaccine for percutaneous administration), a potential vaccine to protect against smallpox and mpox (formerly known as monkeypox), in the second half of 2023.
- Continue development of TNX-2900 (intranasal potentiated oxytocin), a small peptide for the treatment of hyperphagia in Prader-Willi syndrome (PWS), for which the FDA has granted Orphan Drug designation.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 study has been completed, and topline results are expected in the third quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), in development for chronic migraine, is currently enrolling with topline data expected in the fourth quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets), a once-daily formulation being developed as a treatment for major depressive disorder (MDD), is also currently enrolling with interim data expected in the fourth quarter of 2023. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the second quarter of 2023. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox, for which a Phase 1 study is expected to be initiated in the second half of 2023. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease portfolio also includes TNX-3900 and TNX-4000, classes of broad-spectrum small molecule oral antivirals.

*All of Tonix's product candidates are investigational new drugs (IND) or biologics and have not been approved for any indication. TNX-801, TNX-1500, TNX-2900, TNX-3900 and TNX-4000 are in pre-IND stage of development and have not been approved for any indication.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate,” “expect,” and “intend,” among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the 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. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the Securities and Exchange Commission (the “SEC”) on March 13, 2023, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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Exhibit 99.02

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.

TONIX PHARMACEUTICALS

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.**

TONIX PHARMACEUTICALS

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 **$120 M in cash and cash equivalents** as of 12/31/22. Tonix has no debt.

TONIX PHARMACEUTICALS

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 - *FDA Breakthrough Designation*	Mid-Phase 2, Targeted 2Q 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 - *FDA Orphan Drug Designation*	Phase 2 ready
TNX-1500[8]	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1, Targeted 2Q 2023 Start
TNX-801[9]	Smallpox and mpox vaccine	Phase 1, Targeted 2H 2023 Start

*All of Tonix's product candidates are investigational new drugs or biologics and none has been approved for any indication.
[1]TNX-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.
[2]Post-Acute Sequelae of COVID-19.
[3]TNX-1300 (double-mutant cocaine esterase) is licensed from Columbia University.
[4]Acquired from Trigemina; license agreement with Stanford University; Planned investigator-initiated Binge Eating Disorder (BED) study is expected start 2Q 2023.
[5]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900
[6]Phase 1 trial for formulation development was completed outside of the U.S.; Other potential indications include PTSD and neurocognitive dysfunction from steroids
[7]Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)
[8]anti-CD40L humanized monoclonal antibody
[9]Live attenuated vaccine based on horsepox virus

TONIX PHARMACEUTICALS

Five Late-Stage CNS Programs to be in the Clinic by 1H 2023[1]

Three studies Enrolling Now

CNS PORTFOLIO

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 2Q 2023:**
  - TNX-1300 for cocaine intoxication (FDA Breakthrough Therapy Designation) — Potential Pivotal Study

[1]Not approved for any indication

TONIX PHARMACEUTICALS

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-HT2A, adrenergic-α1, 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

Patents Issued

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

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

TONIX PHARMACEUTICALS

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

- Afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women[1]
- 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 completed

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.

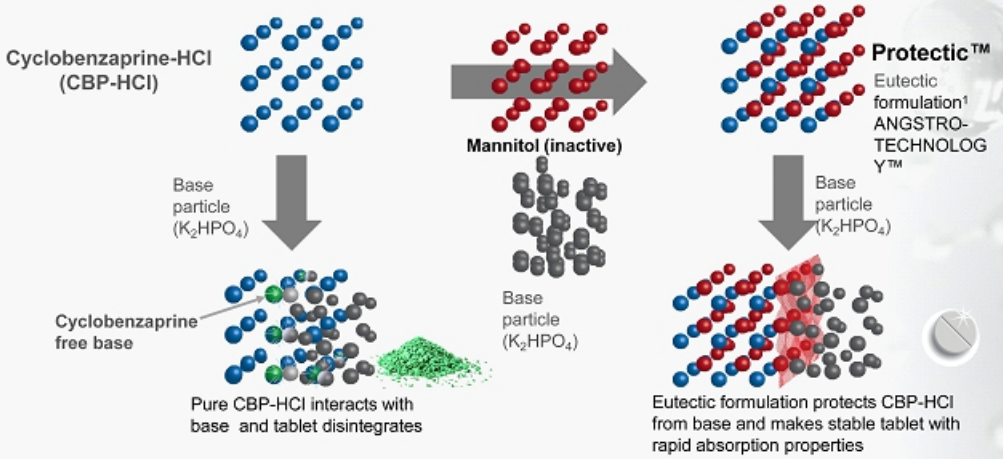
[1]American Chronic Pain Association (www.theacpa.org, 2019)

TONIX PHARMACEUTICALS

TNX-102 SL (Sublingual Cyclobenzaprine HCl tablets)

CNS PORTFOLIO

Proprietary cyclobenzaprine HCl eutectic mixture stabilizes sublingual tablet formulation

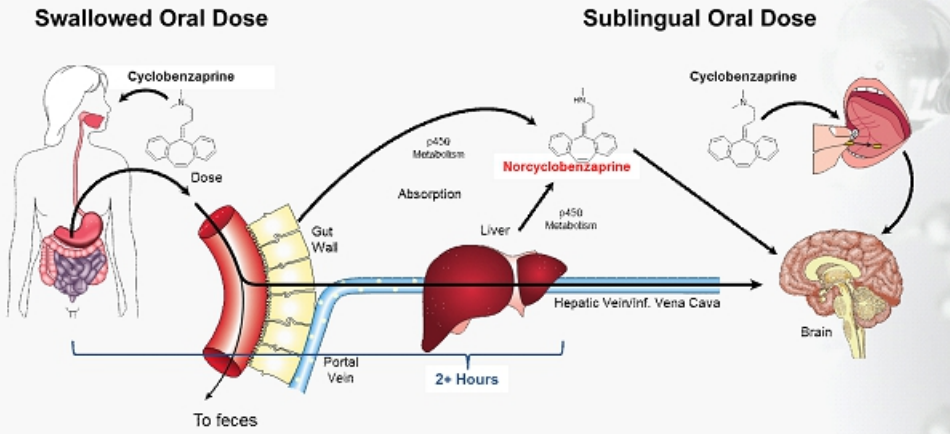


[1] U.S. Patent issued May 2, 2017

TONIX PHARMACEUTICALS

TNX-102 SL Sublingual Administration*

Transmucosal absorption avoids first pass hepatic metabolism



*U.S. Patent issued May 2, 2017

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

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)

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

CNS PORTFOLIO

PROFILE

- Occurs in approximately 13% of recovered COVID-19 patients[1]
- 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 COVID[4] 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.

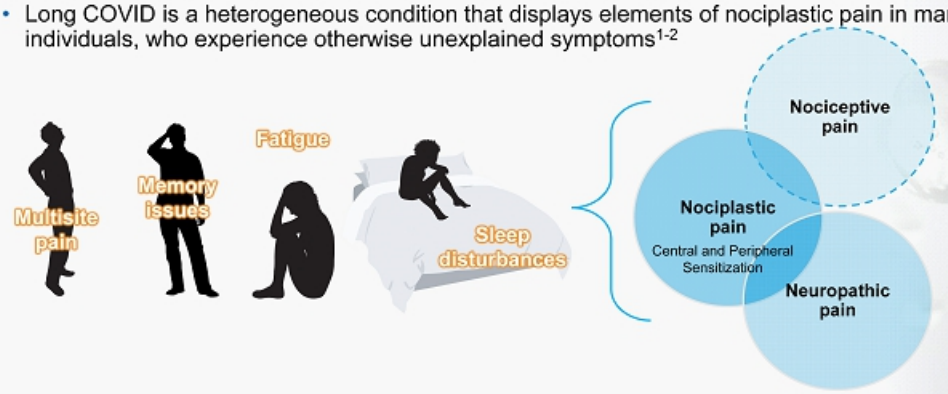
[1]September 1, 2022- CDC - https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html
[2]Harris, H, et al. Tonix data on file. 2022
[3]TriNetX Analytics
[4]Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID. 200 Independence Ave SW, Washington, DC 20201.

TONIX PHARMACEUTICALS

Fibromyalgia-Type Long COVID

CNS PORTFOLIO

- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained symptoms[1-2]



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

Nociplastic pain[3]: (*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

[1]Bierle DM, et al. Central Sensitization Phenotypes in Post Acute Sequelae of SARS-CoV-2 Infection (PASC): Defining the Post COVID Syndrome. J Prim Care Community Health 2021;12:21501327211030826. doi: 10.1177/21501327211030826.
[2]Moghimi, N. et al. The Neurological Manifestations of Post-Acute Sequelae of SARS-CoV-2 infection Curr Neurol Neurosci Rep. 2021;21(9):44. doi: 10.1007/s11910-02101130-1.
[3]Trouvin AP, et al. *Best Pract Res Clin Rheumatol.* 2019;33(3):101415.

TONIX PHARMACEUTICALS

TNX-102 SL: Phase 2 PREVAIL Study Design

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

*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)"

CNS PORTFOLIO

TONIX PHARMACEUTICALS

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

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
- Indirectly modulates the glutamatergic system
- Does not interact with AMPA, NMDA or Kainate receptors[1]

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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder

Additional Indications: PTSD, Neurocognitive Disorder From Corticosteroids, Alzheimer's Disease[2]

Status: Phase 2 study UPLIFT is currently enrolling

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

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

[1]AMPA=α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; NMDA=N-methyl-D-aspartate
[2]Garcia-Alberca JM, et al. Effects of Tianeptine Treatment on Depression and Cognitive Function in Patients with Alzheimer's Disease: A 12-Month Retrospective Observational Study. J Alzheimers Dis. 2022;88(2):707-720. doi: 10.3233/JAD-215630. PMID: 35694919; PMCID: PMC9398087.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

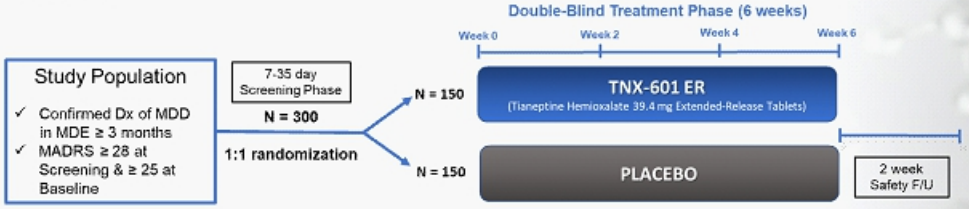
TNX-601 ER: Phase 2 UPLIFT Study Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Major Depressive Disorder
- 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 total score at Week 6



ClinicalTrials.gov Identifier: NCT05686408
Study to Evaluate TNX-601 ER Monotherapy Versus Placebo in Patients With Major Depressive Disorder (MDD) (UPLIFT)

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

CNS PORTFOLIO

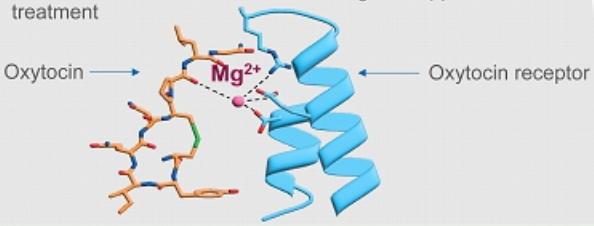
TONIX PHARMACEUTICALS

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

PROFILE

- Intranasal OT has potential utility in treating migraine[1]
- 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 enrolling[4]

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.

[1]Tzabazis A, et al. Oxytocin and Migraine Headache. Headache. 2017 May;57 Suppl 2:64-75. doi: 10.1111/head.13082. PMID: 28485846.
[2]Antoni FA, Chadio SE. Essential role of magnesium in oxytocin-receptor affinity and ligand specificity. Biochem J. 1988 Jan 15;257(2):611-4. doi: 10.1042/bj2570611. PMID: 2838090; PMCID: PMC1135623.
[3]Meyerowitz, J.G., *et al.* The oxytocin signaling complex reveals a molecular switch for cation dependence. *Nat Struct Mol Biol* (2022). (https://doi.org/10.1038/s41594-022-00728-4)
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

CNS PORTFOLIO

TONIX PHARMACEUTICALS

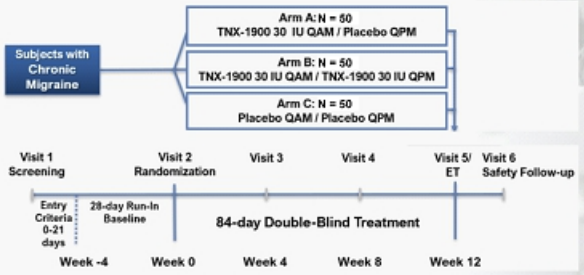
TNX-1900: Phase 2 PREVENTION Study Design

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)

CNS PORTFOLIO

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

PROFILE

Cocaine is the main cause for drug-related ED visits[1]

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 2Q 2023 pending FDA agreement

- 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)

[1]Havakuk O et al. *J Am Coll Cardiol.* 2017;70:101-113.
ED = emergency department.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

 *TNX-1300 has not been approved for any indication.

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

RARE DISEASE PORTFOLIO

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:

Unhealthy behaviors around food[1-4] → Consequences such as obesity, type 2 diabetes, cardiovascular disease[1-5] → Caretaker Burden[1-4]:

Patents Issued

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

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

[1]Miller JL, et al. *Am J Med Genet A*. 2011;155A(5):1040-1049.
[2]Butler MG, et al. *Genet Med*. 2017;19(6):635-642.
[3]Butler MG. NORD. Updated 2018. Accessed May 25, 2022. https://rarediseases.org/rare-diseases/prader-willi-syndrome/
[4]Prader-Willi Syndrome Association USA. Accessed May 25, 2022. https://www.pwsausa.org/what-is-prader-willi-syndrome/
[5]Muscogiuri G, et al. *J Endocrinol Invest*. 2021;44(10):2057-2070.

TONIX PHARMACEUTICALS

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 (FcγR)

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

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

*TNX-1500 is in the pre-IND stage of development and has not been approved for any indication. Patents filed.

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Prevention of Allograft Rejection

Status: Phase 1 ready

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

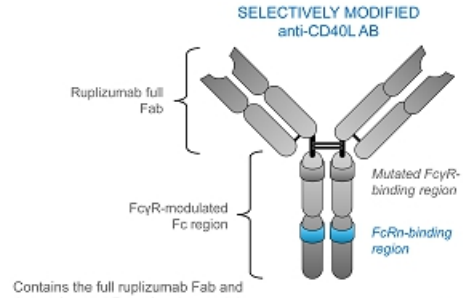
Next Steps: Initiate Phase 1 study 2Q 2023

Autoimmune Diseases

Status: Potential future indications include:

Sjögren's Syndrome, Systemic Lupus Erythematosus

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



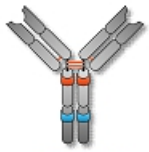
Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

TONIX PHARMACEUTICALS

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

IMMUNOLOGY PORTFOLIO

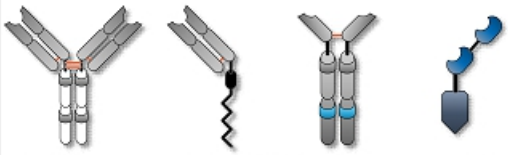
First-generation
anti-CD40L mAbs



Ruplizumab

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

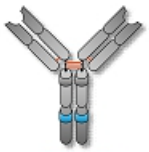
Second-generation
anti-CD40L proteins



Aglycosyl Ruplizumab *Dapirolizumab* *Letolizumab* *Dazodalibep*

Second-generation anti-CD40L proteins exhibited dramatically reduced binding to FcγRIIA[3-6] 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 FcγRIIA 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

[1]Inwald DP, et al. *Circ Res*. 2003;92(9):1041-1048.
[2]Robles-Carrillo L, et al. *J Immunol*. 2010;185(3):1577-1583.
[3]Shock A, et al. *Arthritis Res Ther*. 2015;17(1):234.
[4]Xie JH, et al. *J Immunol*. 2014;192(9):4083-4092.
[5]Ferrant JL, et al. *Int Immunol*. 2004;16(11):1583-1594.
[6]Karnell JL, et al. *Sci Transl Med*. 2019;11(489):eaar6584.
[7]ClinicalTrials.gov identifier: NCT02273960. Updated July 16, 2019. Accessed June 1, 2021. https://clinicaltrials.gov/ct2/show/results/NCT02273960?view=results
[8]Waters J, *Biocentury*; October 26, (2018).
[9]Company data.

TONIX PHARMACEUTICALS

Other anti-CD40L Monoclonal Antibodies in Development

IMMUNOLOGY PORTFOLIO

UCB (Co-developed with Biogen) – Systemic Lupus Erythematosus (SLE)
- Phase 3 Trial Currently Enrolling (NCT04294667)
  - Topline results expected 1H 2024[1]
- Dapirolizumab pegol (pegylated Fab)

Horizon (Agreed to be 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

TONIX PHARMACEUTICALS

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.

[1]Noyce RS, et al. Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLoS One. 2018 Jan 19;13(1):e0188453.
[2]Brennan, Z. Endpoints March 2, 2022 (https://endpts.com/weaker-omicron-variant-is-great-news-for-the-world-but-bad-news-for-covid-related-clinical-trials/)

Mpox and Smallpox Vaccine

Status: Preclinical

- TNX-801 is a cloned version of horsepox[1] (without any insert) purified from cell culture

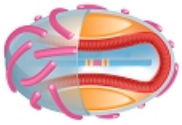
Next Steps: Initiate Phase 1 Trial 2H 2023

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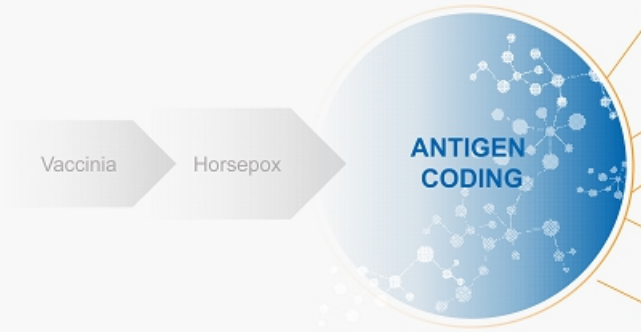
Live Virus Vaccine Platform: Recombinant Pox Vaccine (RPV)
Technology for Emerging Infectious Diseases and Oncolytics



- Mpox and Smallpox
- COVID-19
- Future Pandemics & New Infectious Diseases
- Biodefense
- Oncology

RPV VECTOR BELIEVED SIMILAR TO EDWARD JENNER'S VACCINE[1-3]

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

[1]Shrick, L. N Engl J Med 2017; 377:1491-1492. DOI: 10.1056/NEJMc1707600
[2]Esparza, J. Vaccine. 2020 Jun 19; 38(30): 4773–4779. doi: 10.1016/j.vaccine.2020.05.037
[3]Brinkmann, A. Genome Biol. 2020; 21: 286. doi: 10.1186/s13059-020-02202-0

TONIX PHARMACEUTICALS

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

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

Architectural Rendering

TONIX PHARMACEUTICALS

Pipeline: Key Pre-Clinical Programs

Candidates*	Indication	Status/Next Milestone
TNX-1600[1]	Depression, PTSD and 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

[1]Acquired from TRImaran Pharma; license agreement with Wayne State University
[2]Recombinant trefoil factor 2 (rTFF2) based protein; licensed from Columbia University
[3]Live attenuated vaccine based on horsepox virus vector, expressed SARS-CoV-2 spike protein. TNX-1850 is based on the BA.2 variant spike protein.
[4]Live attenuated vaccine based on bovine parainfluenza (BPI) virus
[5]COVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation with CD40L molecular trigger

TONIX PHARMACEUTICALS

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

IMMUNOLOGY PORTFOLIO

Potential New Cancer Treatment

- TNX-1700 (rTFF2) 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-PD-1 or anti-PD-L1 monoclonal antibodies (mAbs)

Preclinical Evidence for Inhibiting Growth of Cancer Cells

- Data showed that mTFF2-CTP augmented the efficacy of mAb anti-PD-1 therapy. Anti-PD-1 in combination with TFF2-CTP showed greater anti-tumor activity in PD-L1-overexpressing mice
- mTNX-1700 (mTFF2-MSA fusion protein) and anti-PD-1 monotherapy each was able to evoke anti-tumor immunity in the MC38 model of colorectal cancer[1]
- mTNX-1700 augmented the anti-tumor efficacy of anti-PD-1 therapy in both the MC38 and the CT26.wt models[1]

Patents Filed

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

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

[1]Daugherty, B. et al. March 6, 2023 Keystone Poster; www.tonixpharma.com/wp-content/uploads/2023/03/mTFF2-MSA_mTNX-1700_Suppresses-Tumor-Growth-and-Increases-Survival-in-an-Anti-PD-1-Treated-MC38-Colorectal-Cancer-Model-by-Targeting-MDSCs.pdf

TONIX PHARMACEUTICALS

Preclinical Infectious Disease Therapeutics in Development

INFECTIOUS DISEASE PORTFOLIO

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.

TONIX PHARMACEUTICALS


TONIX TEAM, NETWORK
AND FUTURE OUTLOOK
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Key Development Partners
MASSACHUSETTS GENERAL HOSPITAL
HARVARD MEDICAL SCHOOL
TNX-1500: ALLOGRAFT REJECTION
COLUMBIA UNIVERSITY
TNX-1300: COCAINE INTOXICATION
TNX-1700: GASTRIC AND COLORECTAL CANCERS
STANFORD UNIVERSITY
UNIVERSITÉ DE GENÈVE
TNX-1900: MIGRAINE & OTHER INDICATIONS
UNIVERSITY OF ALBERTA
SR SOUTHERN RESEARCH
TNX-801: SMALLPOX AND MONKEYPOX VACCINE
TNX-1850: COVID-19 VACCINE
InsermTransfert
CHU de Toulouse
Aix Marseille université
TNX-2900: PRADER-WILLI SYNDROME
KANSAS STATE UNIVERSITY
TNX-3700: COVID-19 VACCINE (ZINC NANOPARTICLE mRNA TECHNOLOGY)
TNX-2300: BOVINE PARAINFLUEZNA VIRUS
TONIX PHARMACEUTICALS
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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

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

- ❑ 2nd Quarter 2023 Phase 1 study start of TNX-1500 for prevention of allograft rejection
- ❑ 2nd Quarter 2023 Phase 2 study start of TNX-1300 for the treatment of cocaine intoxication
- ❑ 2nd Half 2023 Phase 1 study start of TNX-801 for prevention of mpox and smallpox


THANK YOU
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