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): November 2, 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 November 2, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that the National Institute of Allergy and Infectious Diseases ("NIAID"), a part of the National Institutes of Health, will conduct a Phase 1 clinical trial with the Company's TNX-1800 (recombinant horsepox virus, live vaccine) vaccine candidate to protect against COVID-19. 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 November 2, 2023, the Company announced that the NIAID will conduct a Phase 1 clinical trial with the Company's TNX-1800 vaccine candidate for protection against COVID-19, which is expected to start in the second half of 2024. NIAID will study TNX-1800 by percutaneous administration. The Company's TNX-801 vaccine candidate is the vector on which TNX-1800 is based and has been shown to be more than 1,000-fold attenuated than modern vaccinia virus vaccine strains in immunocompromised mice.

The trial is part of Project NextGen, an initiative by the U.S. Department of Health and Human Services to advance a pipeline of therapeutics for COVID-19. The Phase 1 study involving TNX-1800 is designed to assess safety and immunogenicity in approximately 60 healthy adult volunteers. Upon completion of the trial, the Company and NIAID will assess the results and determine next steps for the development of TNX-1800. NIAID will cover the cost of the clinical trial, including operations and related analysis. The Company will be responsible for providing clinical trial materials, and upon completion will have the right to rely on the findings in regulatory filings with the U.S. Food and Drug Administration to support the approval of its COVID-19 vaccine candidate and other vaccine candidates based on the recombinant pox virus platform

technology.

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, dated November 2, 2023
99.02	Corporate Presentation of the Company for November 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: November 2, 2023

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

Exhibit 99.01

Tonix Pharmaceuticals' Vaccine Candidate, TNX-1800, Selected by NIH/NIAID Project NextGen for Inclusion in Clinical Trials

NIAID is conducting early phase clinical trials on select next generation COVID-19 vaccine candidates with the intent to identify promising vaccine candidates

TNX-1800, a live virus percutaneous vaccine candidate, is based on Tonix's recombinant pox virus (RPV) platform

Phase 1 clinical trial of TNX-1800 expected to start in the second half of 2024

NIAID will cover the full cost of the clinical trial; Tonix will supply the vaccine candidate

CHATHAM, N.J., November 2, 2023 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced that the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health (NIH), will conduct a Phase 1 clinical trial with TNX-1800 (recombinant horsepox virus, live vaccine),[1] Tonix Pharmaceuticals' vaccine candidate to protect against COVID-19.

Tonix is developing a novel vaccine platform initially targeting COVID-19, smallpox and mpox (monkeypox). The intent is to provide durable protection against severe disease and prevent forward transmission, primarily by eliciting a T-cell immune response. TNX-1800 expresses the spike protein of SARS-CoV-2, was immunogenic, well tolerated[2] showed promise in protecting animals from challenge with SARS-CoV-2 delivered directly into the lungs.[3] A related horsepox-based vaccine, TNX-801[1], protected animals against challenge with monkeypox virus delivered directly into the lungs.[4] TNX-801 is also the vector on which TNX-1800 is based and has been shown to be >1,000-fold more attenuated than modern vaccinia virus vaccine (VACV) strains in immunocompromised mice.[5] The Phase 1 trial of TNX-1800 is expected to start in the second half of 2024. NIAID will study TNX-1800 by percutaneous administration.

"We believe our novel vaccine platform technology has the potential to provide durable protection from respiratory pathogens and slow their spread," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "TNX-1800 will be the first vaccine candidate using our live virus recombinant pox virus (RPV) platform technology to enter clinical trials. We hope to expand the portfolio of RPV-based vaccines to address several other known respiratory threats including smallpox, mpox and tuberculosis. We are committed to supporting NIAID in assembling a variety of vaccine platform options to ensure the availability of effective vaccines in the face of known and emerging threats. We look forward to participating in the Project NextGen initiative."

"Project NextGen," is an initiative by the U.S. Department of Health and Human Services (HHS) to advance a pipeline of new, innovative vaccines and therapeutics for COVID-19. NIAID will be conducting clinical trials to evaluate several early-stage vaccine candidates. The Phase 1 study involving TNX-1800 is designed to assess safety and immunogenicity in approximately 60 healthy adult volunteers. Upon completion of the trial, NIAID and Tonix Pharmaceuticals will assess the results and determine the next steps for the development of TNX-1800.

NIAID will cover the full cost of the clinical trial, including operations and related analysis. Tonix will be responsible for providing clinical trial materials, and upon completion will have the right to rely on the findings in regulatory filings with the U.S. Food and Drug Administration (FDA) to support the approval of its COVID-19 vaccine and other vaccines based on the RPV platform.

About Project NextGen

Project NextGen is a $5 billion initiative to develop the next generation of vaccines and therapeutics to combat COVID-19. Based at the HHS and led by the Administration for Strategic Preparedness and Response's Biomedical Advanced Research and Development Authority and the NIH's NIAID, Project NextGen will coordinate across the federal government and the private sector to advance the pipeline of new, innovative vaccines and therapeutics into clinical trials and potential review by the U.S. Food and Drug Administration (FDA) for authorization or approval, and commercial availability for the American people. The program will focus on several areas, including mucosal vaccines, vaccines that provide broader protection against variants of concern and a longer duration of protection, pan-coronavirus vaccines, and new and more durable monoclonal antibodies.

About TNX-1800*

TNX-1800 (recombinant horsepox virus) is a live virus vaccine for percutaneous administration that is designed to express the spike protein of the SARS-CoV-2 virus and to elicit a predominant T cell response. The RPV platform is based on a horsepox vector, which is a live replicating, attenuated virus that has been shown to be >1,000-fold more attenuated than modern VACV strains in immunocompromised mice.[5] Horsepox and the vaccinia vaccine viruses are closely related orthopoxviruses that are believed to share a common ancestor. Molecular analysis shows that horsepox is closer than modern vaccinia vaccines in DNA sequence to the vaccine discovered and disseminated by Dr. Edward Jenner.[6-9] Live replicating orthopoxviruses, like vaccinia or horsepox, can be engineered to express foreign genes and have been explored as platforms for vaccine development because they possess; (1) large packaging capacity for exogenous DNA inserts, (2) precise virus-specific control of exogenous gene insert expression, (3) lack of persistence or genomic integration in the host, (4) strong immunogenicity as a vaccine, (5) ability to rapidly generate vector/insert constructs, (6) readily manufacturable at scale, and (7) ability to provide direct antigen presentation. Relative to vaccinia, horsepox has substantially decreased virulence in mice.[4,6] The current formulation is a frozen liquid, but we believe that future lyophilized versions can be stored and shipped at standard refrigeration. Horsepox-based vaccines are designed to be single dose, vial-sparing vaccines that can be administered without sterile injection, manufactured using conventional cell culture systems with the potential for mass scale production, and packaged in multi-dose vials. Moreover, we believe the low dose of TNX-1800 makes this technology amenable for future implementation in microneedle delivery systems.

About TNX-801*

TNX-801 (recombinant horsepox virus) is a live virus vaccine based on horsepox[4-7] in pre-clinical development to prevent smallpox and mpox. Tonix reported positive preclinical efficacy data, demonstrating that TNX-801 vaccination protected non-human primates against lethal challenge with monkeypox.[4] Tonix has received official written response from a Type B pre-Investigational New Drug Application (IND) meeting with the U.S. Food and Drug Administration (FDA) to develop TNX-801 as a potential vaccine to protect against mpox disease and smallpox.[10] Tonix believes the FDA feedback provides a path to agreement on the design of a Phase 1 /2 study and the overall clinical development plan. The Phase 1/2 clinical trial will assess the safety, tolerability, and immunogenicity of TNX-801, following the submission and clearance of an IND. More than 30,000 people have contracted mpox in the U.S. so far during the 2022-23 epidemic,[11] The recent cluster of mpox in Chicago revealed breakthrough cases of mpox in individuals who had been vaccinated with the currently authorized non-replicating vaccine, which is administered in two doses.[12] In contrast, TNX-801 is delivered percutaneously with only one dose and therefore may achieve higher rates of community protection by eliminating drop-out between doses and limiting forward transmission. Moreover, relying on only one approved mpox vaccine at present is a risk for the global supply chain that has already led to insufficient availability of vaccines to meet global health needs, especially in Africa. TNX-801 has the potential to make a global impact on mpox and the risk of smallpox because of its durable T-cell immune response, the potential to manufacture at scale, and the use of a lower dose than non-replicating vaccines.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults. Tonix's development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS development portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment of a potentially confirmatory Phase 3 study in the third quarter of 2023, with topline data expected in late December 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 proof-of-concept study has been completed, and topline results were reported in the third quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), is in development as a preventive treatment for chronic migraine, and enrollment has been completed in a Phase 2 proof-of-concept study with topline data expected in early December 2023. TNX-1900 is also being studied in binge eating disorder, pediatric obesity and social anxiety disorder by academic collaborators under investigator-initiated INDs. 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 fourth quarter of 2023. Tonix's rare disease development 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 development 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 rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 was initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases, including TNX-1800, in development as a vaccine to protect against COVID-19. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals.

*Tonix's product development candidates are investigational new drugs or biologics and have not been approved for any indication.

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[1] TNX-1800 and TNX-801 are experimental new vaccines and have not been approved for any indication.

[2] Awasthi, M. et al. *Viruses*. 2023. 15(10):2131.

[3] Awasthi, M. et al. *BioRxiv*. 2023.

[4] Trefry S, et al. *BioRxiv*. 2023.

[5] Noyce RS, et al. *Viruses*. 2023. 15(2):356.

[6] Jenner E. "An Inquiry Into the Causes and Effects of the Variole Vaccinae, a Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire and Known by the Name of the cow-pox." London: Sampson Low, 1798.

[7] Noyce RS, et al. *PloS One.* 2018. 13(1):e0188453.

[8] Schrick L et al. *N Engl J Med.* 2017. 377:1491-1492.

[9] Tulman ER, et al. *J Virol*. 2006. 80(18):9244-58.

[10] TNX-801 PR pre-IND meeting August 20, 2023: https://ir.tonixpharma.com/news-events/press-releases/detail/1417/tonix-pharmaceuticals-announces-results-of-pre-ind-meeting

[11] McQuiston JH, et al. *MMWR Morb Mortal Wkly Rep.* 2023. 72:547–552.

[12] Centers for Disease Control. *MMWR Morb Mortal Wkly Rep.* 2023. 72(25);696-698.

This press release and further information about Tonix can be found at www.tonixpharma.com.

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; risks related to the failure to successfully market any of our products; 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; risks related to the failure to successfully market any of our products; 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

Tonix is committed to developing and marketing therapeutics to treat pain, neurologic, psychiatric and addiction conditions through our ***central nervous system portfolio*** and within other areas of ***high unmet need***, including immunology, infectious disease, and rare disease

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CNS-Focused Biopharma with Preclinical to Commercial Stage Products

Robust Development Pipeline

Topline data for two late-stage CNS programs expected by end of 2023

Internal Facilities

For R&D and clinical-scale manufacturing

Marketed Products

For the treatment of acute migraine

Strategic Partnerships

With world-class academic & research organizations to bring innovative therapeutics to market faster

TONIX PHARMACEUTICALS

Late-Stage Clinical Portfolio

Molecule*	Indication	Phase 1	Phase 2	Phase 3	NDA Submission
TNX-102 SL Cyclobenzaprine Protectio® Sublingual Tablets	Fibromyalgia (FM)	*Phase 3 Topline Results Expected 4Q'23 (Late December)*			
	FM-Type Long COVID	*Phase 2 Topline Results Reported 3Q'23*			
TNX-1900 Intranasal Potentiated Oxytocin with Magnesium	Chronic Migraine	*Phase 2 Topline Results Expected 4Q'23 (Early December)*			
TNX-1300 Cocaine Esterase	Cocaine Intoxication	*Phase 2 Study Start Expected 4Q'23*			

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

TONIX PHARMACEUTICALS

Two Marketed Proprietary Migraine Drugs
Non-oral Formulations of Sumatriptan

Zembrace® SymTouch®
(sumatriptan injection) 3 mg[1]

Tosymra®
(sumatriptan nasal spray) 10 mg[2]

- Each indicated for the ***treatment of acute migraine with or without aura in adults***
- Sumatriptan remains the acute migraine 'gold standard' treatment for many patients and continues to represent the largest segment of the market in terms of unit sales[3]
- Each may provide migraine ***pain relief in as few as 10 minutes*** for some patients[1,2,4,5]
- Patents to 2036 (Zembrace) and 2031 (Tosymra)

Acquired from Upsher-Smith Laboratories which has managed care contracts covering ~200 M lives
- Contract includes a transition period during which Tonix expects to secure its own contracts

Retail Product Sales for the 12 months ended December 31st 2022
- Retail sales: ~$23 M (Zembrace ~$19.6 M and Tosymra ~$3.5 M)[4]

Tonix is prepared to meet potential increased demand for Tosymra following GSK's planned discontinuation of Imitrex® (sumatriptan) nasal spray after January 2024

[1]Zembrace SymTouch [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: February 2021 - For more information, talk to your provider and read the Patient Information and Instructions for Use. – Important Safety Information is provided in the appendix
[2]Tosymra [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: Feb 2021. For more information, talk to your provider and read the Patient Information and Instructions for Use. – Important Safety Information is provided in the appendix
[3]Upsher-Smith Laboratories, LLC; Data On File, 2023
[4]Mathew NT, et al. Dose ranging efficacy and safety of subcutaneous sumatriptan in the acute treatment of migraine. US Sumatriptan Research Group. Arch Neurol. 1992;49(12):1271-1275.
[5]Wendt J, et al. A randomized, double-blind, placebo-controlled trial of the efficacy and tolerability of a 4-mg dose of subcutaneous sumatriptan for the treatment of acute migraine attacks in adults. Clinical Therapeutics. 2006;28(4):517-526.

Zembrace and Tosymra Bypass the GI Tract

Bypassing gastrointestinal (GI) tract is *potential advantage for treating acute migraine*
- GI absorption may be inconsistent in migraineurs due to gastric stasis (also called "gastroparesis")[1-4]
- Nausea and vomiting are symptoms of migraine[5] which can complicate oral treatment

Existing intranasal products
- Imitrex® nasal spray (sumatriptan)
- Migranal® (dihydroergotamine) nasal spray – developed by Novartis, sold by Bausch Health

New intranasal products bringing attention to non-oral route
- Pfizer's Zavzpret® (zavegepant), FDA approved in March, 2023[1] is the first intranasal gepant
- Impel NeuroPharma's Trudhesa® (dihydroergotamine) FDA approved 2021[2]

[1]Pfizer Press Release March 10, 2023. – https://www.pfizer.com/news/press-release/press-release-detail/pfizers-zavzpretttm-zavegepant-migraine-nasal-spray
[2]Impel Press Release September 3, 2021 - https://impelpharma.com/2021/09/03/impel-neuropharma-announces-u-s-fda-approval-of-trudhesa-dihydroergotamine-mesylate-nasal-spray-for-the-acute-treatment-of-migraine/

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-1900 for Chronic Migraine

Topline Results Expected – early December

Phase 2 Proof-of-Concept Study

TNX-102 SL for Fibromyalgia

Topline Results Expected – late December

Phase 3 Potential NDA Enabling Study

TONIX PHARMACEUTICALS

TNX-102 SL

Cyclobenzaprine (Protectic®)

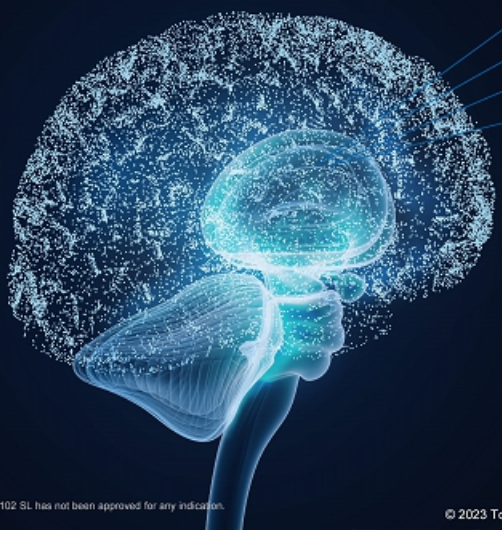
A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

TONIX PHARMACEUTICALS

TNX-102 SL: Unique MOA Facilitates Restorative Sleep

Centrally Acting Analgesic

Potent binding and antagonist activities at four key receptors facilitate ***restorative sleep***



- *serotonergic-5-HT2A*
- *adrenergic-α1*
- *histaminergic-H1*
- *muscarinic-M1*

Key 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 nor with recognized abuse potential

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

TONIX PHARMACEUTICALS

About Fibromyalgia

*Fibromyalgia (FM) is a **chronic pain disorder** resulting from amplified sensory and pain signaling within the CNS. Symptoms include chronic widespread pain, **nonrestorative sleep**, fatigue, and cognitive dysfunction*

6-12 million adults **Fibromyalgia afflicts an estimated 6-12 million adults in the US, predominantly women**[1]

Large unmet need:

- Patients struggle with daily activities, have impaired quality of life, and frequently are disabled
- Physicians and patients report common dissatisfaction with currently marketed products
  - Average patient has 20 physician office visits per year[2]

Current standard of care:

- FDA-approved products include Lyrica, Cymbalta, and Savella
- Fewer than half of those treated for fibromyalgia receive sustained benefit from the approved drugs[3]
  - Majority (60%) fail therapy due to lack of a response (25%) or poor tolerability (35%)[4]
  - Opioid usage is not uncommon

[1]American Chronic Pain Association (www.theacpa.org, 2019)
[2]Robinson et al, Pain Medicine 2013;14:1400
[3]The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[4]Market research by Frost & Sullivan, commissioned by Tonix

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Fibromyalgia Program Status

TNX-102 SL Cyclobenzaprine Protectio® Sublingual Tablets	**Fibromyalgia**	***Phase 3 Topline Results Expected 4Q'23 (Late December)***
	FM-Type Long COVID	*Phase 2 Topline Results Reported 3Q'23*

1) One **positive Phase 3 study (RELIEF) completed**[1]
2) Second Phase 3 study (RALLY) missed primary endpoint
   - Unexpected increase in adverse event-related discontinuations in both drug and placebo arms, potentially due to recruiting during COVID-19
3) Confirmatory Phase 3 study (RESILIENT) **enrollment complete**

Next Steps: ***Potentially confirmatory topline results expected 4Q 2023 (Late December)***

*TNX-102 SL has not been approved for any indication.
[1]Lederman 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", doi: 10.1002/acr.25142. Epub ahead of print. PMID: 37165930.

TNX-102 SL: Phase 3 RESILIENT Study Design

RESILIENT Study

CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia
- U.S. sites only, ***completed enrollment of 457 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
- Threshold for potential NDA-enabling study is $p < 0.05$

Key Secondary Endpoints:

- 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
- 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)

TONIX PHARMACEUTICALS

About Fibromyalgia-Type Long COVID

CNS PORTFOLIO

Long COVID is broadly defined as signs, symptoms, and conditions that continue or develop after acute COVID-19 infection[1]

Many Long-COVID symptoms <u>overlap with core symptoms of fibromyalgia</u>
and are hallmarks of other chronic pain syndromes like myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

19% **Long COVID occurs in approximately 19% of recovered COVID-19 patients**[2]

40% **As many as 40% of Long COVID patients experience multi-site pain**[3,4]

[1]CDC - https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html#:~:text=Some%20people%20who%20have%20been,after%20acute%20COVID%2D19%20infection.
[2]CDC Press Release, June 22, 2022 - https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm
[3]Harris, H, et al. Tonix data on file. 2022
[4]TriNetX Analytics

TONIX PHARMACEUTICALS

TNX-102 SL: Phase 2 PREVAIL Study Design

PREVAIL Study

CNS PORTFOLIO

Study characteristics:

- Randomized, double-blind, placebo-controlled study of TNX-102 SL in fibromyalgia-type Long COVID
- U.S. sites only, ***completed enrollment of 63 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)*

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

Placebo once-daily at bedtime

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

Next Steps: ***End of Phase 2 Meeting with FDA 1Q 2024***

TONIX PHARMACEUTICALS

TNX-102 SL: Phase 2 PREVAIL Topline Results[1]

CNS PORTFOLIO

Did not meet the primary endpoint of multi-site pain reduction at Week 14

However, findings fulfill the objectives of proof-of-concept study, supporting the decision to advance the program based on a proposed primary endpoint using the PROMIS Fatigue scale

- TNX-102 SL showed robust effect size in improving fatigue and consistent activity across secondary measures of sleep quality, cognitive function, disability and Patient Global Impression of Change (PGIC)
- Was generally well tolerated with an adverse event (AE) profile comparable to prior studies with TNX-102 SL:
  - AE-related discontinuations were similar in drug and placebo arms
  - No new safety signals were observed

Fatigue is the signature symptom of Long COVID and has been identified as the dominant symptom contributing to disability[2]

- We observed numerical improvement in the PROMIS fatigue score (in RELIEF p=0.007 MMRM and in RALLY p=0.007 MMRM) in both prior Phase 3 studies of TNX-102 SL in fibromyalgia,
- We believe the results of PREVAIL, together with extensive data from studies in other chronic conditions[3-5], makes PROMIS Fatigue a solid candidate for the primary endpoint of future Long COVID registrational studies

[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z8FQHQ
[2]Walker S, *et al. BMJ Open* 2023;13:e069217. doi: 10.1136/ bmjopen-2022-069217
[3]Cook, K.F., *et al.* 2016. *Journal of Clinical Epidemiology*, 73, 89- 102
[4]Cella, D., et al. 2016. *Journal of Clinical Epidemiology*, 73, 128–134
[5]Lai, J.S., et al. 2011. *Archives of Physical Medicine and Rehabilitation*, 92(10 Supplement), S20-S27.

TONIX PHARMACEUTICALS

Acute Stress Reaction (ASR)/ Acute Stress Disorder (ASD)

ASR/ASD are acute stress conditions resulting from trauma which can affect both civilian and military populations.

Large unmet need:

- According to National Center for PTSD, about 60% of men and 50% of women in the US are exposed least one traumatic experience in their lives[1]
- In the US alone, one-third of emergency department visits (40-50 million patients per year) are for evaluation after trauma exposures[2]

Current standard of care:

- No medications are currently available at or near the point of care to treat patients suffering from acute traumatic events and support long-term health

[1]National Center for PTSD. How Common is PTSD in Adults? https://www.ptsd.va.gov/understand/common/common_adults.asp
[2]Wisco et al. *J Clin Psychiatry*. 2014;75(12):1338-46

ASR/ASD Program Status

Status: Expect to start Phase 2 in 1Q 2024

Phase 2 Trial Funded by DoD grant to University of North Carolina (UNC)

- UNC Institute for Trauma Recovery awarded a $3M grant from the Department of Defense (DoD)
- OASIS trial will build upon infrastructure developed through the UNC-led, $40M AURORA initiative
  - AURORA study is a major national research initiative to improve the understanding, prevention, and recovery of individuals who have experienced a traumatic event
  - Supported in part by funding from the National Institutes of Health (NIH) and the health care arm of Google's parent company Alphabet
- Opportunity to investigate the correlation between motor vehicle collisions and the emergence of ASD and PTSD
- Supported by multiple clinical trials:
  - Phase 2 trial in military-related PTSD (AtEase or NCT02277704)
  - Phase 3 trial in military-related PTSD (HONOR or NCT03062540)
  - Phase 3 trial in primarily civilian PTSD (RECOVERY or NCT03841773)
- In each of these studies, early and sustained improvements in sleep were associated with TNX-102 SL treatment by the PROMIS sleep disturbance (SD) scale and the Clinician Administered PTSD Scale (CAPS-5) "sleep disturbance" item.

Together these studies provide preliminary evidence that TNX-102 SL is well-tolerated and may promote recovery from PTSD via a pharmacodynamic facilitation of sleep-dependent emotional memory processing

TNX-102 SL: Phase 2 OASIS Study Design

CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Acute Stress Reaction (ASR) / Acute Stress Disorder (ASD)
- The proposed Optimizing Acute Stress reaction Interventions with TNX-102 SL (OASIS) trial will examine the safety and efficacy of TNX-102 SL to reduce adverse posttraumatic neuropsychiatric sequelae among patients presenting to the emergency department after a motor vehicle collision (MVC)
- The trial will enroll approximately 180 individuals who acutely experienced trauma at study sites across the US
- Participants will be randomized in the emergency department to receive a two-week course of either TNX-102 SL or placebo
- Investigator-initiated IND

Objective:

- Investigate the potential of Tonix's TNX-102 SL (cyclobenzaprine HCl sublingual tablets) to reduce the frequency and severity of the adverse effects of traumatic exposure, including acute stress reaction (ASR), acute stress disorder (ASD), and posttraumatic stress disorder (PTSD).
- ASR refers to the body's immediate response to trauma, whereas ASD is the short-term effects of trauma (within 1 month), and PTSD is the long-term effects of trauma (beyond 1 month)

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

Placebo once-daily at bedtime

2 weeks

*First dose of TNX-102 SL 5.6 mg versus placebo taken in the emergency department, and then daily at bedtime to finish 2 weeks of treatment

A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With ASR/ ASD (OASIS)

- Primary outcome measure: Acute Stress Disorder Scale (ASDS) assessed at 7 and 21 days post MVC
- Posttraumatic stress symptom severity assessed at 6 and 12 weeks post MVC using the PTSD Checklist for DSM-5 (PCL-5)
- Standardized survey instruments of sleep disturbances, anxiety and depression symptoms, general physical and mental health, and clinical global improvement also employed
- Detailed and brief neurocognitive assessments are performed from baseline to 12 weeks after MVC at specific timepoints throughout study participation period

TONIX PHARMACEUTICALS

TNX-1900 and TNX-2900

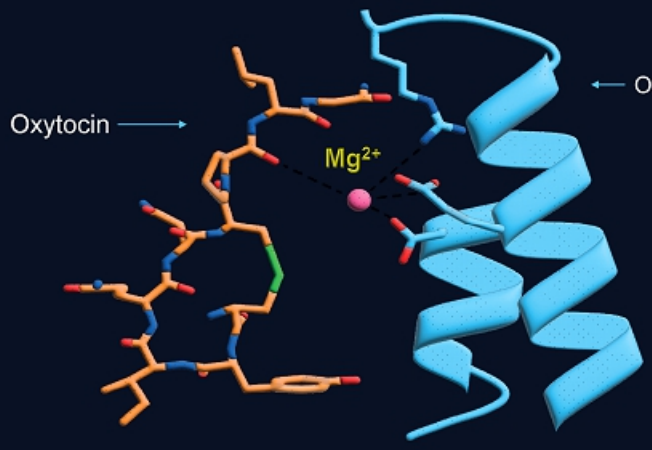
Intranasal Potentiated Oxytocin with Magnesium

A novel, non-CGRP antagonist approach to treatment

TONIX PHARMACEUTICALS

TNX-1900 & TNX-2900: Novel Formulation of Intranasal Oxytocin (OT) Potentiated with Magnesium

*Magnesium is known to **potentiate the binding of OT** to its receptor*[1,2]



Key Differentiators

- Targeted intranasal delivery
  - Low systemic exposure
- Blocks release of CGRP from trigeminal ganglia neurons
  - CGRP is a key peptide in the pathogenesis of migraine

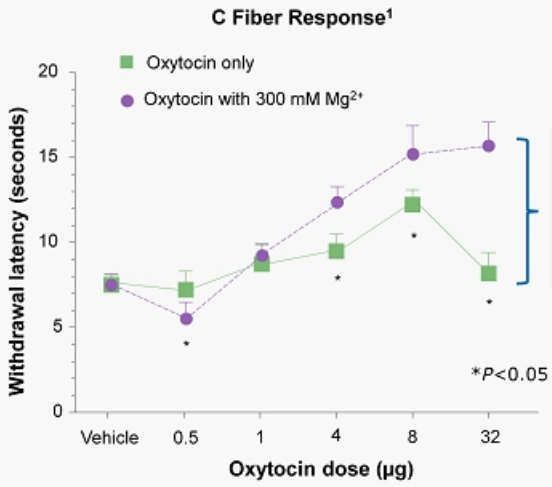
[1]Antoni et al., 1989. *Biochem J.* 257(2):511-4
[2]Meyerowitz et al., 2022. *Nat Struct Mol Biol.* (3):274-281
*TNX-1900 and TNX-2900 have not been approved for any indication.

TONIX PHARMACEUTICALS

Oxytocin Effects – Addressing the "Inverted U" Dose Response

Addition of Mg^{2+} Augments Oxytocin-Induced Analgesia in Animal Model

- A ***nonlinear dose response*** decreases efficacy at higher doses
- Addition of ***Mg^{2+} rescues the efficacy*** of oxytocin at high doses



[1]Adapted from: Bharadwaj VN, et al. *Pharmaceutics.* 2022;14(5):1105.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

About Chronic Migraine

*Chronic migraine involves frequent (>15 days per month) or long-lasting episodes of headaches and migraines over the course of at least 3 months. Migraines can occur with or without an aura and are often **debilitating for patients.***

3-7 *million adults*

Chronic migraine afflicts 3-7 million adults in the US[1]

Current standard of care:

- Anti-CGRP antibodies and Botox® (onabotulinumtoxinA) are specifically approved to prevent headaches in chronic migraine
- Nurtec® (Rimegepant), a gepant, is approved for both prevention of migraine and acute treatment

Large unmet need:

- Anti-CGRP antibodies and oral gepants involve systemic exposure
- Long term safety concerns with prolonged systemic blockade of CGRP receptor[2]

[1]Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[2]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: Phase 2 PREVENTION Study Design

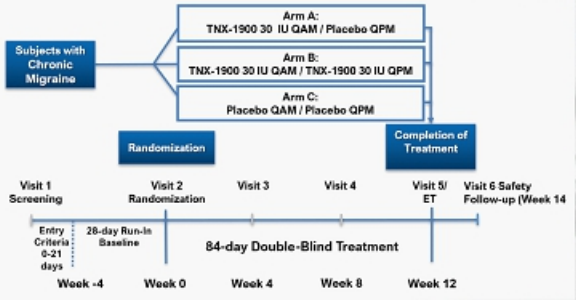
PREVENTION Study

General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms– two treatment regimens and one placebo) in chronic migraine
- U.S. sites only, ***completed enrollment with 88 patients***

Primary Endpoint:

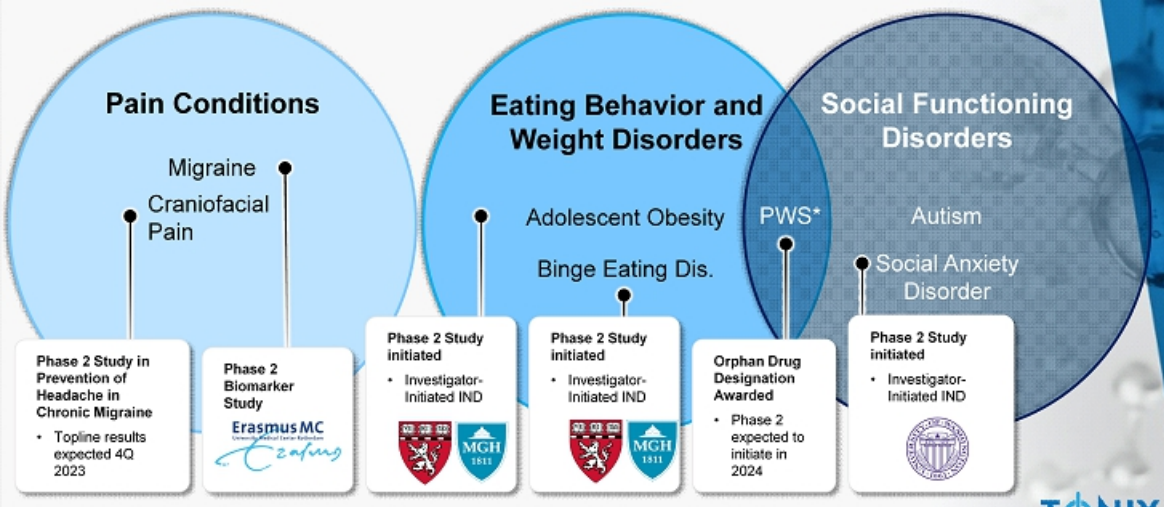
- Mean change in the number of migraine headache days between the 28-day Run-In phase and the last 28-days of the Treatment phase (TNX-1900 vs. placebo)
- Threshold for achieving positive proof-of-concept is Effect Size (ES) > 0.2



ClinicalTrials.gov Identifier: NCT05679908
A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)

Next Steps: ***Topline results expected 4Q 2023 (Early December)***

Potential Applications of TNX-1900 & TNX-2900: Investigator Led Studies



*Prader-Willi Syndrome

TONIX PHARMACEUTICALS

About Prader-Willi Syndrome

*Prader-Willi Syndrome (PWS) is the most common genetic cause of life-threatening childhood obesity. PWS causes unhealthy behaviors around food[1-4], consequences such as **obesity, type 2 diabetes, and cardiovascular disease**[1-5], and creates significant caretaker burden[1-4]*

10-20 *thousand individuals* **Rare genetic disease that afflicts 10-20 thousand individuals in the US**

Current standard of care:

- Human growth hormone treatment is FDA-approved for growth failure in PWS children

Large unmet need:

- Currently no cure, and no treatment for PWS-related hyperphagia
- Consequences can be life threatening - obesity and cardiovascular disease are leading cause of death

Tonix has been granted FDA Orphan Drug Designation

[1]Miller et al., 2011. *Am J Med Genet A.* 155A(5):1040-1049
[2]Butler et al., 2017. *Genet Med.* 19(5):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 et al., 2021. *J Endocrinol Invest.* 44(10):2057-2070

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

TNX-1300
Cocaine Esterase

Fast acting antidote for life threatening cocaine intoxication

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TNX-1300: Recombinant Protein Rapidly Degrades Cocaine in the Bloodstream

Drops plasma exposure by 90% in 2 minutes

FDA Breakthrough Therapy Designation

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

Key Differentiators

- Rapidly metabolizes cocaine within matter of minutes
- No other product currently on the market for this indication

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

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About Cocaine Intoxication

Over 5 million Americans reported current cocaine use in 2020, which is almost 2% of the population[1]. In 2021, more than 24,900 individuals in the US died from drug overdose deaths involving cocaine[2]

500k **Over 500,000 emergency department visits for cocaine, annually[3,4]**

Current standard of care:

- Patients are currently managed only by supportive care for the adverse effects of cocaine intoxication on the cardiovascular and central nervous systems

Large unmet need:

- No other product currently on the market for this indication
- TNX-1300 could significantly reduce the time and resources required for other detox services
- Potentially reduces the risk of morbidity and mortality

[1]Substance Abuse and Mental Health Services Administration. (2021). Results from the 2020 National Survey on Drug Use and Health: Detailed Tables: Prevalence Estimates, Standard Errors, and Sample Sizes.
[2]Centers for Disease Control and Prevention (CDC) - https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

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

TONIX PHARMACEUTICALS

TNX-1500

Anti-CD40L Monoclonal Antibody

Next Generation mAb preserves efficacy without risk of thrombosis

TNX-1500: Next Generation anti-CD40L mAb

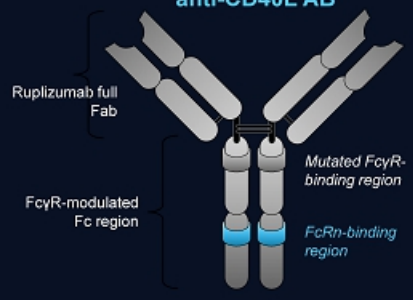
Re-engineered to better modulate the binding of FcγR and mitigate risk of thrombosis

Key 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.

Selectively Modified anti-CD40L AB



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

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

TNX-1500 Strategy and Status

1 Proposed Initial Indication: Prevention of Allograft Rejection

Status: ***Phase 1 currently enrolling***

- Collaborations ongoing with Mass General Hospital on heart and kidney transplantation in non-human primates
- Collaboration with Boston Children's on bone marrow transplantation in non-human primates

Next Steps: Initiate Phase 2 study in Kidney Transplant Recipients

2 Second Indication: Hematopoetic Cell Transplant (Bone Marrow Transplant)

- Potential to reduce GvHD

3 Third Indication (and beyond): Autoimmune Diseases (e.g., Multiple Sclerosis, Sjögen's Syndrome, Systemic Lupus Erythematosus)

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

IMMUNOLOGY PORTFOLIO

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TNX-1500 Preclinical Data and Publications

Non-human Primate Kidney Allo-Transplantation

- TNX-1500 monotherapy consistently prevents kidney transplant rejection with no thrombosis observed
- April 2023 Publication: Lassiter, G., et al. (2023). TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Renal Allograft Survival. *American Journal of Transplantation*. www.sciencedirect.com/science/article/pii/S1600613523003714

Non-human Primate Heart Heterotopic Allo-Transplantation

- TNX-1500 monotherapy consistently prevents heart transplant rejection. Similar activity to chimeric hu5c8[2] during treatment phase in prior studies
- April 2023 Publication: Miura, S., et al. (2023) TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Cardiac Allograft Survival. *American Journal of Transplantation*. www.sciencedirect.com/science/article/pii/S1600613523003969

Non-Human Primate Kidney Xenograft Transplantation

- TNX-1500 therapy is part of a regiment to prevent rejection in kidney xenograft transplants
  - Anand, R.P., Layer, J.V., Heja, D. et al. (2023). Design and testing of a humanized porcine donor for xenotransplantation. *Nature*. https://www.nature.com/articles/s41586-023-06594-4
  - Kozlov, M. (2023). Monkey survives two years after gene-edited pig-kidney transplant. *Nature*. https://www.nature.com/articles/d41586-023-03176-2
  - Mohiuddin, M. (2023). Pig-to-primate organ transplants require genetic modifications of donor. *Nature*. https://www.nature.com/articles/d41586-023-02817-w

IMMUNOLOGY PORTFOLIO

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TNX-1700

Recombinant Trefoil Factor Family Member 2 (rTFF2-HSA) Fusion Protein

Targeting the toxic tumor micro-environment

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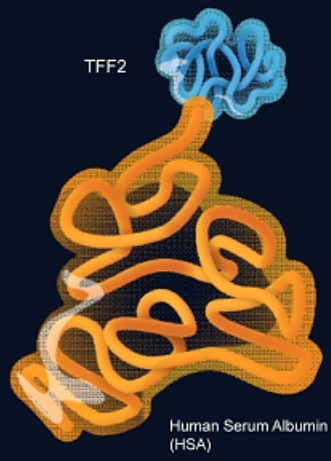
TNX-1700: Fighting Cancer by Targeting the Tumor Micro-Environment

Suppresses myeloid-derived suppressor cells (MDSCs) and activates anti-cancer CD8+ T cells



Key Differentiators

- Different MOA than checkpoint inhibitors
- ***Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies***

Preclinical Evidence

- 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]

*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. https://bit.ly/48nIRHM

TONIX PHARMACEUTICALS

About Gastric and Colorectal Cancer

Gastric and colorectal cancer are both leading cancers in the US. Colorectal cancer is the 3rd leading cause of cancer-related deaths in both men and women.[1]

>1.3M People living with colorectal cancer in the US[2]

>125k People living with gastric cancer in the US[3]

Current standard of care:

- PD-1 blockade
  - However, gastric and colorectal cancer are relatively unresponsive

Large unmet need:

- Gastric and colorectal cancer have a relative 5-year survival rate of 35.7% and 65%, respectively
  - Despite advances in the field, patients are still in need of life saving treatment

IMMUNOLOGY PORTFOLIO

[1]American Cancer Society, accessed September 2023 - https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html
[2]NIH, accessed September 2023 - https://seer.cancer.gov/statfacts/html/colorect.html
[3]NIH, accessed September 2023 - https://seer.cancer.gov/statfacts/html/stomach.html

TONIX PHARMACEUTICALS

Internal Development & Manufacturing Capabilities

R&D Center (RDC): Frederick, MD

- Research advancing CNS and immunology drugs
- Accelerated development of vaccines and antiviral drugs against infectious diseases
- ~48,000 square feet, BSL-2 with some areas designated BSL-3

Advanced Development Center (ADC): North Dartmouth, MA

- Development and clinical scale manufacturing of biologics
- ~45,000 square feet, BSL-2

INFECTIOUS DISEASE PORTFOLIO

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Broad-Spectrum Antiviral Discovery Programs

Host-directed antiviral discovery programs

CD45 targeted therapeutics

- Small molecule therapeutics that reduce endogenous levels of CD45, a protein tyrosine phosphatase
- Reduction in CD45 protects against many viruses including the Ebola virus

Cathepsin inhibitors

- Small molecule therapeutics that inhibit ***essential cathepsins*** which are required by viruses such as coronaviruses and filoviruses to infect cells
- Activity as monotherapy and in combination with other antivirals

Virus-directed antivirals discovery program

Viral glycan-targeted engineered biologics

- Bind to viral densely branched high-mannose (DBH) glycans
- ***Neutralize circulating virus*** and stop the entry of the progeny virus into cells
- Antiviral activity against a broad range of RNA viruses
- Activity as monotherapy and in combination with other antivirals

INFECTIOUS DISEASE PORTFOLIO

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TNX-801

Live Virus Vaccine

Live virus vaccine platform with multitude of potential applications

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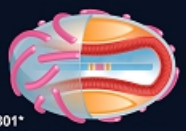
TNX-801: Recombinant Pox Vaccine (RPV) Platform Using Live Virus Technology

Cloned version of horsepox[1] purified from cell culture



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

Vaccinia → Horsepox → **ANTIGEN CODING**

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

Key Differentiators

Live virus vaccines are the most established vaccine technology

- 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 administration

Standard refrigeration for shipping and storage

*TNX-801 is in the pre-IND stage of development and has not been approved for any indication.
[1]Noyce et al., 2018. *PLoS One*. 13(1):e0188453.

TONIX PHARMACEUTICALS

TNX-1800: Designed to Express the SARs-CoV-2 Spike Protein

TNX-1800 (recombinant horsepox virus) is a live virus vaccine based on Tonix's TNX-801 that is designed to express the spike protein of the SARS-CoV-2 virus and to elicit a predominant T cell response

- Immunogenic and well tolerated[1]
- Showed promise in protecting animals from challenge with SARS-CoV-2 delivered directly into the lungs[1]

Status: ***National Institute of Allergy and Infectious Diseases (NIAID) will conduct a Phase 1 clinical trial with TNX-1800***

- Expected to start in 2H 2024
- First vaccine candidate using Tonix's live virus recombinant pox virus (RPV) platform technology to enter clinical trials
- "Project NextGen" is an initiative by the U.S. Department of Health and Human Services (HHS) to advance a pipeline of new, innovative vaccines and therapeutics for COVID-19. NIAID will be conducting clinical trials to evaluate several early-stage vaccine candidates, including TNX-1800
- Phase 1 study is designed to assess safety and immunogenicity in approximately 60 healthy adult volunteers
- Upon completion of the trial, NIAID and Tonix will assess the results and determine the next steps for the development of TNX-1800

[1]Awasthi, M. et al. *Viruses*. 2023. 15(10):2131.
[2]Awasthi, M. et al. *BioRxiv*. 2023.

Key Development Partners

TNX-1500: ALLOGRAFT REJECTION

Massachusetts General Hospital · Harvard Medical School

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

Columbia University

TNX-1900: MIGRAINE & OTHER INDICATIONS

Stanford University · Université de Genève · Massachusetts General Hospital · Harvard Medical School

TNX-801: SMALLPOX AND MONKEYPOX VACCINE

University of Alberta · SR Southern Research

TNX-2900: PRADER-WILLI SYNDROME

Inserm Transfert · CHU de Toulouse · Aix Marseille université

Management Team

Seth Lederman, MD
Co-Founder, CEO & Chairman

TARGENT · Fusilev (levoleucovorin) for injection · vela

Gregory Sullivan, MD
Chief Medical Officer

Columbia University Department of Psychiatry · New York State Psychiatric Institute

Bradley Saenger, CPA
Chief Financial Officer

Shire · VERTEX · Steward · pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank · svb Silicon Valley Bank · American Capital

Summary of Upcoming Milestones

Clinical Trial Initiations

- **Phase 2 study of TNX-1300 for the treatment of cocaine intoxication – expected 4Q 2023**
- **Phase 1 study of TNX-1800 with NIAID – expected 2H 2024**

4th Quarter 2023 Data Readouts

- **Phase 2 PREVENTION study of TNX-1900 for chronic migraine – topline early December 2023**
  - Affects approximately 3-7 M adults in the U.S[1]
- **Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia – topline late December 2023**
  - Affects approximately 6-12 M adults in the U.S[2]

[1]Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[2]American Chronic Pain Association (www.theacpa.org, 2019)

TONIX PHARMACEUTICALS

Zembrace® Important Safety Information (1 of 2)

Zembrace SymTouch (Zembrace) can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop use and get emergency help if you have any signs of a heart attack:

- Discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back; severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw; pain or discomfort in your arms, back, neck, jaw or stomach; shortness of breath with or without chest discomfort; breaking out in a cold sweat; nausea or vomiting; feeling lightheaded

Zembrace is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam shows no problem.

Do not use Zembrace if you have:

- History of heart problems; narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease); uncontrolled high blood pressure; hemiplegic or basilar migraines. If you are not sure if you have these, ask your provider.
- Had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation; severe liver problems; taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, dihydroergotamine; are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- An allergy to sumatriptan or any of the components of Zembrace

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Zembrace can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

Zembrace® Important Safety Information (2 of 2)

Zembrace may cause serious side effects including:

- Changes in color or sensation in your fingers and toes; sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever; cramping and pain in your legs or hips; feeling of heaviness or tightness in your leg muscles; burning or aching pain in your feet or toes while resting; numbness, tingling, or weakness in your legs; cold feeling or color changes in one or both legs or feet; increased blood pressure including a sudden severe increase even if you have no history of high blood pressure; medication overuse headaches from using migraine medicine for 10 or more days each month. If your headaches get worse, call your provider.
- Serotonin syndrome, a rare but serious problem that can happen in people using Zembrace, especially when used with anti-depressant medicines called SSRIs or SNRIs. Call your provider right away if you have: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- Hives (itchy bumps); swelling of your tongue, mouth, or throat
- Seizures even in people who have never had seizures before

The most common side effects of Zembrace include: pain and redness at injection site; tingling or numbness in your fingers or toes; dizziness; warm, hot, burning feeling to your face (flushing); discomfort or stiffness in your neck; feeling weak, drowsy, or tired.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Zembrace. For more information, ask your provider.

This is the most important information to know about Zembrace but is not comprehensive. For more information, talk to your provider and read the Patient Information and Instructions for Use. You can also visit www.upsher-smith.com or call 1-888-650-3789. For full Prescribing Information, visit: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6e5b104f-2b9e-416e-92fb-ef1bdaea867d

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Zembrace is a prescription medicine used to treat acute migraine headaches with or without aura in adults who have been diagnosed with migraine.

Zembrace is not used to prevent migraines. It is not known if it is safe and effective in children under 18 years of age.

Tosymra® Important Safety Information (1 of 2)

Tosymra® can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop Tosymra and get emergency medical help if you have any signs of heart attack:

- Discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back; severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw; pain or discomfort in your arms, back, neck, jaw, or stomach; shortness of breath with or without chest discomfort; breaking out in a cold sweat; nausea or vomiting; feeling lightheaded

Tosymra is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam is done and shows no problem.

Do not use Tosymra if you have:

- History of heart problems; narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease); uncontrolled high blood pressure; severe liver problems; hemiplegic or basilar migraines. If you are not sure if you have these, ask your healthcare provider.
- Had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation; taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, or dihydroergotamine. Ask your provider if you are not sure if your medicine is listed above
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure
- An allergy to sumatriptan or any ingredient in Tosymra

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements. Tosymra can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

Tosymra® Important Safety Information (2 of 2)

Tosymra may cause serious side effects including:

- Changes in color or sensation in your fingers and toes; sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever; cramping and pain in your legs or hips, feeling of heaviness or tightness in your leg muscles, burning or aching pain in your feet or toes while resting, numbness, tingling, or weakness in your legs, cold feeling or color changes in one or both legs or feet; increased blood pressure including a sudden severe increase even if you have no history of high blood pressure; medication overuse headaches from using migraine medicine for 10 or more days each month. **If your headaches get worse, call your provider**.
- Serotonin syndrome, a rare but serious problem that can happen in people using Tosymra, especially when used with anti-depressant medicines called SSRIs or SNRIs. **Call your provider right away if you have**: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- Seizures even in people who have never had seizures before

The most common side effects of Tosymra include: tingling, dizziness, feeling warm or hot, burning feeling, feeling of heaviness, feeling of pressure, flushing, feeling of tightness, numbness, application site (nasal) reactions, abnormal taste, and throat irritation.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Tosymra. For more information, ask your provider.

This is the most important information to know about Tosymra but is not comprehensive. For more information, talk to your provider and read the Patient Information and Instructions for Use. You can also visit www.upsher-smith.com or call 1-888-650-3789. For full Prescribing Information, visit: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=015a5cf9-f246-48bc-b91e-cd730a53d8aa

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Tosymra is a prescription medicine used to treat acute migraine headaches with or without aura in adults.

Tosymra is not used to treat other types of headaches such as hemiplegic or basilar migraines or cluster headaches.

Tosymra is not used to prevent migraines. It is not known if Tosymra is safe and effective in children under 18 years of age.

CNS PORTFOLIO

TONIX PHARMACEUTICALS