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): September 27, 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 September 27, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that the University of North Carolina Institute for Trauma Recovery ("UNC") has been awarded a $3 million grant from the U.S. Department of Defense ("DoD") to investigate the potential of the Company's TNX-102 SL (cyclobenzaprine HCl sublingual tablets) product candidate to reduce the frequency and severity of adverse effects of acute trauma. 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 September 27, 2023, the Company announced that UNC has been awarded a $3 million grant from the DoD to investigate the potential of TNX-102 SL to reduce the frequency and severity of adverse effects of acute trauma, including acute stress reaction, acute stress disorder, and posttraumatic stress disorder. The proposed OASIS study (Optimizing Acute Stress reaction Interventions with TNX-102 SL) trial, that 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. As cost sharing in this pubic/private partnership, the Company has committed to contribute approximately $1.3 million to the study over three years, $75,000 of which is payable on initiation, and afterwards monthly as incurred: approximately $217,000 in the first year, $374,000 in the second year, and $664,000 in the third year. The trial will enroll approximately 180 trauma survivors at study sites around the U.S. Participants will be randomized in the emergency department to receive a two-week course of either TNX-102 SL or placebo. Initiation of patient enrollment in the proposed investigator sponsored OASIS trial is anticipated in the beginning of 2024, subject to an Investigational New Drug application submission and U.S. Food and Drug

Administration clearance.

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 September 27, 2023
99.02	Corporate Presentation by the Company for September 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: September 27, 2023

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

Exhibit 99.01

Tonix Pharmaceuticals Announces Department of Defense Grant to Support the University of North Carolina's Proposed Investigator Sponsored OASIS Trial of TNX-102 SL for Treatment of Acute Stress Reaction, Acute Stress Disorder, and Posttraumatic Stress Disorder

$3 million awarded by DoD to University of North Carolina Institute of Trauma Recovery to support a proposed 180-patient, randomized, placebo-controlled trial in acute trauma patients

Investigator sponsored trial to evaluate the potential for TNX-102 SL[1] to reduce the frequency and severity of acute stress reaction, acute stress disorder, and post-traumatic stress disorder (PTSD)

Acute stress disorder is identified in 13-21% of motor vehicle accidents;[2,3] Individuals with acute stress disorder have an increased risk of developing PTSD; U.S. lifetime PTSD prevalence is approximately 6%[4-7]

CHATHAM, N.J., September 27, 2023 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company, today announced that the University of North Carolina (UNC) Institute for Trauma Recovery has been awarded a $3 million grant from the Department of Defense (DoD) to investigate the potential of Tonix's TNX-102 SL (cyclobenzaprine HCl sublingual tablets) to reduce the frequency and severity of adverse effects of acute trauma. Such adverse effects include 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 represents the short-term effects of trauma, and PTSD represents the long-term effects of trauma.

"In addition to emergency care to treat and help patients recover from physical wounds, whether in the emergency room or on the battlefield, we must also address the unmet need for treatment options to address 'invisible wounds' that survivors may experience following a traumatic event," said Samuel McLean, M.D., Professor of Psychiatry and Emergency Medicine at the UNC School of Medicine at UNC, School of Medicine, and lead principal investigator of the proposed study. "To address these needs, we are investigating TNX-102 SL as a potential treatment for patients who experience trauma and traumatic stress."

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. The trial will enroll approximately 180 trauma survivors at study sites around the U.S. Participants will be randomized in the emergency department to receive a two-week course of either TNX-102 SL or placebo.

Initiation of patient enrollment in the proposed investigator sponsored OASIS trial is anticipated in the beginning of 2024, subject to Investigational New Drug (IND) application submission and U.S. Food and Drug Administration (FDA) clearance.

The OASIS trial will build upon a foundation of knowledge and infrastructure developed through the UNC-led, $40 million AURORA initiative. The AURORA study is a major national research initiative to improve the understanding, prevention, and recovery of individuals who have experienced a traumatic event. AURORA is supported by funding from the National Institutes of Health (NIH), leading brain health nonprofit One Mind, private foundations, and partnerships with leading tech companies such as Mindstrong Health and Verily Life Sciences, the health care arm of Google's parent company Alphabet.

"No medications are currently available at or near the point of care to treat patients suffering from traumatic events and support long-term health, whether U.S. military exposed to life-threatening events or civilians experiencing traumatic events such as motor vehicle collisions," said Seth Lederman, M.D., Chief Executive Officer of Tonix. "Acute stress reaction and posttraumatic stress symptoms are common among civilian motor vehicle collision survivors. The AURORA study, which has collected thousands of data points from motor vehicle collisions, will allow us to better investigate the correlation between motor vehicle collisions and the emergence of acute stress disorder or PTSD symptoms. And leveraging support from the AURORA study and utilizing the DoD's non-dilutive capital to primarily fund OASIS allows Tonix and UNC to streamline trial efficiency, reduce costs and increase trial power through enriching the target patient population."

Added Brandon Staglin, President of One Mind, "For individuals who experience trauma and traumatic stress, the need for effective treatments is an urgent one. The OASIS trial's focus on evaluating a promising potential treatment option exemplifies the kind of evidence-based outcomes One Mind and our partners hoped to achieve as part of the AURORA initiative's broader efforts to improve the lives of trauma survivors."

Acute and chronic stress disorders can affect both civilian and military populations. According to the National Center for PTSD, in the U.S. about 60% of men and 50% of women experience at least one trauma in their lives.[5] In the U.S. alone, one-third of emergency department visits (40-50 million patients per year) involve evaluation after trauma exposures, and in a 2014 study involving 3,157 US veterans, 87% reported exposure to at least one potentially traumatic event during their service.[8] Moreover, as many as 500,000 U.S. troops who served in wars between 2001 and 2015 were diagnosed with PTSD.[9]

About TNX-102 SL in Post-Traumatic Stress Disorder

Sleep disturbances in PTSD are a potential target for pharmacotherapy. TNX-102 SL is a sublingual formulation of cyclobenzaprine designed for once-daily bedtime dosing and rapid transmucosal absorption such that cyclobenzaprine plasma levels rapidly rise during the onset of sleep and first four hours of sleep, then rapidly fall through the second half of sleep through awakening. Cyclobenzaprine has potent binding and antagonist activity at 5-HT_{2A}, α_1-adrenergic, H_1-histaminergic, and M_1 muscarinic receptors, each of which play roles in the pharmacological management of insomnia. The sublingual transmucosal formulation of cyclobenzaprine is designed to bypass first-pass hepatic metabolism, increasing the ratio in plasma of the parent cyclobenzaprine to the long-lived active metabolite, norcyclobenzaprine, which has a longer half-life and consequently less circadian variation with once-daily dosing. The use of TNX-102 SL 5.6 mg administered daily at bedtime to reduce PTSD symptoms and improve sleep quality in patients with PTSD is supported by the results of a Phase 2 trial (AtEase NCT02277704 in military-related PTSD) and two Phase 3 trials (HONOR or NCT03062540 in military-related PTSD and RECOVERY or NCT03841773 in PTSD). [10-12] In each of these studies, early improvements in sleep were associated with TNX-102 SL treatment as measured by the PROMIS sleep disturbance (SD) scale. Moreover, in AtEase and HONOR, early and sustained improvement in sleep were associated with TNX-102 SL treatment by the Clinician Administered PTSD Scale (CAPS-5)[13] "sleep disturbance" item. Primary analyses comparing change from baseline CAPS-5 total severity between TNX-102 SL 5.6 mg and placebo at week 12 were not significant in AtEase, HONOR or RECOVERY. However, in HONOR and RECOVERY at week 4, TNX-102 SL treatment was associated with an improvement in CAPS-5 total severity as compared to placebo. Moreover, secondary analyses in all three studies showed TNX-102 SL treatment was associated with benefits on the patient global impression of change (PGIC), indicating that across studies TNX-102 SL treated patients self-reported greater symptom improvement than those treated with placebo. The most common side-effects were administration site reactions described as tongue numbness or abnormal taste and reported by approximately 30% of participants. There were no unexpected safety findings. Together these studies, with approximately 650 trauma-exposed patients (included 254 patients treated with TNX-102

SL 5.6 mg), provide preliminary evidence that TNX-102 SL is well-tolerated and may promote recovery from PTSD via a pharmacodynamic mechanism of sleep-dependent emotional memory processing.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which provides rapid transmucosal absorption and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. As a multifunctional agent with potent binding and antagonist activities at the 5-HT2A-serotonergic, α1-adrenergic, H1-histaminergic, and M1-muscarinic receptors, TNX-102 SL is in development as a daily bedtime treatment for fibromyalgia, Long COVID (formally known as post-acute sequelae of COVID-19 [PASC]), alcohol use disorder and agitation in Alzheimer's disease. The United States Patent and Trademark Office (USPTO) issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in the patent are important elements of Tonix's proprietary TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.

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 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 the fourth quarter of 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-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in the fourth quarter of 2023.

TNX-4300 (estianeptine) is a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the μ-opioid receptor while maintaining activity in the rat Novel Object Recognition test *in vivo* and the ability to activate PPAR-β/δ and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment in a Phase 2 proof-of-concept study with topline data expected in the fourth quarter of 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. 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.

1. TNX-102 SL has not been approved for any indication
2. Diagnostic and statistical manual of mental disorders (5th ed.). American Psychiatric Association.Pg 284
3. Dai W, et al. *BMC Psychiatry.* 2018. 18, 188
4. U.S. Department of Veterans Affairs. Epidemiology and Impact of PTSD.www.ptsd.va.gov/professional/treat/essentials/epidemiology.asp#one
5. Goldstein RB, et al. *Soc Psychiatry Psychiatr Epidemiol.* 2016. 51(8):1137-48
6. Kessler RC, et al. *Arch Gen Psychiatry.* 2005. 62(6):593-602
7. U.S. Department of Veteran Affairs. How Common is PTSD in Adults?www.ptsd.va.gov/understand/common/common_adults.asp
8. Wisco BE, et al. *J Clin Psychiatry*. 2014. 75(12):1338-46
9. Thompson M. *Time*. 2015;185(12):40-3
10. Sullivan GM, et al. *Psychiatry Res*. 2021. 301:113974
11. Rauch SAM, et al. *J Clin Psychiatry.* 2021. 82(4)
12. Ivanova A, et al. *J Biopharm Stat.* 2022. 32(3):441-449
13. U.S. Department of Veterans Affairs. PTSD Checklist for DSM-5 (PCL-5).https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp#obtain

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.

Investor Contact

Jessica Morris
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(862) 904-8182

Peter Vozzo
ICR Westwicke
peter.vozzo@westwicke.com
(443) 213-0505

Media Contact

Ben Shannon
ICR Westwicke
ben.shannon@westwicke.com
(919) 360-3039

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.

Investment Highlights

MARKETED PRODUCTS

Tonix Medicines **markets two FDA-approved products** Zembrace® SymTouch® (sumatriptan injection) and Tosymra® (sumatriptan nasal spray) for the treatment of acute migraine in adults with or without aura

RICH PIPELINE OF THERAPEUTICS CANDIDATES IN DEVELOPMENT

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

Internal **capabilities in R&D and biologics process development and GMP manufacturing** to accelerate development timelines.

STRATEGIC PARTNERSHIPS

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

[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
Zembrace, SymTouch and Tosymra are registered trademarks of Tonix Medicines. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc.

TONIX PHARMACEUTICALS

Pipeline: Key Clinical Development Programs

Candidates*	Indication	Status/Next Milestone
TNX-601 ER	Depression	Phase 2 – Topline expected early November[1]
TNX-1900[2]	Prevention of Chronic Migraine	Phase 2 – Topline expected early December
TNX-102 SL[3]	Fibromyalgia (FM) Long COVID (PASC[4])	Mid-Phase 3 – Topline expected late December Phase 2 – Topline Reported
TNX-2900[5]	Prader-Willi Syndrome - *FDA Orphan Drug Designation*	Phase 2 ready
TNX-1300[6]	Cocaine Intoxication - *FDA Breakthrough Designation*	Mid-Phase 2, Targeted 4Q 2023 Start
TNX-1500[7]	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1 – currently ongoing

*All of Tonix's product candidates are investigational new drugs or biologics and none has been approved for any indication.
[1]Phase 1 trial for formulation development was completed outside of the U.S.; Other potential indications include PTSD and neurocognitive dysfunction from steroids
[2]Acquired from Trigemina; license agreement with Stanford University; Investigator-initiated Binge Eating Disorder (BED) and adolescent obesity studies initiated 3Q 2023.
[3]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). AAD and AUD are Phase 2 ready, and PTSD is Phase 3 ready..
[4]Post-Acute Sequelae of COVID-19.
[5]Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)
[6]TNX-1300 (double-mutant cocaine esterase) is licensed from Columbia University
[7]anti-CD40L humanized monoclonal antibody –Phase 1 trial in healthy volunteers is currently ongoing

TONIX PHARMACEUTICALS

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-601 ER for Depression

Topline Results Expected – early November

Phase 2 Proof-of-Concept Study

Registration-Quality

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

Registration-Quality

TONIX PHARMACEUTICALS

Two Marketed Proprietary Migraine Drugs
Autoinjector and Nasal Spray (Non-oral) Formulations of Sumatriptan

CNS PORTFOLIO

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

- 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)

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

Consolidated Product Sales for the 12 months ended March 31st 2023
- Factory sales: $30.4M[3]
- Net sales: $16.4M[3]

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]

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

[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][3]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.

TONIX PHARMACEUTICALS

Administration of Zembrace and Tosymra Bypass the GI Tract

CNS PORTFOLIO

Bypassing the gastrointestinal (GI) tract is a potential advantage for treating acute migraine
- Potential to provide a treatment option for migraines complicated by severe nausea and vomiting

Need for acute non-oral treatments
- GI absorption may be inconsistent in migraineurs due to gastric stasis (also called "gastroparesis")[1-4]
- Nausea and vomiting are symptoms of migraine[5]

Existing intranasal branded products
- Imitrex® nasal spray (sumatriptan)
  - GSK has announced that this product will be discontinued in January 2024
- Migranal® (dihydroergotamine) nasal spray – developed by Novartis, sold by Bausch Health

New intranasal products bring attention to this 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/

TONIX PHARMACEUTICALS

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-601 ER for Depression

Topline Results Expected – early November

Phase 2 Proof-of-Concept Study

Registration-Quality

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

Registration-Quality

TONIX PHARMACEUTICALS

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

CNS PORTFOLIO

PROFILE

- A novel, oral, extended-release once-daily tablet
- Treatment effect of tianeptine sodium immediate release *t.i.d.* in depression is well-established
- Tianeptine restores neuroplasticity in animal models
- PPAR-β/δ and PPAR-γ agonist[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 less weight gain or sexual side effects than traditional antidepressants
- Tianeptine's side effects are described in labeling in countries in which it is marketed[2]

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder (MDD)

Additional Indications: PTSD, Neurocognitive Dysfunction From Corticosteroids, Alzheimer's Disease[3]

Status: Phase 2 MDD study UPLIFT enrollment complete

Next Steps:

Topline results expected early November 2023

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

[1]Sullivan G et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. https://bit.ly/42o3jnV
[2]Summary of product characteristics (SmPC), European Medicines Agency, Stablon®, https://www.servier.com.ve/sites/default/files/spc-pil/spc-stablon.pdf accessed 9-25-23.
[3]Garcia-Alberca et al., 2022. *J Alzheimers Dis.* 88(2):707-720
Abbreviations: IR, immediate release; *t.i.d.*, three times a day

TONIX PHARMACEUTICALS

TNX-601 ER - Phase 2 UPLIFT* Study Design

UPLIFT Study

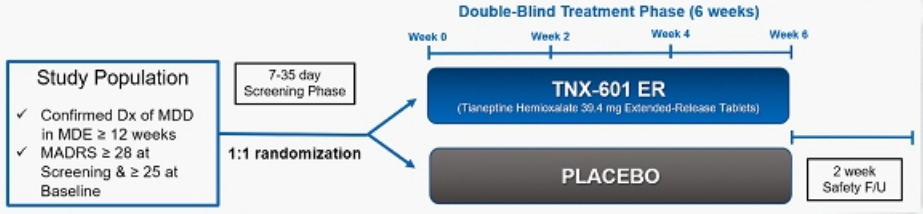
CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Major Depressive Disorder to evaluate monotherapy with TNX-601 ER versus placebo
- Parallel design with two arms – treatment with tianeptine hemioxalate 39.4 mg or placebo
- U.S. sites only, completed enrollment of 132 patients

Primary Endpoint:

- Mean change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at Week 6 analyzed via MMRM with MI
- Threshold for achieving proof-of-concept is ES > 0.20
- Threshold for potential registrational study is *p*-value < 0.05



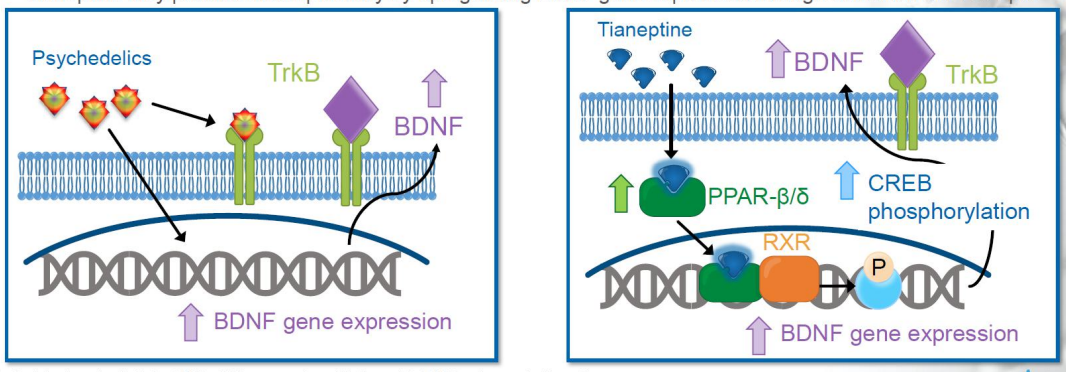
*ClinicalTrials.gov Identifier: NCT05686408
Abbreviations: Dx, diagnosis; ER, extended-release; F/U, follow-up; MDD, major depressive disorder; MDE, major depressive episode; N, number; ES, effect size; MMRM, mixed models for repeated measures; MI, multiple imputation

TONIX PHARMACEUTICALS

Tianeptine Shares a Neuroplasticity-Promoting Mechanism With Psychedelics

The neurotrophic growth factor BDNF plays a key role in the regulation of synaptic plasticity, and is diminished in populations suffering from anxiety and depression[1]

- Psychedelics may promote neuroplasticity both by directly binding to BDNF receptor TrkB, and by increasing BDNF gene expression[1,2]
- Tianeptine may promote neuroplasticity by upregulating BDNF gene expression through activation of PPAR-β/δ[3,4]



BDNF=brain-derived neurotrophic factor; CREB=cAMP response element binding protein; TrkB=tyrosine receptor kinase B

[1]de Vos CMH, et al. *Front Psychiatry*. 2021;12:724606
[2]Moliner R, et al. *Nat Neurosci*. 2023;26(6):1032-1041
[3]Ji MJ, et al. *Int J Neuropsychopharmacol*. 2015;19(1):pyv083
[4]Seo MK, et al. *Psychopharmacology (Berl)*. 2016;233(13):2617-2627

TONIX PHARMACEUTICALS

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

Racemic tianeptine:
- Approved in Europe and ex-US
- 1:1 mixture of 2 mirror-image isomers[1,2]
- Weak μ-opioid receptor agonism[2]
  - Risk of abuse or diversion for euphoric effects[3]

(S)-Tianeptine: PPAR-β/δ agonist, no opioid liability[4]
- New mechanism of action for treating depression

(R)-Tianeptine: opioid liability[4]
- Weak μ-opioid receptor agonism[4]

	Racemic-Tianeptine	(S)-Tianeptine TNX-4300	(R)-Tianeptine
Activates PPAR-β/δ	+	+	-
Neuroplasticity	+	+	-
Novel Object Recognition Test[5]	+	+	-
μ-Opioid Receptor	+	-	+
Forced Swim Test[6]	+	-	+
Activates PPAR-γ	+	+	+

***(S)*-tianeptine**

***(R)*-tianeptine**

[1]Stablon. Summary of product characteristics. Les Laboratoires Servier Industrie; 2014.
[2]PubChem. Accessed November 10, 2022. https://pubchem.ncbi.nlm.nih.gov/compound/Tianeptine
[3]Drug Enforcement Administration. May 2019. Accessed November 11, 2022. https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf
[4]Sullivan GM et al. Poster presentation at the American Society of Clinical Psychopharmacology. June 2023. https://bit.ly/42q3jnV
[5]Rat Novel Object Recognition Test
[6]Mouse Porsolt Forced Swim Test

CNS PORTFOLIO

TONIX PHARMACEUTICALS

TNX-4300*: Depression, Alzheimer's & Parkinson's diseases
Estianeptine (Single *(S)*-isomer of Tianeptine)

CNS PORTFOLIO

PROFILE

- Single isomer, oral treatment
- Proposed mechanism of action from lab studies indicates estianeptine is the active ingredient of TNX-601 ER[1]
  - PPAR-β/δ and PPAR-γ agonist
  - Free of μ-opioid receptor activity
- Estianeptine restores neuroplasticity in tissue culture

Differentiators:

Relative to racemic tianeptine IR or TNX-601 ER:

- Lack of opioid liability

Relative to traditional antidepressants:

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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder (MDD)

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

Status: Pre-clinical

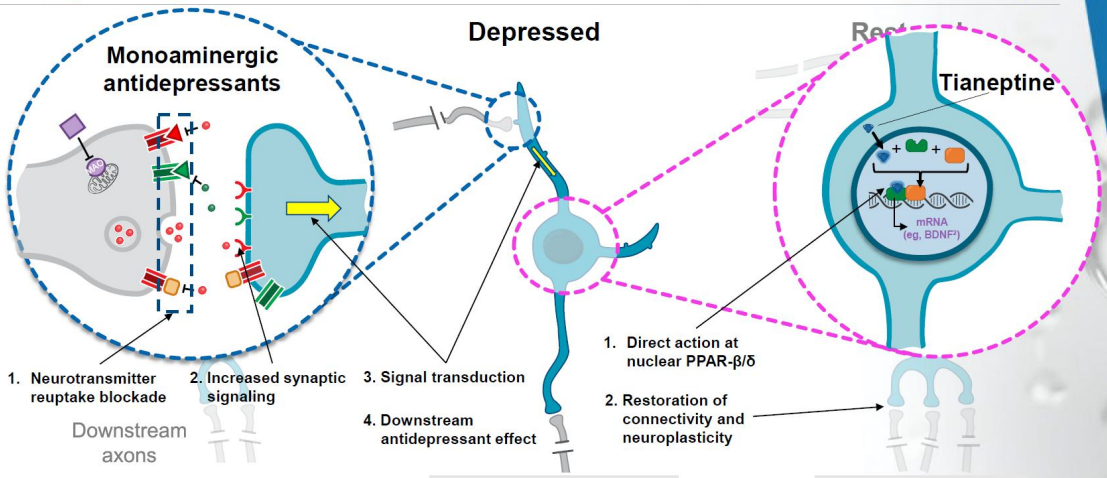
Next Steps: Potential for IND to be supported by pre-clinical and clinical data from TNX-601 (racemic tianeptine) development

*TNX-4300 is in the pre-IND stage of development and has not been approved for any indication

[1]Sullivan GM et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. https://bit.ly/42o3jnV
[2]Garcia-Alberca et al., 2022. *J Alzheimers Dis.* 88(2):707-720

TONIX PHARMACEUTICALS

While Monoaminergic Antidepressants Work at the Synapse, *(S)*-Tianeptine "Cuts in Line" to More Directly Affect Neuroplasticity[1]



[1]Sullivan GM et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. https://bit.ly/42o3jnV
[2]BDNF=brain-derived neurotrophic factor.

TONIX PHARMACEUTICALS

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-601 ER for Depression	**TNX-1900 for Chronic Migraine**	TNX-102 SL for Fibromyalgia
Topline Results Expected – early November	Topline Results Expected – early December	Topline Results Expected – late December
Phase 2 Proof-of-Concept Study	Phase 2 Proof-of-Concept Study	*Phase 3 Potential NDA Enabling Study*
Registration-Quality		Registration-Quality

TONIX PHARMACEUTICALS

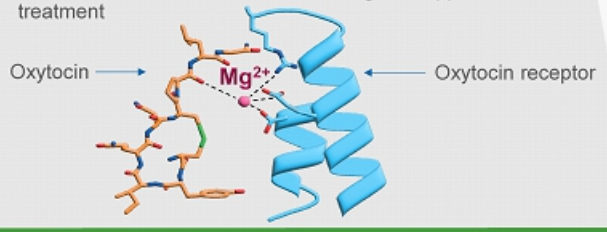
TNX-1900*: Prevention of Headache in Chronic Migraine
Intranasal Potentiated Oxytocin (OT) with Magnesium

CNS PORTFOLIO

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 enrollment complete[4]

Next Steps: Topline results from PREVENTION expected early December 2023

Investigator initiated Phase 2 trials in adolescent obesity, social anxiety disorder, and binge eating disorder are enrolling 3Q 2023

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

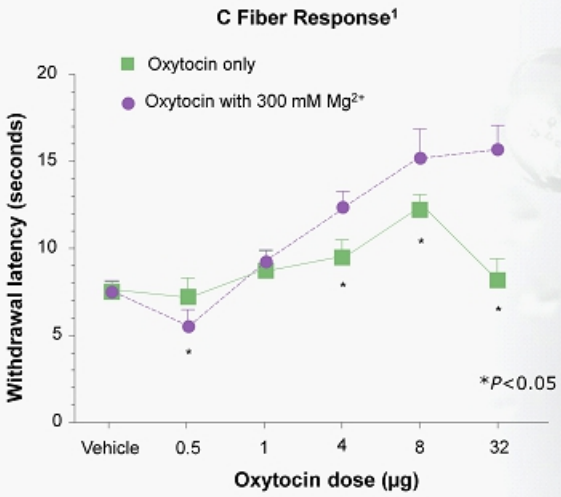
[1]Tzabazis et al., 2017. *Headache*. 57 Suppl 2:64-75
[2]Antoni et al., 1989. *Biochem J*. 257(2):611-4
[3]Meyerowitz et al., 2022. *Nat Struct Mol Biol*. (3):274-281
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

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

***In vivo* effect of Mg^{2+} ion addition with intranasal oxytocin-induced craniofacial analgesia on the withdrawal response time to noxious heat stimulation of the cheek of pre-inflamed rat[2]**



[1]Adapted from: Bharadwaj VN, et al. *Pharmaceutics*. 2022;14(5):1105.
[2]Oxytocin receptors are upregulated in response to stress, including inflammation

---

TNX-1900: Phase 2 PREVENTION Study Design

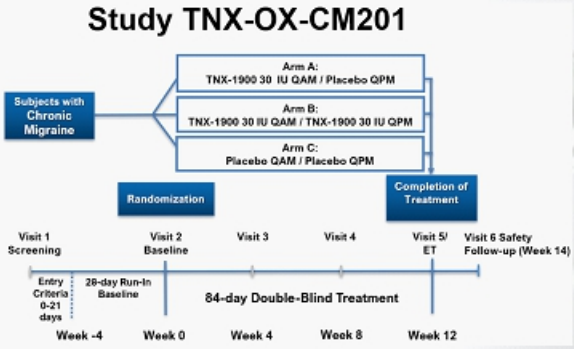
PREVENTION Study

General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms– two oxytocin treatment regimens and one placebo) in chronic migraine
- U.S. sites only
- Fully enrolled with 88 patients
- Topline results expected 4Q'23

Primary Endpoint:

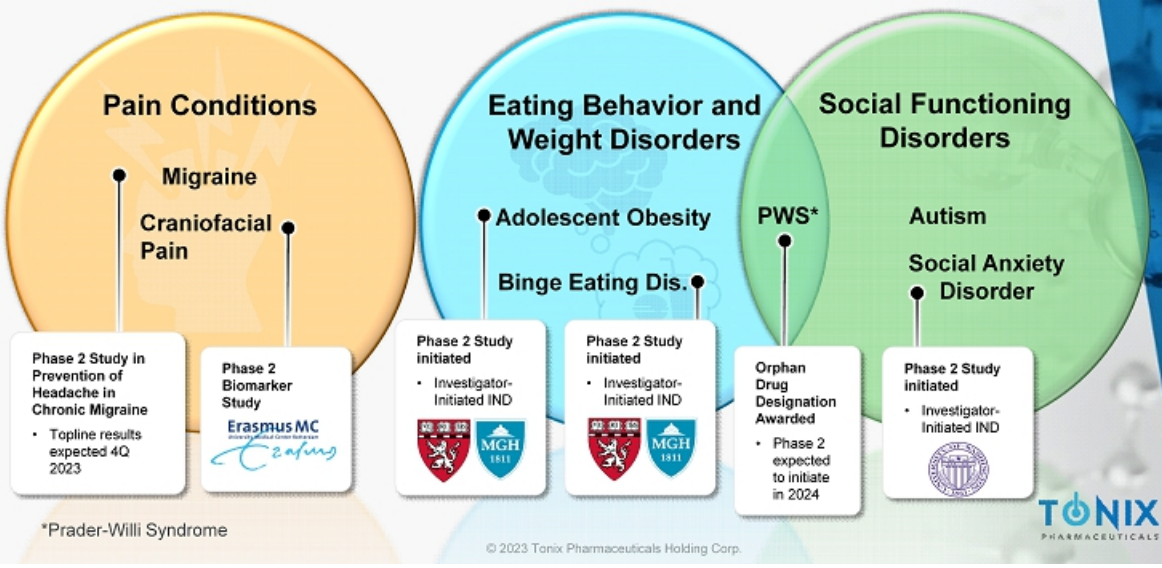
- Mean change in the number of migraine headache days between the 28-day Run-In phase and the last 28-days of the Treatment phase (TNX-1900 vs. placebo), analyzed via MMRM
- Threshold for achieving proof-of-concept is ES > 0.2



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

ES, effect size; MMRM, mixed models for repeated measures

Potential Applications of TNX-1900 and TNX-2900



*Prader-Willi Syndrome

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-601 ER for Depression	TNX-1900 for Chronic Migraine	TNX-102 SL for Fibromyalgia
Topline Results Expected – early November	Topline Results Expected – early December	Topline Results Expected – late December
Phase 2 Proof-of-Concept Study	Phase 2 Proof-of-Concept Study	***Phase 3 Potential NDA Enabling Study***
Registration-Quality		Registration-Quality

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
- Not scheduled with no recognized abuse potential

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) enrollment complete

Next Steps: Topline results expected late December 2023

Fibromyalgia-Type Long COVID

Status: Phase 2
- Phase 2 study (PREVAIL) enrollment complete

Next Steps: Topline results reported 3Q 2023

Planning End of Phase 2 Meeting with FDA 1Q 2024

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., predominantly 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[2]

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT enrollment complete

Next Steps: Topline results expected late December 2023

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

[1]American Chronic Pain Association (www.theacpa.org, 2019)
[2]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.

TONIX PHARMACEUTICALS

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 analyzed via MMRM with MI
- 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

*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)

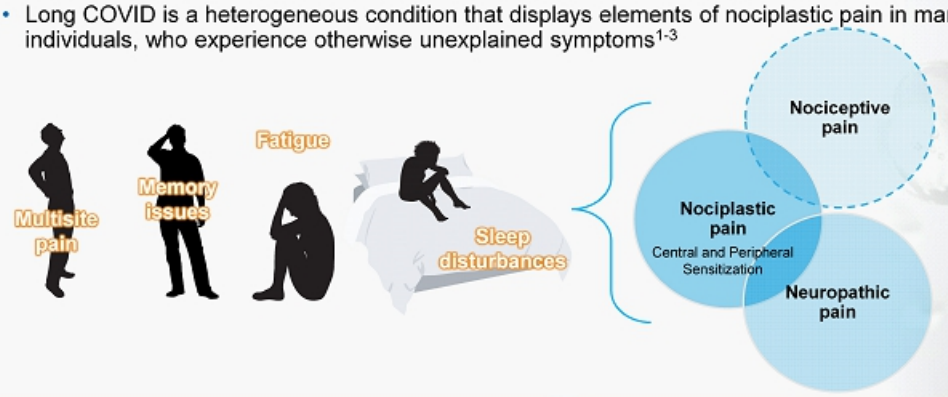
MMRM, mixed models for repeated measures; MI, multiple imputation

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[1-3]



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

Nociplastic pain[4]: (*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 et al., 2021. *J Prim Care Community Health*. 12:21501327211030826
[2]Moghimi et al., 2021. *Curr Neurol Neurosci Rep*. 21(9):44
[3]Thaweethai T, et al. 2023. JAMA. 2023 329(22):1934-1946
[4]Trouvin et al., 2019. *Best Pract Res Clin Rheumatol*. 33(3):101415

TONIX PHARMACEUTICALS

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

CNS PORTFOLIO

PROFILE

- Occurs in approximately 19% 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 ME/CFS

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 topline reported

Next Steps: End of Phase 2 Meeting with FDA expected 1st Quarter 2024

Patents Issued

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

[1]June 22, 2022- CDC - https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm
[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.

TONIX PHARMACEUTICALS

TNX-102 SL: Phase 2 PREVAIL Study Design
Proof-of-Concept Study

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, 63 patients enrolled

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: 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)"

TONIX PHARMACEUTICALS

PREVAIL Topline Results[1]

TNX-102 SL showed a robust effect size of 0.5 in improving fatigue and showed consistent activity across secondary measures of sleep quality, cognitive function, disability and Patient Global Impression of Change, but did not meet the primary endpoint of multi-site pain reduction at week 14

- There is currently no drug approved to treat Long COVID

TNX-102 SL 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

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

- Fatigue is the signature symptom of Long COVID and it has been identified as the dominant symptom contributing to disability[2]
- In both of our prior Phase 3 studies of TNX-102 SL 5.6 mg in fibromyalgia, we observed numerical improvement in the PROMIS fatigue score (in RELIEF p=0.007 MMRM and in RALLY p=0.007 MMRM)
- Although the validity of PROMIS Fatigue is not yet established in Long COVID, we believe the results of PREVAIL, together with extensive data from studies in other chronic conditions[3-5] – including Tonix's studies in fibromyalgia – make 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.

PREVAIL Next Steps

Tonix plans to meet with FDA to discuss a path to registration

- Expected date of End of Phase 2 meeting is 1st Quarter 2024

Fatigue is the principal symptom overlapping with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and fibromyalgia syndromes

- Expected date of fibromyalgia topline is late December 2023

TNX-102 SL*: Acute Stress Reaction (ASR)/ Acute Stress Disorder (ASD)
Cyclobenzaprine Protectic® Sublingual Tablets

CNS PORTFOLIO

PROFILE

ASR/ASD are acute stress conditions resulting from trauma

- Can affect both civilian and military populations
- 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]

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

Patents Issued

DEVELOPMENT PROGRAM

Target Indication: ASR/ASD

Status: Expect to start Phase 2 in 1Q 2024

Next Steps: Investigator-initiated IND

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

[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

TONIX PHARMACEUTICALS

TNX-102 SL*: ASR/ASD
Cyclobenzaprine Protectic® Sublingual Tablets

CNS PORTFOLIO

Significant unmet need

- 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
- Trauma patients include U.S. military exposed to life-threatening events or civilians who experienced traumatic events such as motor vehicle collisions

Rationale for TNX-102 SL Evaluation in Post-Traumatic Stress Disorder

- 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.
  - Primary analysis comparing change from baseline in Clinician-Administered PTSD Scale (CAPS-5) total severity between TNX-102 SL and placebo at week 12 was not significant.
- Across studies at week 4, TNX-102 SL treatment was associated with an improvement in CAPS-5 total severity as compared to placebo
- Secondary analyses showed TNX-102 SL treatment was associated with benefits on Clinical Global Impression – Improvement (CGI-I) scale at week 4 and the Patient Global Impression of Change scale at week 12
- The most common side-effects were administration-site reactions, reported as tongue/mouth numbness (~34%), tingling (~7%), and abnormal taste (~6%) in the active groups. No unexpected safety findings

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

[1]Sullivan GM, et al. *Psychiatry Research*. 2021;301, Article 113974
[2]Rauch SAM, et al. *J Clin Psychiatry*. 2021. 82(4):20m13752
[3]Ivanova A, et al. *Statistics*. 2022. 32:3, 441-449

TONIX PHARMACEUTICALS

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
- 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)

TONIX PHARMACEUTICALS

TONIX PHARMACEUTICALS

IMMUNOLOGY: KEY CANDIDATES

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 has not been approved for any indication. Patents filed.

Prevention of Allograft Rejection

Status: Phase 1 currently enrolling

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

Next Steps: Initiate Phase 2 study in Kidney Transplant Recipients

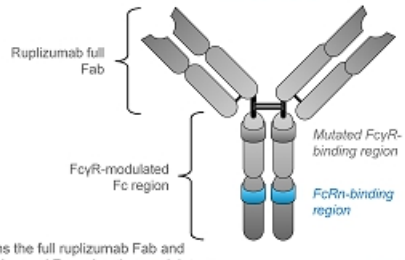
Autoimmune Diseases

Status: Planning for future indications including:

Sjögren's Syndrome, Systemic Lupus Erythematosus and Multiple Sclerosis

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

SELECTIVELY MODIFIED anti-CD40L AB



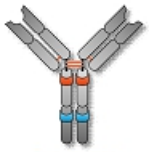
Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

TONIX PHARMACEUTICALS

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

IMMUNOLOGY PORTFOLIO

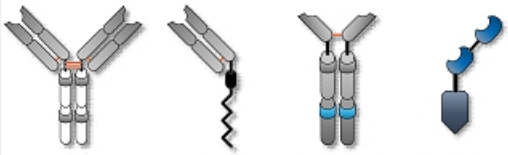
First-generation anti-CD40L mAbs



Ruplizumab

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

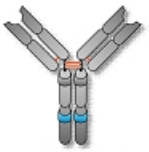
Second-generation anti-CD40L proteins



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 et al., 2003. *Circ Res.* 92(9):1041-1048
[2]Robles-Carrillo et al., 2010. *J Immunol.* 185(3):1577-1583
[3]Shock et al., 2015. *Arthritis Res Ther.* 17(1):234
[4]Xie et al., 2014. *J Immunol.* 192(9):4083-4092
[5]Ferrant et al., 2004. *Int Immunol.* 16(11):1583-1594
[6]Karnell et al., 2019. *Sci Transl Med.* 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, 2018. *Biocentury.*
[9]Company data

TONIX PHARMACEUTICALS

TNX-1500 anti-CD40L Monoclonal Antibody

Proposed indication - prevention of rejection in kidney transplant:

- Supported by pre-clinical studies

Phase 1 study initiated:

- A Phase 1 study of TNX-1500 was initiated in the third quarter of 2023.

Peer reviewed articles:

- Two articles have recently published in the *American Journal of Transplantation* that demonstrate TNX-1500 prolongs non-human primate renal and heart allograft survival.[1,2]

[1]Lassiter, G., et al. (2023). TNX-1500, a crystallizable fragment–modified anti-CD154 antibody, prolongs non-human primate renal allograft survival. *American Journal of Transplantation*. April 3, 2023. https://doi.org/10.1016/j.ajt.2023.03.022
[2]Miura, S., et al. (2023) TNX-1500, a crystallizable fragment–modified anti-CD154 antibody, prolongs non-human primate cardiac allograft survival. *American Journal of Transplantation*. April 6, 2023. https://doi.org/10.1016/j.ajt.2023.03.025

Other anti-CD40L Monoclonal Antibodies in Development

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) – positive results reported[1,2]
- Frexalimab, f.k.a.SAR441344 (Fc-modified)

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

- Two Positive Phase 2 studies reported[3,4]
- Dazodalibep (tn03 fusion protein)

Eledon – 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)

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

- Phase 3 Trial Currently Enrolling (NCT04294667)
  - Topline results expected 1H 2024[5]
- Dapirolizumab pegol (pegylated Fab)

[1]Sanofi press release May 31, 2023 "Press Release: Positive Phase 2 data of novel investigational anti-CD40L antibody frexalimab show significantly reduced disease activity in relapsing multiple sclerosis": www.sanofi.com/en/media-room/press-releases/2023/2023-05-31-05-00-00-2678891 (accessed August 11 2023)
[2]Carvalho, T. *Nature Medicine* (News) (2023). 29:1882
[3]Horizon press release September 12, 2022 "Horizon Therapeutics plc Announces Phase 2 Trial Evaluating Dazodalibep for the Treatment of Sjögren's Syndrome Meets Primary Endpoint" https://ir.horizontherapeutics.com/news-releases/news-release-details/horizon-therapeutics-plc-announces-phase-2-trial-evaluating (accessed August 11 2023)
[4]Horizon Press Release January 18, 2023 "Horizon Therapeutics plc Announces Phase 2 Trial Evaluating Dazodalibep for the Treatment of Sjögren's Syndrome Meets Primary Endpoint in the Second Study Population; Only Phase 2 Trial to Meet Primary Endpoint in Both Patient Populations
[5]https://www.ucb.com/our-science/pipeline

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

Internal Development & Manufacturing Capabilities

R&D Center (RDC) – Frederick, MD

- **Functions:**
  - Research advancing CNS and immunology drugs
  - Accelerated development of vaccines and antiviral drugs against COVID-19, its variants and other infectious diseases
- **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

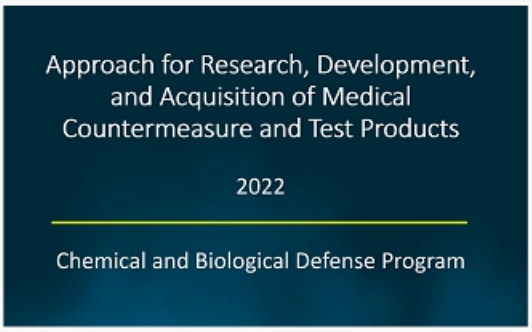
INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Broad Spectrum Antivirals

New DoD approach[1,2] raises importance of broad-spectrum medical counter measures

- Need to improve medical readiness of the warfighter in biological threat environments
- Beyond "one bug, one drug" approach
- Issued Dec 2022



[1]Vergun, D. DOD News. January 10, 2023. DoD aims to shield warfighters from novel biological agents. https://www.defense.gov/News/News-Stories/Article/Article/3261095/dod-aims-to-shield-warfighters-from-novel-biological-agents/

[2]US Department of Defense, Chemical and Biological Defense Program, "Approach for Research, Development and Acquisition of Medical Countermeasure and Test Products, Dec. 2022. https://media.defense.gov/2023/Jan/10/2003142624/-1/-1/0/APPROACH-RDA-MCM-TEST-PRODUCTS.PDF

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

DTRA RFP for Broad Spectrum Antivirals Through Medical CBRN

DTRA Through Medical CBRN Defense Consortium: New DoD approach raises importance of broad-spectrum medical counter measures

- MCDC issued a request for project proposals in the Fall of November 2021 on behalf of DTRA for, "Novel Biologics as Medical Countermeasures(MCM) against Biological Threats of Concern."

Who We Are

The Medical CBRN Defense Consortium (MCDC) was formed in response to the Government's expressed interest to establish an Other Transaction Agreement (OTA) with an eligible entity or group of entities, to include industry, academic, and not-for-profit partners, for advanced development efforts to support the Department of Defense's (DoD) medical, pharmaceutical and diagnostic requirements as related to enhancing the mission effectiveness of military personnel.

Through the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND), the Medical Countermeasures Systems (MCS) Joint Project Management Office is always looking for innovative, safe and effective medical solutions to counter CBRN threats. The usage of an OTA allows government to partner with the MCDC to leverage cutting edge R&D and develop prototypes from commercial sources. This gives MCS an agile and flexible way to develop medical countermeasures using new and innovative technology.

RFP = request for proposals
DTRA = Defense Threat Reduction Agency
CBRN = Chemical, Biological, Radiological and Nuclear

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

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

Mpox and Smallpox Vaccine

Status: Preclinical

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

Milestone: Successful completion of pre-IND meeting

Next Steps: Preparation of IND submission

Vaccine for Future Emerging Infectious Diseases

Example: TNX-1850 for COVID-19

Status: Model System

TONIX PHARMACEUTICALS

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

Massachusetts General Hospital · Harvard Medical School

TNX-1900: Binge Eating Disorder, Adolescent Obesity

TONIX PHARMACEUTICALS

Upcoming: Expected Topline Clinical Data and Trial Initiations 2023

4th Quarter

- **Phase 2 UPLIFT study of TNX-601 ER for major depressive disorder – expected early November**
  - Affects approximately 47 M adults in the U.S (18.4% of population)[1]
- **Phase 2 PREVENTION study of TNX-1900 for chronic migraine – expected early December**
  - Affects approximately 3-7 M adults in the U.S[2]
- **Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia – expected late December**
  - Affects approximately 6-12 M adults in the U.S[3]

3rd Quarter Clinical Trial Initiations

- **Phase 1 study of TNX-1500 for prevention of allograft rejection - started**

4th Quarter Clinical Trial Initiations

- **Phase 2 study of TNX-1300 for the treatment of cocaine intoxication - expected**

[1]CDC - https://www.cdc.gov/mmwr/volumes/72/wr/mm7224a1.htm?s_cid=mm7224a1_w
[2]Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[3]American Chronic Pain Association (www.theacpa.org, 2019)

TONIX PHARMACEUTICALS

THANK YOU

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.

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.

TONIX PHARMACEUTICALS