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 11, 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, NJ 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Tonix Pharmaceuticals Holding Corp. (the "Company") updated its investor presentation, which is used to conduct meetings with investors, stockholders and analysts and at investor conferences, and which the Company intends to place on its website, which may contain nonpublic information. A copy of the presentation is filed as Exhibit 99.01 hereto and incorporated herein by reference.

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

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	**Description.**
99.01	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 11, 2023

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

Exhibit 99.01

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.

TONIX PHARMACEUTICALS

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-102 SL[1]	Fibromyalgia (FM) Long COVID (PASC[2])	Mid-Phase 3 – enrollment complete Phase 2 – Topline Reported
TNX-1300[3]	Cocaine Intoxication - *FDA Breakthrough Designation*	Mid-Phase 2, Targeted 4Q 2023 Start
TNX-1900[4]	Prevention of Chronic Migraine	Phase 2 – enrollment complete[5]
TNX-601 ER	Depression	Phase 2 – enrollment complete[6]
TNX-2900[7]	Prader-Willi Syndrome - *FDA Orphan Drug Designation*	Phase 2 ready
TNX-1500[8]	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1 – currently enrolling

**All of Tonix's product candidates are investigational new drugs or biologics and none has been approved for any indication.*
[1]TNX-102 SL (cyclobenzaprine HCl sublingual tablets) also has active INDs for Agitation in Alzheimer's Disease (AAD), Alcohol Use Disorder (AUD), and Posttraumatic Stress Disorder (PTSD). All indications are Phase 2 ready.
[2]Post-Acute Sequelae of COVID-19.
[3]TNX-1300 (double-mutant cocaine esterase) is licensed from Columbia University.
[4]Acquired from Trigemina; license agreement with Stanford University; Planned investigator-initiated Binge Eating Disorder (BED) study initiated 3Q 2023.
[5]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900
[6]Phase 1 trial for formulation development was completed outside of the U.S.; Other potential indications include PTSD and neurocognitive dysfunction from steroids
[7]Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)
[8]anti-CD40L humanized monoclonal antibody – IND cleared

TONIX PHARMACEUTICALS

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-102 SL for Fibromyalgia

Topline Results Upcoming

Phase 3 Potential NDA Enabling Study

Registration-Quality

TNX-1900 for Chronic Migraine

Topline Results Upcoming

Phase 2 Proof-of-Concept Study

Registration-Quality

TNX-601 ER for Depression

Topline Results Upcoming

Phase 2 Proof-of-Concept Study

Registration-Quality

TONIX PHARMACEUTICALS

TONIX MEDICINES: MARKETED PRODUCTS

Two Marketed Proprietary Migraine Drugs
Autoinjector and Nasal Spray (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)

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]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):1271-1276.
[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.

Administration of Zembrace and Tosymra Bypass the GI Tract

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 products
- Imitrex® nasal spray (sumatriptan)
- 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]
  - Precision Olfactory Delivery (POD) technology targets vascular-rich upper nasal space

[1]Pfizer Press Release March 10, 2023. – https://www.pfizer.com/news/press-release/press-release-detail/pfizers-zavzprettm-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/

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 4Q 2023

Fibromyalgia-Type Long COVID

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

Next Steps: Topline results reported 3Q 2023

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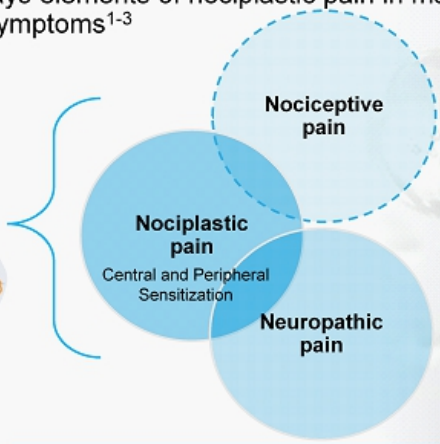
Fibromyalgia-Type Long COVID

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

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

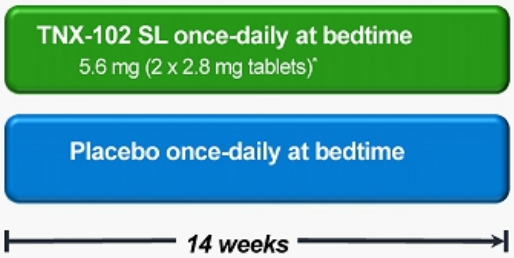
CNS PORTFOLIO

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



*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: Demographics and Baseline Characteristics

CNS PORTFOLIO

Demographics and Baseline Characteristics

Variable	Placebo N=31	TNX-102 SL N=32	Total N=63
Age, mean years (SD)	51.4 (10.01)	48.6 (8.80)	50.0 (9.45)
Female, number (%)	25 (80.6%)	21 (65.6%)	46 (73.0%)
Male, number (%)	6 (19.4%)	11 (34.4%)	17 (27.0%)
Ethnicity			
Hispanic or Latino	3 (9.7%)	2 (6.3%)	5 (7.9%)
Not Hispanic or Latino	28 (80.6%)	30 (93.8%)	58 (92.1%)
Race			
American Indian or AN, number (%)	1 (3.2%)	0 (0.0%)	1 (1.6%)
Asian, number (%)	0 (0.0%)	1 (3.1%)	1 (1.6%)
Black or African American, number (%)	5 (16.1%)	7 (21.9%)	12 (19.0%)
Native Hawaiian or PI, number (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
White or Caucasian, number (%)	24 (77.4%)	21 (65.6%)	45 (71.4%)
Multiple Races, number (%)	1 (3.2%)	3 (9.4%)	4 (6.3%)
BMI, mean kg/m^2 (SD)	29.5 (4.44)	29.8 (4.07)	29.6 (4.22)
Employed, number (%)	26 (83.9%)	25 (78.1%)	51 (81.0%)

Abbreviations: AN, Alaskan Native; BMI, body mass index; PI, Pacific Islander; SD, standard deviation

[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ

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.

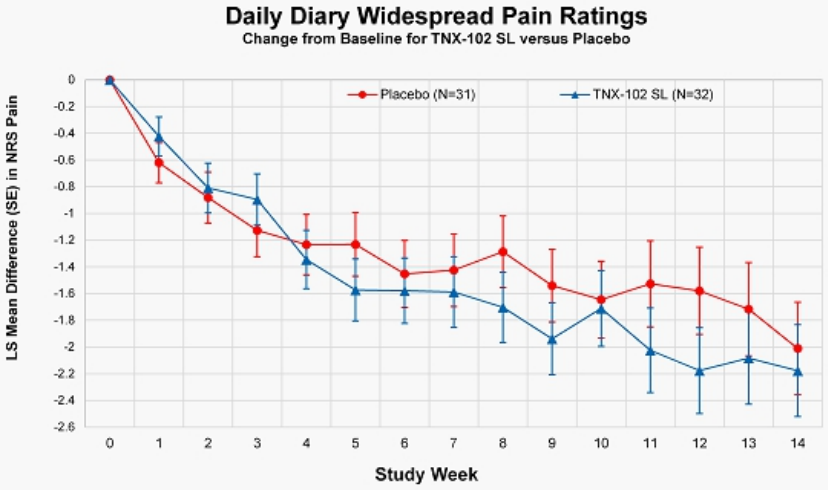
- AE-related discontinuations were similar in drug and placebo arms.
- No new safety signals were observed

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.

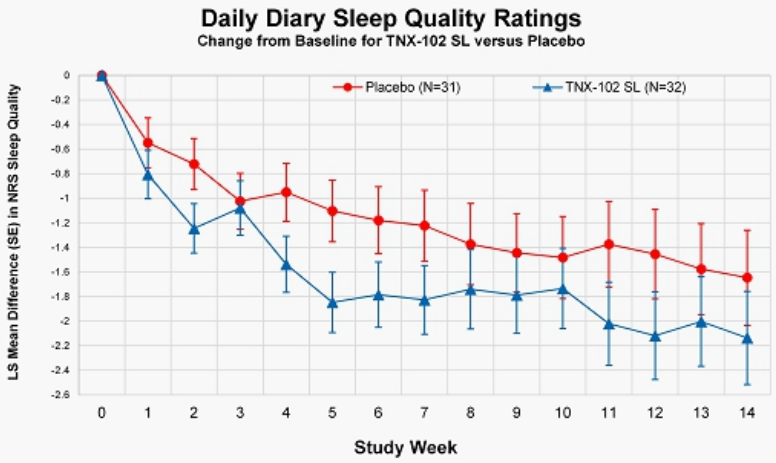
[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ
[2]Walker S, *et al. BMJ Open* 2023;13:e069217. doi:10.1136/ bmjopen-2022-069217
[3]Cook, K.F., et al. 2016. *Journal of Clinical Epidemiology*, 73, 89- 102
[4]Cella, D., et al. 2016. *Journal of Clinical Epidemiology*, 73, 128–134
[5]Lai, J.S., et al. 2011. *Archives of Physical Medicine and Rehabilitation*, 92(10 Supplement), S20-S27.

Primary Endpoint: Weekly Summary of Daily Pain Scores[1-3]



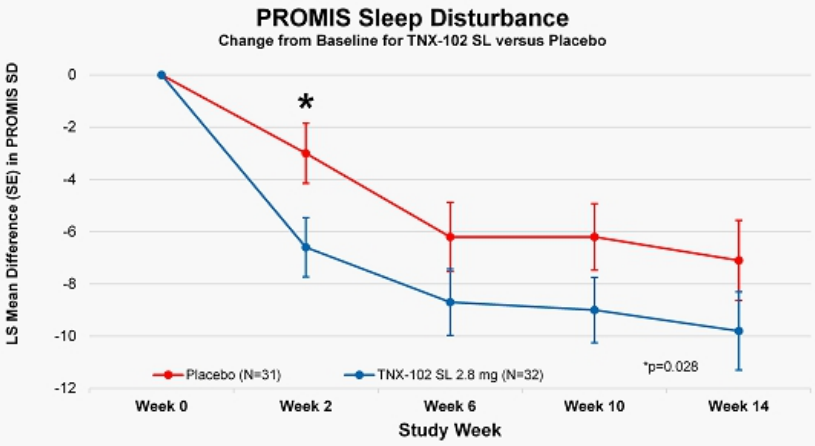
[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ
[2]Change from baseline in the diary numerical rating scale (NRS) weekly average of daily self-reported worst Long COVID pain intensity scores for TNX-102 SL versus placebo; Mixed Model for Repeated Measures (MMRM). Abbreviations: LS, least squares; SE, standard error.
[3]Primary endpoint, at week 14 (effect size (ES) = 0.08

PREVAIL: Weekly Summary of Daily Sleep Scores[1-3]



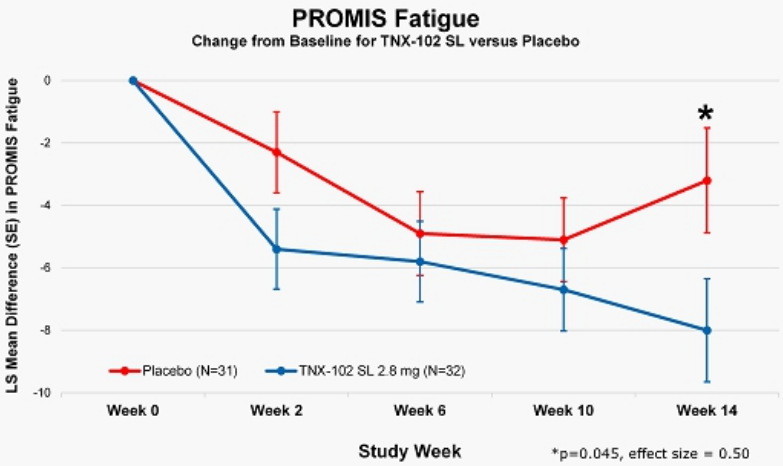
[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ
[2]Change from baseline in the diary numerical rating scale (NRS) weekly average of daily self-reported sleep quality scores for TNX-102 SL versus placebo; Mixed Model for Repeated Measures (MMRM). Abbreviations: LS, least squares; SE, standard error.
[3]Pre-specified secondary endpoint, at week 14 (effect size (ES) = 0.23

PREVAIL: PROMIS Sleep Disturbance[1,2]



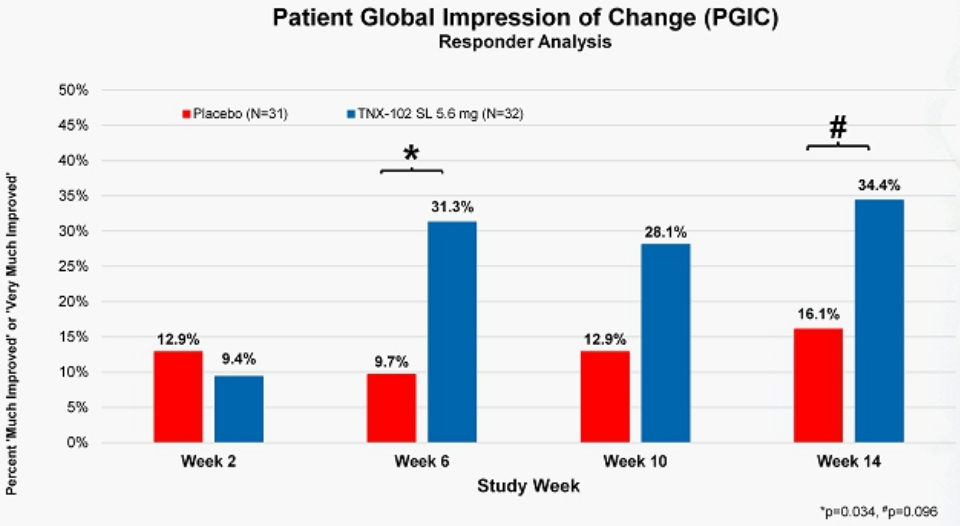
[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ
[2]Mixed Model for Repeated Measures (MMRM). Abbreviations: LS, least squares; SE, standard error; SD, sleep disturbance

PREVAIL: PROMIS Fatigue Score[1-5]



[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ
[2]Mixed Model for Repeated Measures (MMRM), Abbreviations: LS, least squares; SE, standard error
[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: Patient Global Impression of Change – Responder Analysis (Very Much Improved or Much Improved)[1]



[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ

PREVAIL: Adverse Events[1]

Adverse Events Occurring in ≥ 2 Participants in Either Treatment Group

		Placebo N=31	TNX-102 SL N=32	Total N=63
Administration Site Reactions				
	Hypoaesthesia oral	0	6	6
	Product taste abnormal	0	3	3
	Glossodynia	0	2	2
	Oral pain	0	2	2
	Paraesthesia oral	0	2	2
Systemic Adverse Events				
	Influenza like illness	2	0	2

[1]Tonix Press Release, September 5, 2023 - https://bit.ly/3Z6FQHQ

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 4th Quarter 2023

Upcoming Expected Topline Results

Fourth Quarter
2023

TNX-102 SL for Fibromyalgia
Topline Results Upcoming
Phase 3 Potential NDA Enabling Study
Registration-Quality

TNX-1900 for Chronic Migraine
Topline Results Upcoming
Phase 2 Proof-of-Concept Study
Registration-Quality

TNX-601 ER for Depression
Topline Results Upcoming
Phase 2 Proof-of-Concept Study
Registration-Quality

TONIX PHARMACEUTICALS

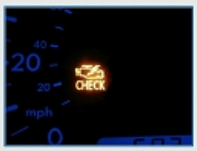
TNX-102 SL*: Fibromyalgia
Cyclobenzaprine Protectic® Sublingual Tablets

CNS PORTFOLIO

PROFILE

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

- Afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women[1]
- Symptoms include chronic widespread pain, nonrestorative sleep, fatigue, and cognitive dysfunction
- Patients struggle with daily activities, have impaired quality of life, and frequently are disabled
- Physicians and patients report common dissatisfaction with currently marketed products



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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia

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

Status: One Positive Phase 3 study RELIEF completed[2]

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT enrollment complete

Next Steps: Topline results expected 4Q 2023

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

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

Key Secondary Endpoints:

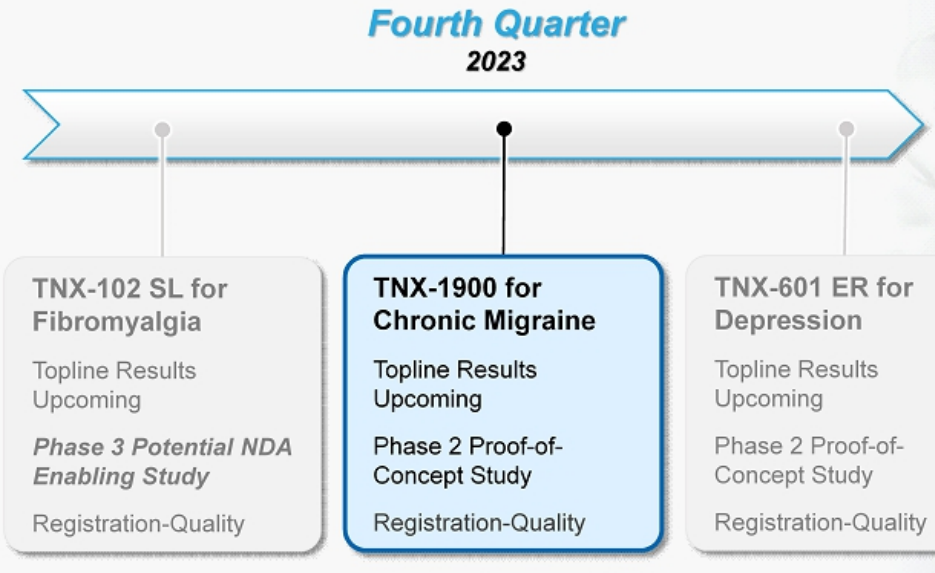
- Fibromyalgia Impact Questionnaire - Revised (FIQ-R) Symptom Domain score
- Patient Global Impression of Change responder analysis
- FIQ-R Function Domain score
- PROMIS Sleep Disturbance instrument
- PROMIS Fatigue instrument
- Weekly average of the daily diary assessment of sleep quality

*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

Upcoming Expected Topline Results



TONIX PHARMACEUTICALS

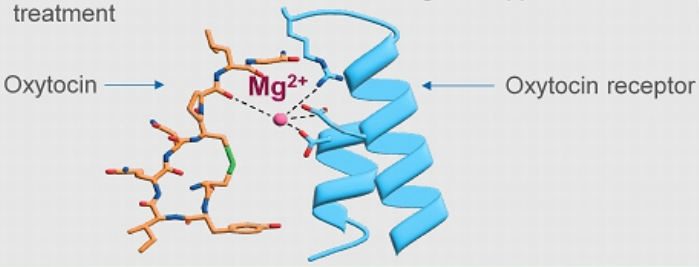
TNX-1900*: Prevention of Headache in Chronic Migraine
Intranasal Potentiated Oxytocin (OT) with Magnesium

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 4Q 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

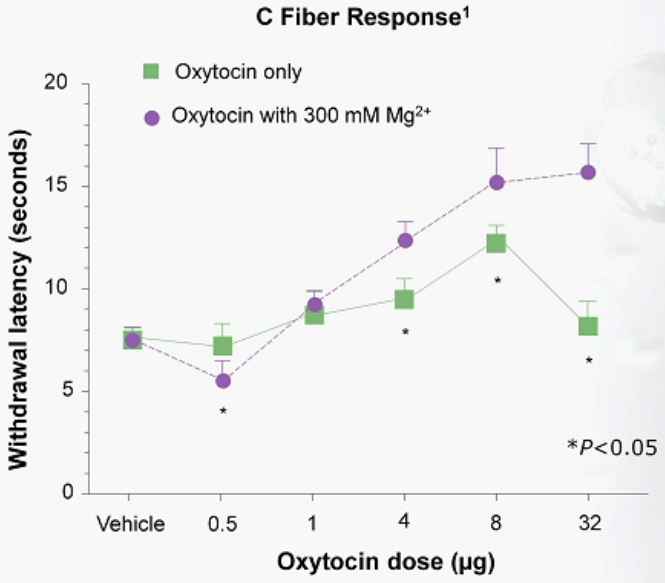
TONIX PHARMACEUTICALS

Oxytocin Effects – Addressing the "Inverted U" Dose Response
Addition of Mg^{2+} Augments Oxytocin-Induced Analgesia in Animal Model

CNS PORTFOLIO

- 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**



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

TONIX PHARMACEUTICALS

TNX-1900: Phase 2 PREVENTION Study Design

PREVENTION Study

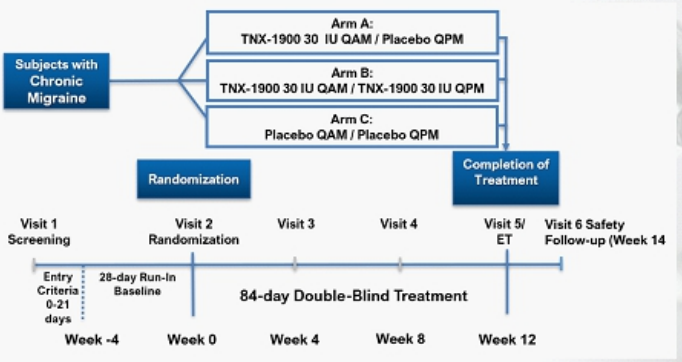
CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms– two 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)

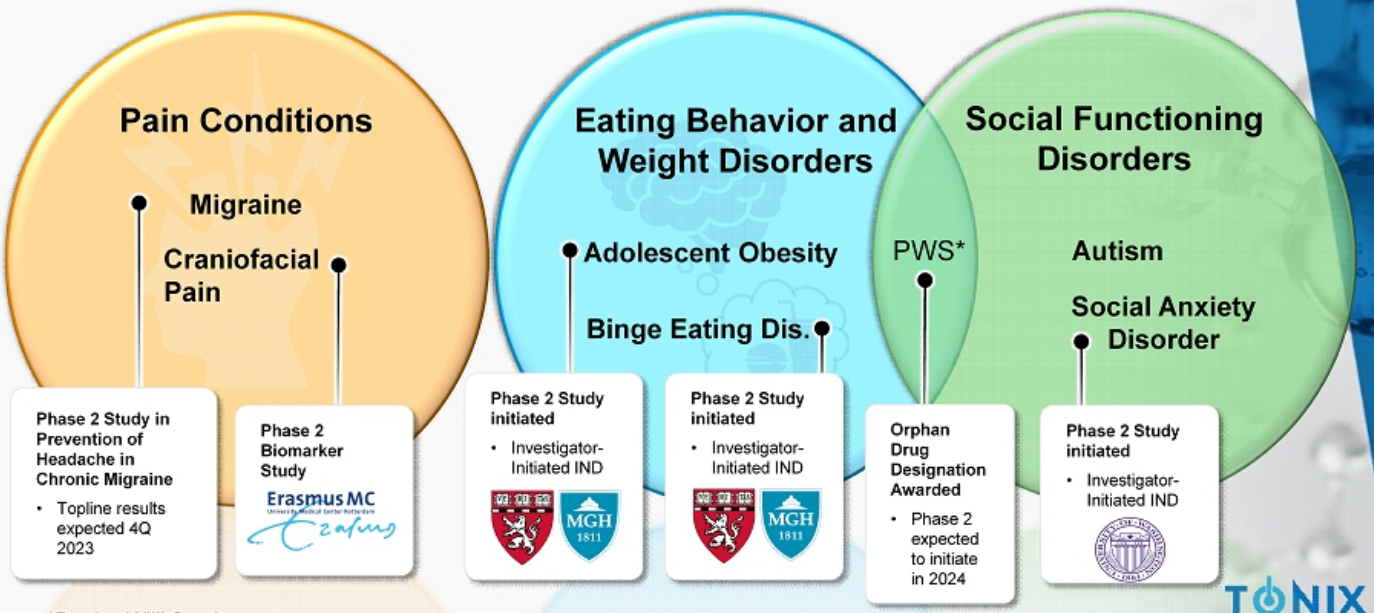


ClinicalTrials.gov Identifier: NCT05679908
A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)

TONIX PHARMACEUTICALS

Potential Applications of TNX-1900 and TNX-2900

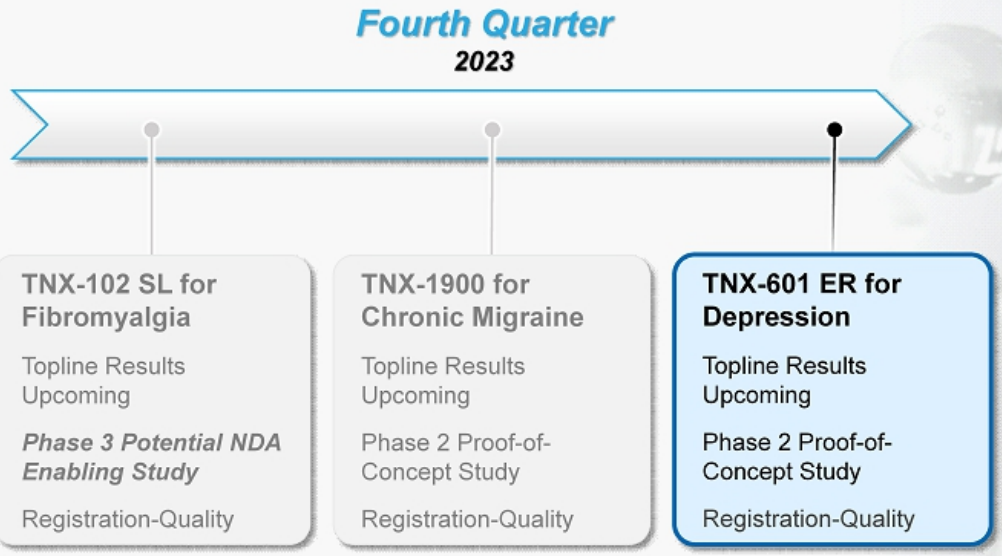
CNS PORTFOLIO



*Prader-Willi Syndrome

TONIX PHARMACEUTICALS

Upcoming Expected Topline Results



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 Disorder From Corticosteroids, Alzheimer's Disease[3]

Status: Phase 2 MDD study UPLIFT enrollment complete

Next Steps:

Topline results expected 4Q 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®, www.servier.ci/sites/default/files/spc-pil/SPC_Stablon_1.pdf accessed 7-16-23.
[3]Garcia-Alberca et al., 2022. *J Alzheimers Dis.* 88(2):707-720

TNX-601 ER - Phase 2 UPLIFT* Study Design

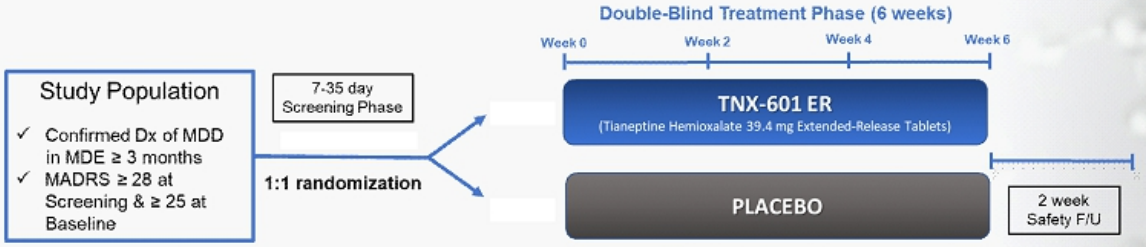
UPLIFT Study

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Major Depressive Disorder to evaluate monotherapy with TNX-601 ER versus placebo
- Parallel design with two arms – treatment with tianeptine hemioxalate 39.4 mg or placebo
- 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



*ClinicalTrials.gov Identifier: NCT05686408

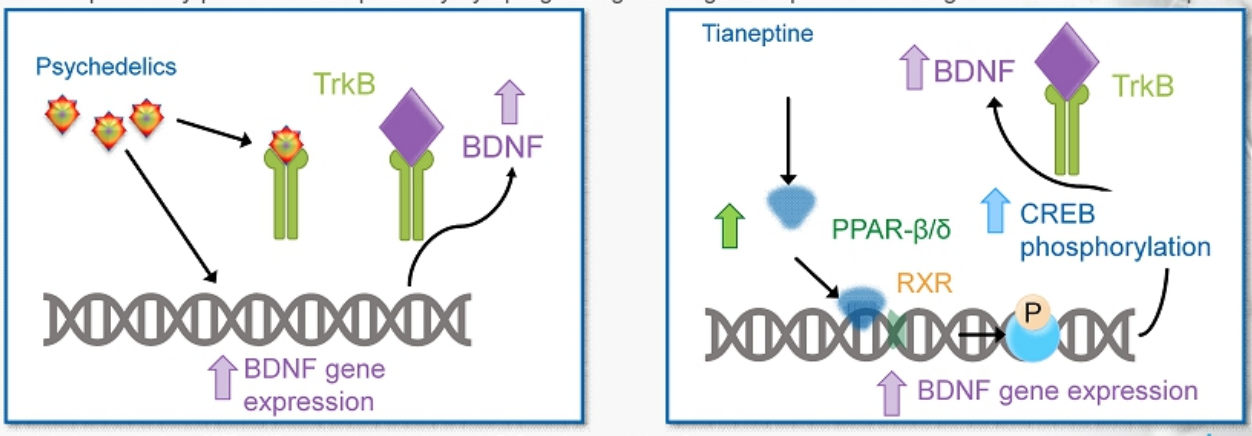
Abbreviations: Dx, diagnosis; ER, extended-release; F/U, follow-up; MDD, major depressive disorder; MDE, major depressive episode; N, number

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 mirrorr-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 opiate liability[4]
- New mechanism of action for treating depression

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

	Racemic-Tianeptine	*(S)*-Tianeptine TNX-4300	*(R)*-Tianeptine
Activates PPAR-β/δ	+	+	-
Neuroplasticity	+	+	-
Novel Object 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 G et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. https://bit.ly/42o3jnV
[5]Rat Novel Object Recognition Test
[6]Mouse Porsolt Forced Swim Test

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

PROFILE

- Single isomer, oral treatment
- Proposed mechanism of action from lab studies indicates estianeptine is the active ingredient of TNX-601 ER[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]

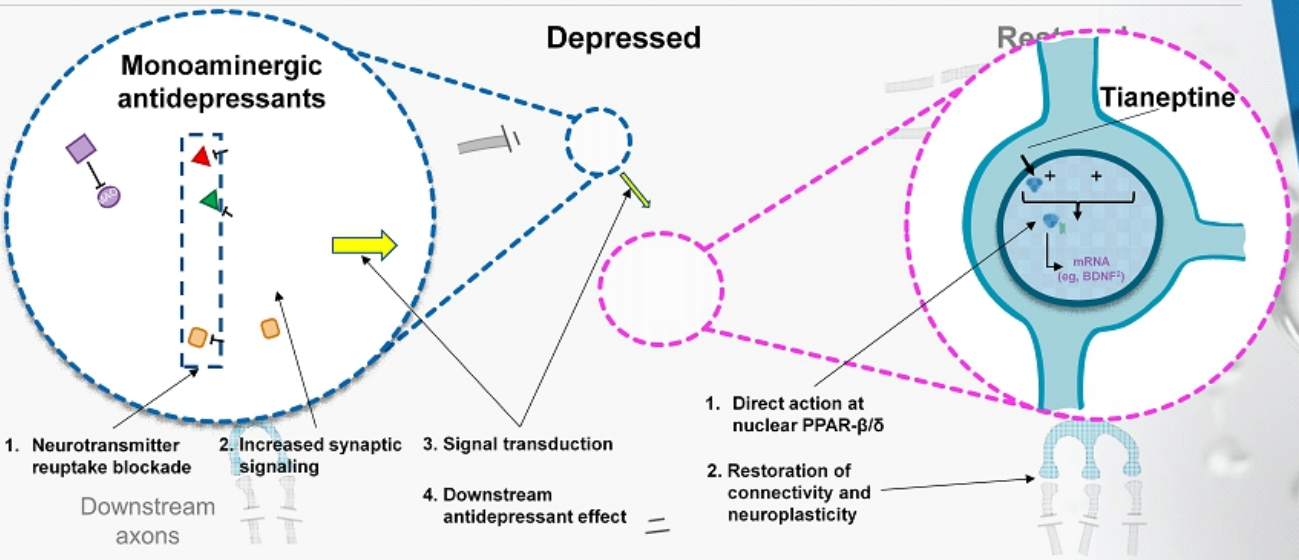
Status: Pre-clinical

Next Steps: Expect IND can 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 G 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

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



[1]Sullivan G 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

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

CNS PORTFOLIO

PROFILE

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

CocE is a recombinant protein that degrades cocaine in the bloodstream

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

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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Cocaine Intoxication

Status: Mid-Phase 2

Next Steps: Initiate new Phase 2 trial 4Q 2023

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

FDA Breakthrough Therapy Designation

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

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

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

TONIX PHARMACEUTICALS

TNX-1500*

Next Generation α-CD40 Ligand (CD40L) Antibody

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

Differentiators: Expected to deliver efficacy without compromising safety

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

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

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

*TNX-1500 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

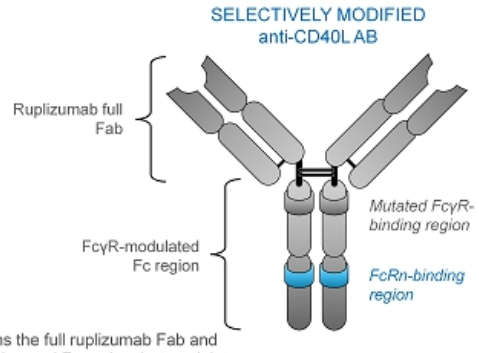
Next Steps: Initiate Phase 2 study in Kidney Transplant Recipients

Autoimmune Diseases

Status: Potential future indications include:

Sjögren's Syndrome, Systemic Lupus Erythematosus

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

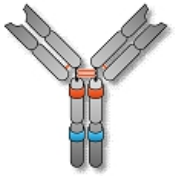


Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

TONIX PHARMACEUTICALS

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

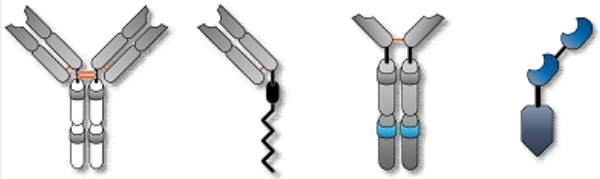
First-generation
anti-CD40L mAbs



Ruplizumab

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

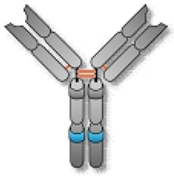
Second-generation
anti-CD40L proteins



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

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/2023/2023-05-31-05-00-00-2678991 (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-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

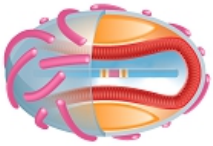
Next Steps: Preparation of IND submission

Vaccine for Future Emerging Infectious Diseases

Example: TNX-1850 for COVID-19

Status: Model System

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

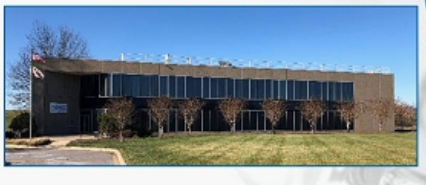


TONIX PHARMACEUTICALS

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

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

Kansas State University

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

TONIX PHARMACEUTICALS

Upcoming: Expected Topline Clinical Data and Trial Initiations 2023

4th Quarter

- **Phase 2 PREVENTION study of TNX-1900 for chronic migraine**
  - Affects approximately 3-7 M adults in the U.S[2]
- **Phase 2 UPLIFT study of TNX-601 ER for major depressive disorder**
  - Affects approximately 47 M adults in the U.S (18.4% of population)[3]
- **Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia**
  - Affects approximately 6-12 M adults in the U.S[4]

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/nchs/pressroom/nchs_press_releases/2022/20220622.htm
[2]Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalagia, 2010, 30:599-609
[3]CDC - https://www.cdc.gov/mmwr/volumes/72/wr/mm7224a1.htm?s_cid=mm7224a1_w
[4]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