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): January 2, 2024

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.

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 8.01 Other Events.

The Company expects a decision by the U.S. Food and Drug Administration on the new drug application for its TNX-102 SL (cyclobenzaprine HCl sublingual tablets) product candidate for the management of fibromyalgia in the second half of 2025.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	**Description.**
99.01	Corporate Presentation by the Company for January 2024
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: January 2, 2024

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.

Who We Are

Focus on Filing the New Drug Application (NDA) to the US Food and Drug Administration (FDA) for TNX-102 SL for Fibromyalgia

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

TONIX PHARMACEUTICALS

CNS-Focused Biopharma with Preclinical to Commercial Stage Products

TNX-102 SL for Fibromyalgia: Preparing New Drug Application (NDA)

- Two positive Phase 3 trials completed
- NDA filing expected 2H'24
- FDA decision on NDA approval expected 2H'25

Marketed Products

- Zembrace® and Tosymra® indicated for the treatment of acute migraine

Strategic Partnerships

- With government institutions, world-class academic & research organizations

Pipeline

- Phase 2 biologic cocaine antidote, FDA "Breakthrough Therapy Designation"
- Phase 1 anti-CD40L monoclonal antibody to prevent organ transplant rejection

Internal Capabilities

- Commercial prescription drug sales
- R&D and clinical-trial scale manufacturing

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Clinical Portfolio: Tonix-Sponsored Programs

Molecule*	Indication	Phase 1	Phase 2	Phase 3	NDA Submission
TNX-102 SL Cyclobenzaprine Protectic® Sublingual Tablets	Fibromyalgia (FM)	*Positive Phase 3 Topline Results Reported 4Q'23*			Expected 2H'24
TNX-1300 Cocaine Esterase	Cocaine Intoxication	*Phase 2 Study Start Expected 1Q'24*			
TNX-1500 Anti-CD40L mAb	Organ Transplant Rejection and Autoimmune Conditions	*Phase 1 Study Ongoing*			
TNX-2900 Intranasal Potentiated Oxytocin	Prader Willi Syndrome	IND Cleared for Phase 2 Study			

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

TONIX PHARMACEUTICALS

TNX-102 SL

Cyclobenzaprine (Protectic®)

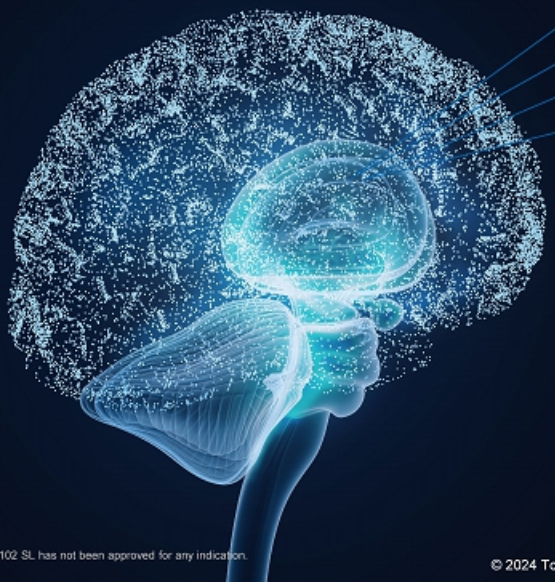
A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

TONIX PHARMACEUTICALS

TNX-102 SL: Unique MOA Facilitates Restorative Sleep

Centrally Acting Analgesic

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



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

Key Differentiators

Relative to Oral Cyclobenzaprine

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

Relative to Standard of Care

- Potential for better tolerability while maintaining efficacy
- Not scheduled nor with recognized abuse potential

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

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About Fibromyalgia

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

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

Large unmet need:

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

Current standard of care:

- FDA-approved products include Lyrica®, Cymbalta®, and Savella® - each approved 10 or more years ago
- Fewer than half of those treated for fibromyalgia receive sustained benefit from the approved drugs[3]
  - Majority (60%) fail therapy due to lack of a response (25%) or poor tolerability (35%)[4]
  - Opioid usage is not uncommon

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

Fibromyalgia Program Status

TNX-102 SL
Cyclobenzaprine Protectic®
Sublingual Tablets

Fibromyalgia — ***Positive 2nd Phase 3 Topline Results Reported 4Q'23***

1) **Positive Phase 3 study (*RELIEF*) reported – December 2020[1]**
2) Second Phase 3 study (*RALLY*) missed primary endpoint
   - Unexpected increase in adverse event-related discontinuations in both drug and placebo arms, potentially due to recruiting during COVID-19
3) **Positive 2nd (confirmatory) Phase 3 study (*RESILIENT*) reported – December 2023**

Next Steps:
Pre-NDA meeting with FDA expected 1H'24
NDA filing expected 2H'24
FDA decision on NDA approval expected 2H'25

*TNX-102 SL has not been approved for any indication.
[1]Lederman et al., (2023) *Arthritis Care & Research* "Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results From the RELIEF Trial". doi: 10.1002/acr.25142. Epub ahead of print. PMID: 37165930.

TNX-102 SL: Phase 3 *RESILIENT* Study Design

RESILIENT Study

CNS PORTFOLIO

General study characteristics:

- Randomized, double-blind, multicenter, placebo-controlled study in fibromyalgia
- 33 U.S. sites enrolled 457 participants with fibromyalgia as defined by 2016 Revisions to the 2010/2011 FM Diagnostic Criteria[1]

Primary Endpoint:

- Change from baseline to Week 14 (TNX-102 SL vs. placebo) in weekly averages of daily diary average pain severity score
- ***Primary Endpoint, p-value = 0.00005***

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

Placebo once-daily at bedtime

14 weeks

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

ClinicalTrials.gov Identifier: **NCT05273749**

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

Trial ID: TNY-CY-F307 ('RESILIENT')

[1]Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, Mease PJ, Russell AS, Russell IJ, Walitt B. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016; 46(3):319-329.

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RESILIENT Primary Outcome Measure
Reduction in Widespread Pain

RESILIENT Study

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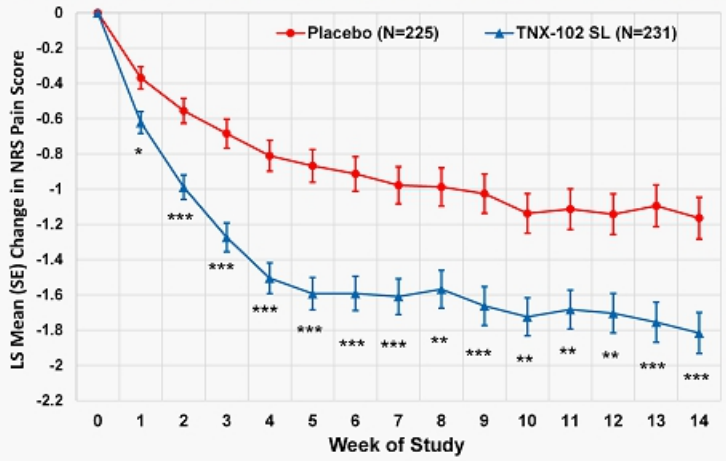
Weekly Average of Daily Diary NRS Ratings of Average Pain Over Prior 24 Hours



*p<0.01; **p<0.001; ***p<0.0001

Week 14 LS mean (SE) change from baseline for TNX-102 SL -1.82 (0.12) and for placebo -1.16 (0.12); LSMD from placebo -0.65 (0.16); **p=0.00005**[#]

[#]Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction. Abbreviations: LS, least squares; LSMD, least squares mean difference; NRS, numerical rating scale; SE, standard error

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RESILIENT Pre-Specified Primary Endpoint

RESILIENT Study

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Summary

- **TNX-102 SL demonstrated statistically significant improvement in mean weekly pain scores over placebo at Week 14**
- ***P*-value of *0.00005* is *highly* statistically significant**

Additional Findings

- **Effect size 0.38**
- **All pre-specified sensitivity analyses of the primary endpoint show statistical significance ($p \leq 0.001$)**
- **Rapid onset of action: *p*-values <0.01 at each weekly time point, including Week 1**

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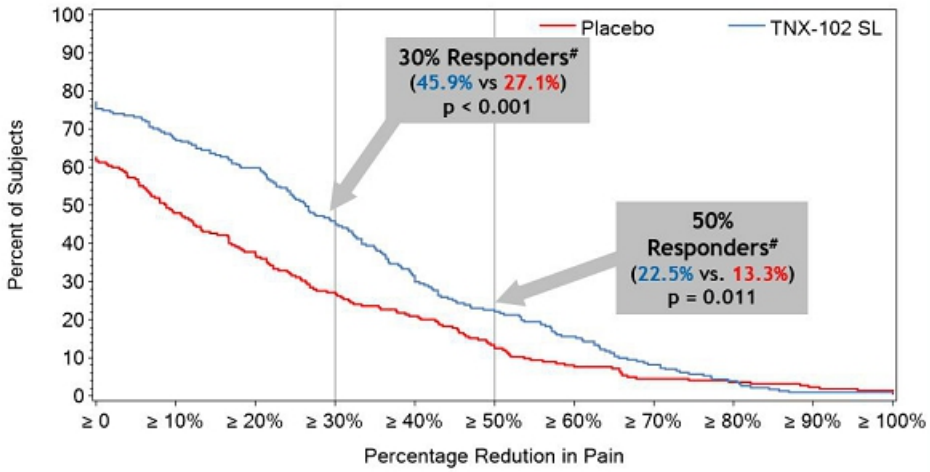
RESILIENT Continuous Pain Responder Graph

RESILIENT Study

CNS PORTFOLIO



#Analyses: Pearson's Chi Squared test for equality of proportions
Abbreviations: CI, confidence interval; DIP, difference in proportions
^pre-specified analyses but not key secondary analyses

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Summary of Key Pre-Specified Secondary Outcome Measures

Rating Scale	Week 14	Met**
Patient Global Impression of Change (PGIC)	*p < 0.001*	✓
Fibromyalgia Impact Questionnaire - Symptoms	*p < 0.001*	✓
Fibromyalgia Impact Questionnaire - Function	*p = 0.001*	✓
PROMIS Sleep Disturbance	*p < 0.001*	✓
PROMIS Fatigue	*p < 0.001*	✓
Weekly average of daily Sleep Quality scores	*p < 0.001*	✓

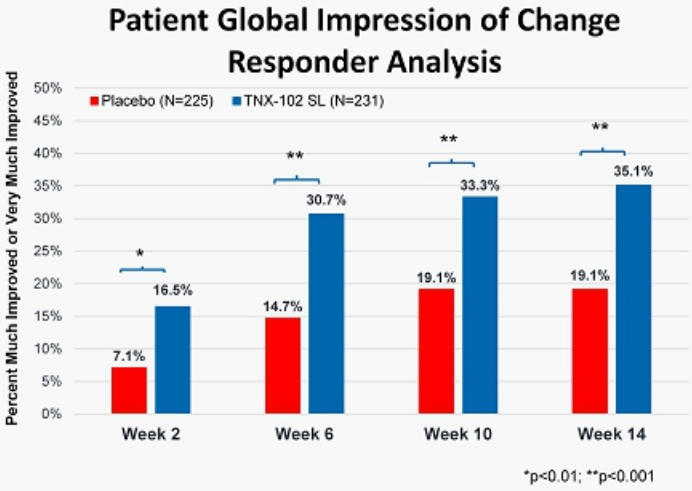
*In order of statistical serial gate-keeping hierarchy (or, "waterfall") to control overall Type 1 error
**Statistical significance met

CNS PORTFOLIO

RESILIENT Study TONIX PHARMACEUTICALS

RESILIENT Patient Global Impression of Change
Key Secondary Outcome Measure

RESILIENT Study



*p<0.01; **p<0.001

Week 14 TNX-102 SL responders 35.1%, and placebo responders 19.1%; difference in proportions (95% CI) 16% (7.9%, 24.0%); **p=0.00013#**

#Based on a Pearson Chi-Squared with differences in proportions 95% CIs from difference in proportions Z-test
Responders defined as subject that reply 'very much improved' or 'much improved' at Week 14; all others are non-responders
CI, confidence interval

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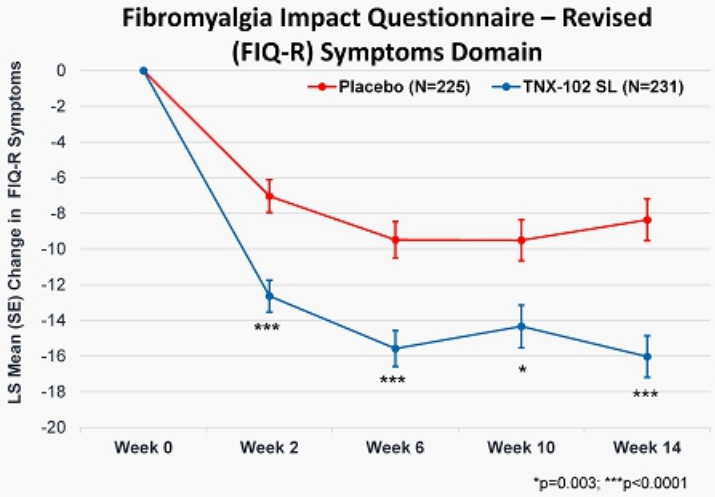
RESILIENT FIQ-R Symptoms Domain
Key Secondary Outcome Measure

RESILIENT Study



Week 14 LS mean (SE) change from baseline for TNX-102 SL -16.0 (1.17) and for placebo -8.4 (1.17); LSMD from placebo -7.7 (1.62); **p=0.000002[#]**

[#]Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction.

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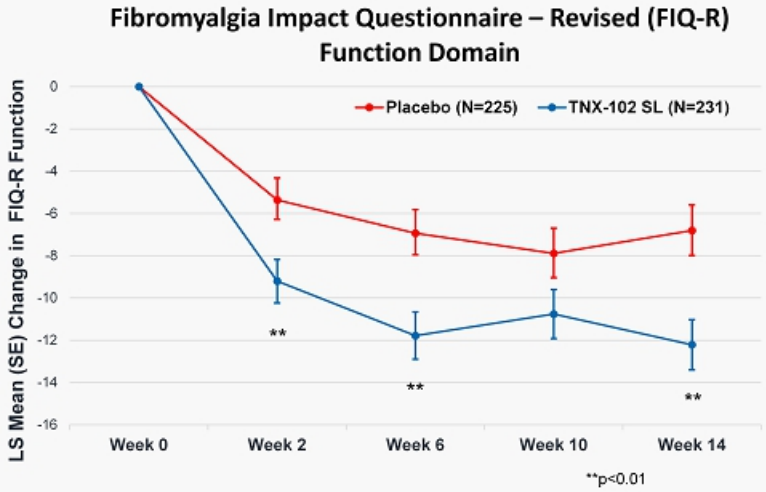
RESILIENT FIQ-R Function Domain
Key Secondary Outcome Measure

RESILIENT Study



Week 14 LS mean (SE) change from baseline for TNX-102 SL -12.2 (1.19) and for placebo -6.8 (1.21); LSMD from placebo -5.4 (1.66); **p=0.001[#]**

[#]Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction.

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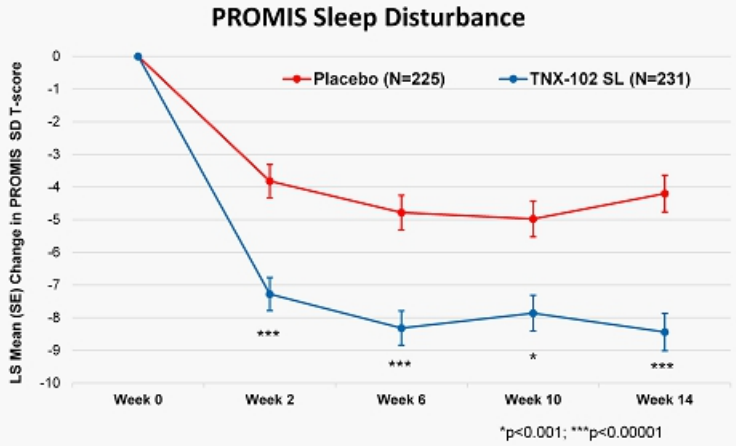
RESILIENT PROMIS Sleep Disturbance Invento
Key Secondary Outcome Measure

RESILIENT Study



Week 14 LS mean (SE) change from baseline for TNX-102 SL -8.4 (0.57) and for placebo -4.2 (0.56); LSMD from placebo -4.2 (0.79); **p=0.0000001#**

#Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction.

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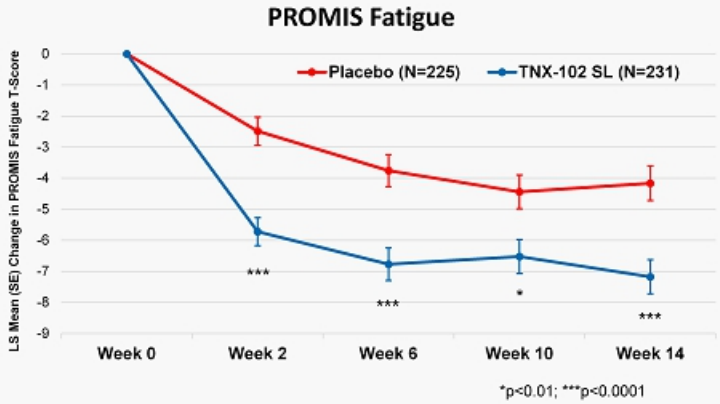
RESILIENT PROMIS Fatigue Inventory
Key Secondary Outcome Measure

RESILIENT Study



Week 14 LS mean (SE) change from baseline for TNX-102 SL -7.2 (0.55) and for placebo -4.2 (0.56); LSMD from placebo -3.0 (0.77); **p=0.00009#**

#Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction.

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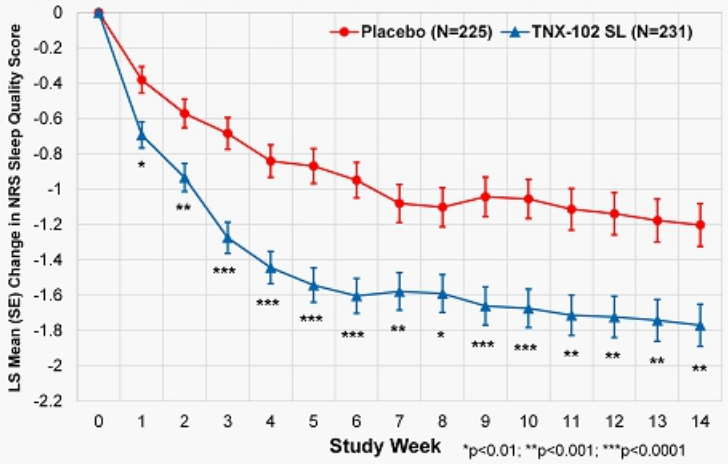
RESILIENT Sleep Quality by Daily Diary
Key Secondary Outcome Measure

RESILIENT Study

Weekly Average of Daily Diary NRS Ratings of Prior Night Sleep Quality



Week 14 LS mean (SE) change from baseline for TNX-102 SL -1.77 (0.12) and for placebo -1.20 (0.12); LSMD from placebo -0.57 (0.17); **p=0.0007#**

#Based on Mixed Model Repeated Measures with Multiple Imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction.

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RESILIENT Safety Summary

RESILIENT Study

**Treatment-Emergent Adverse Events (TEAEs)
at Rate of ≥ 3% in Either Treatment Group**

System Organ Class Preferred Term	TNX-102 SL N=231	Placebo N=226	Total* N=457
Oral Cavity Adverse Events			
Hypoaesthesia oral	55 (23.8%)	1 (0.4%)	56 (12.3%)
Product taste abnormal	27 (11.7%)	2 (0.9%)	29 (6.3%)
Paraesthesia oral	16 (6.9%)	2 (0.9%)	18 (3.9%)
Tongue discomfort	16 (6.9%)	0 (0.0%)	16 (3.5%)
Systemic Adverse Events			
COVID-19	10 (4.3%)	7 (3.1%)	17 (3.7%)
Somnolence	7 (3.0%)	3 (1.3%)	10 (2.2%)
Headache	7 (3.0%)	4 (1.8%)	11 (2.4%)

*Safety Population

Changes in Sexual Functioning Questionnaire short form (CSFQ-14) was a safety measure in the study

- In females, CFSQ-14 total score improved (indicating better sexual functioning) to a greater extent in the TNX-102 SL group compared with placebo, p=0.010
  - Potential tolerability advantage over pharmacotherapeutics with potent serotonin reuptake inhibition
- 7 males on TNX-102 SL and 12 on placebo had Week 14 CSFQ-14 completed; but it was notable that the desire/interest subscore improved and separated from placebo in this small sample, p=0.049 (12/14 placebo and 7/7 active patients completed the survey.)

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Fibromyalgia: Market Characteristics

Prevalence

- One of the more common chronic pain disorders (2-4% of US Population)[1]

Diagnosed population

- Large population but underdiagnosed[2] relative to prevalence rate
- Majority receive drug treatment[3]

Treatment Pattern

- Polypharmacy the norm - average 2.6 drugs/patient[3]
- Rotation through therapy common: average ~5 drugs/year[3]
- Estimated that >22 million prescriptions are issued for the treatment of fibromyalgia (on- and off-label usage) each year[4,5]

Unmet Need

- Majority of patients do not respond or cannot tolerate therapy[6]

[1]American College of Rheumatology (www.ACRPatientInfo.org accessed May 7, 2019) – prevalence rate of 2-4% for U.S. adult population (~250 million)
[2]Vincent et al., 2013; diagnosed prevalence rate was 1.1% of adult population or 50% of the prevalent population
[3]Robinson, et al., 2012; 85% received drug treatment
[4]Vincent et al, Arthritis Care Res 2013;65:786
[5]Product sales derived from IMS MIDAS; IMS NDTI used to factor usage for fibromyalgia; data accessed April 2015.
[6]Market research by Frost & Sullivan, commissioned by Tonix, 2011

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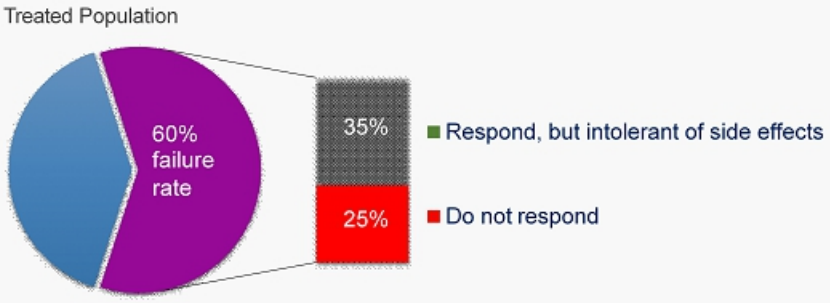
Fewer than Half of Those Treated for Fibromyalgia Receive Sustained Benefit from the Three FDA-Approved Drugs[1]

- The treatment objective is to **restore functionality** and **quality of life** by broadly improving symptoms while avoiding significant side effects
- The majority fail therapy due to **lack of a response** or **poor tolerability**[2]



[1] The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[2] Market research by Frost & Sullivan, commissioned by Tonix (2011)

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Large Need for New Fibromyalgia Therapies that Provide Broad Symptom Improvement with Better Tolerability

- Currently-approved medications may have side effects that limit long-term use[1]
  - Many patients skip doses or discontinue altogether within months of treatment initiation
- Medication-related side effects may be similar to fibromyalgia symptoms
- High rates of discontinuation, switching and augmentation
  - Attempt to treat multiple symptoms and/or avoid intolerable side effects
  - Average of 2-3 medications used simultaneously[2]
  - The typical patient has tried six different medications[3]
- Substantial off-label use of narcotic painkillers and prescription sleep aids[3]
  - Among those diagnosed, more than one-third have used prescription opioids as a means of treatment[4]
- TNX-102 SL is a non-opioid, centrally-acting analgesic that could provide a new therapeutic option for fibromyalgia patients

[1] Nuesch et al, Ann Rheum Dis 2013;72:955-62.
[2] Robinson RL et al, Pain Medicine 2012;13:1366.
[3] Patient Trends: Fibromyalgia", Decision Resources, 2011.
[4] Berger A, Dukes E, Martin S, Edelsberg J, Oster G, Int J Clin Pract, 2007; 61(9):1498–1508.

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

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., the majority 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

Status: One Positive Phase 3 study RELIEF completed, *p*-value = 0.01[2]

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT positive, *p*-value = 0.00005

Next Steps: Pre-NDA meeting with FDA

Additional Indications: Fibromyalgia-type Long COVID, Acute Stress Disorder (ASD), PTSD, Agitation in Alzheimer's, Alcohol Use Disorder

*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.

Additional Potential Indications for TNX-102 SL

Fibromyalgia-Type Long COVID

Status: Phase 2

- Phase 2 study (*PREVAIL*) completed
- Topline results reported 3Q 2023

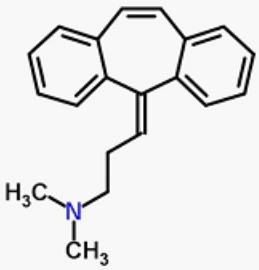
Next Steps: Meeting with FDA regarding primary endpoint

Acute Stress Reaction/ Acute Stress Disorder

- Phase 2 ready investigator-initiated study
- Department of Defense funded/ UNC will perform study

Next Steps: Expect to start Phase 2 in 1Q 2024

Cyclobenzaprine Long-Term Utilization



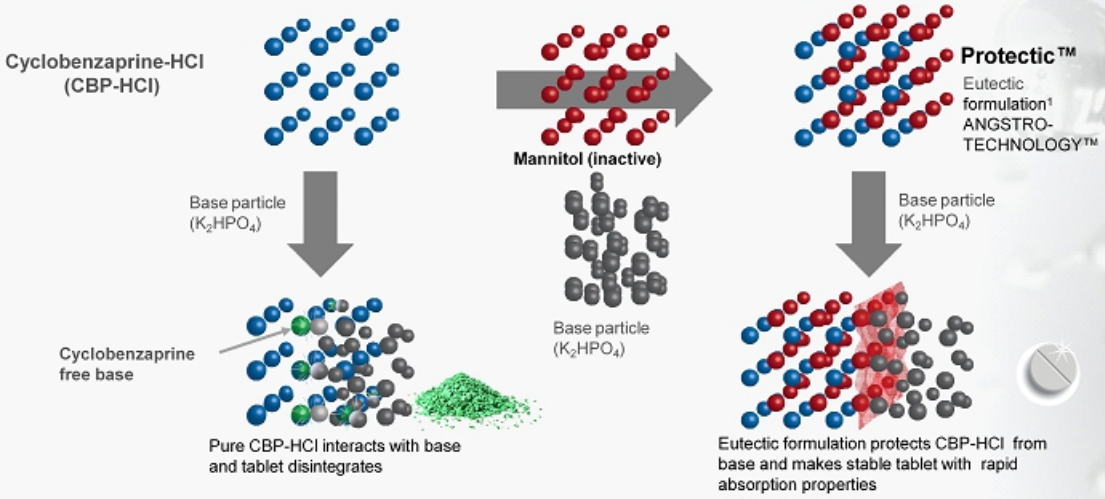
- **Flexeril® approved in 1977 by Merck for the treatment of muscle spasm**
  - 10 mg T.I.D. for acute use (2-3 weeks)
  - 1999 OTC AdCom Briefing Package: original NDA included "*8 long term safety studies* in which patients with various neurologic disorders received cyclobenzaprine up to *80 mg per day for 1 month up to 3 years*."

  6 published studies in fibromyalgia
  - N=246, placebo controlled, 4-24 week treatment period
  - Generally well tolerated, no new or unexpected AEs

  Extensive safety record in humans for over 30 years
  - In recent years, ~20 million prescriptions and ~ 1 billion tablets dispensed *per year*
  - Chronic cyclobenzaprine use is common *(*~12% of users)
- **Post-marketing surveillance program**
  - 7,607 patients included 297 patients treated with 10 mgs for ≥ 30 days
  - Incidence of most common AEs was much lower than in controlled studies

TNX-102 SL – Proprietary Eutectic Formulation

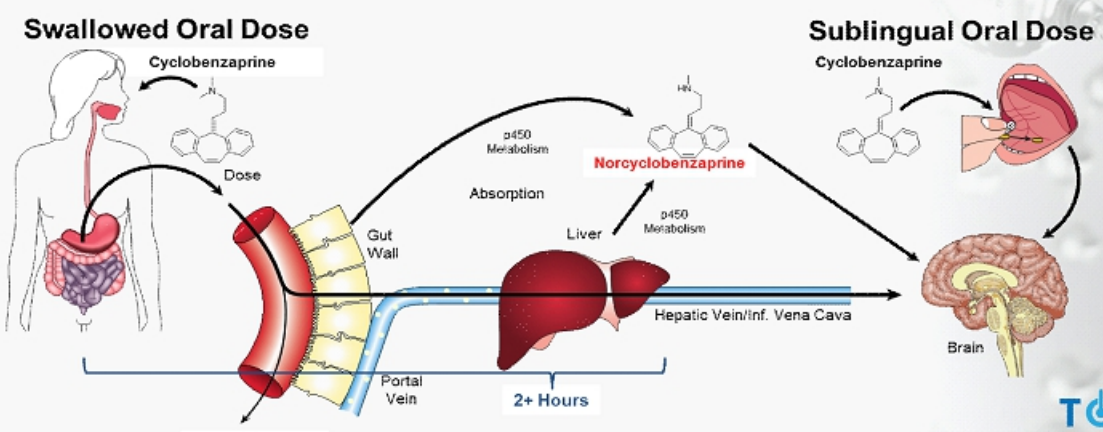
- **Proprietary Cyclobenzaprine HCL Eutectic Mixture Stabilizes Sublingual Tablet Formulation**



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

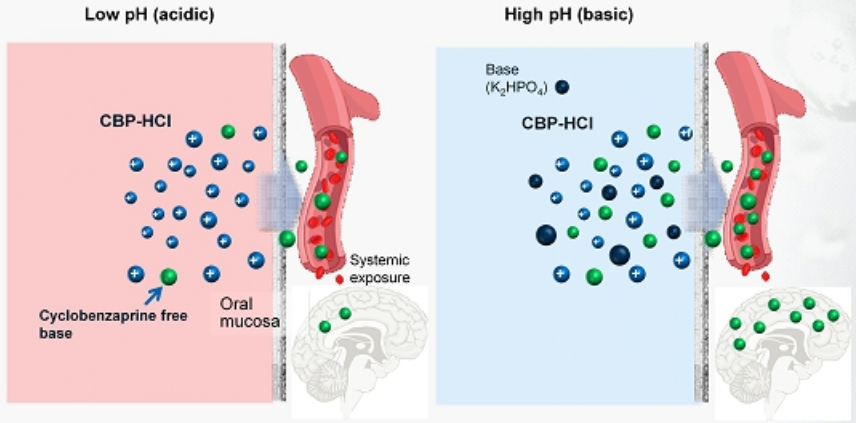
TNX-102 SL – Sublingual Administration and Transmucosal Delivery

- Advantages of the sublingual route
- Faster absorption provides PK that is ideal for bedtime dosing
- Bypasses "first-pass" hepatic metabolism
- Reduced metabolism of parent CBP to active metabolite norcyclobenzaprine (nCBP)



Formulation with Base Increases Systemic Absorption of Sublingual Cyclobenzaprine[1]

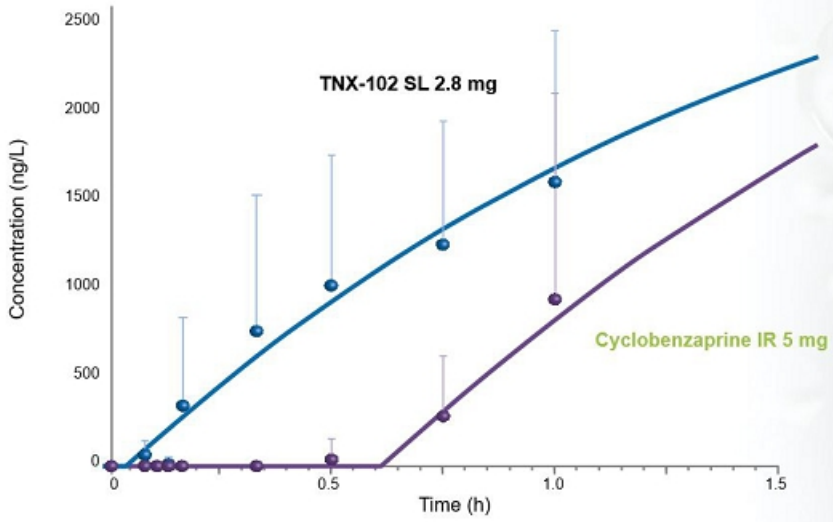
Concentration gradient increases diffusion of free base across oral mucosa (Le Chatelier's Principle)



[1]US Patent applications 13/918,692. 14/214,433 and 14/776,624 - Eutectic Formulations

TNX-102 SL –Cyclobenzaprine Detected in Plasma Within Minutes Following Sublingual Administration

Plasma Concentration Versus Time of TNX-102 SL Compared to Cyclobenzaprine IR



TNX-102 SL Single Dose PK Differentiation from Oral IR CBP

TNX-102 SL 2.8 mg v. Oral IR CBP 5 mg: Single Dose Pharmacokinetics

Parameter	TNX-102 SL 2.8 mg	Oral IR CBP 5 mg	TNX-102 SL Compared to Oral IR
	Cyclobenzaprine		
Absorption Lag Time	0.050 hr (3 min)	0.622 hr (37 min)	12x faster
Relative Bioavailability	154%	-	54% higher
C_{max}	3.41 ng/mL	4.26 ng/mL	20% lower
AUC_{0-48}	57.4 ng•hr/mL	69.5 ng•hr/mL	17% lower
	Norcyclobenzaprine		
C_{max}	0.81 ng/mL	1.71 ng/mL	53% lower
AUC_{0-48}	30.5 ng•hr/mL	58.6 ng•hr/mL	48% lower
	Cyclobenzaprine/Norcyclobenzaprine		
Ratio AUC_{0-48}	1.88	1.18	59% higher

PK = pharmacokinetics
IR = immediate release
CBP = cyclobenzaprine
C_{max} = maximum concentration
AUC = Area under the curve

TNX-102 SL Multi-Dose PK Differentiation from Simulated Oral IR CBP

TNX-102 SL: Proprietary sublingual formulation of cyclobenzaprine (CBP) with transmucosal absorption

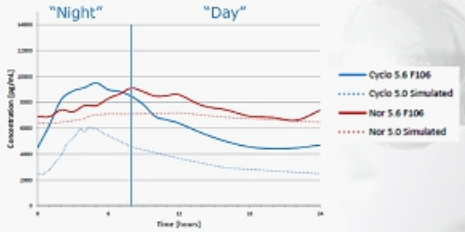
- Rapid systemic exposure
- Increases bioavailability during sleep
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, norcyclobenzaprine (norCBP)

CBP undergoes extensive first-pass hepatic metabolism when orally ingested

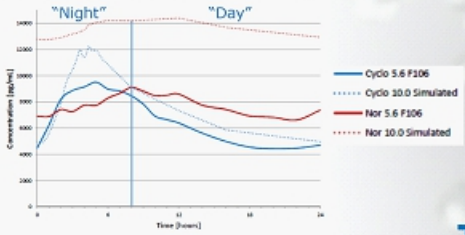
- Active major metabolite, norCBP

Steady State Pharmacokinetics (after 20 days dosing)

Day 20 TNX-102 SL 5.6 mg v. Simulated Oral IR 5 mg



Day 20 TNX-102 SL 5.6 mg v. Simulated Oral IR 10 mg



PK = pharmacokinetics
IR = immediate release
CBP = Cyclo = cyclobenzaprine
Nor = norCBP = norcyclobenzaprine

Multi-Functional Mechanism Involves Antagonism at Four Neuronal Receptors

CNS PORTFOLIO

Active ingredient, cyclobenzaprine, interacts with four receptors

- Antagonist at 5-HT_{2A} receptors
  - Similar activity to trazodone and Nuplazid® (pimivanserin)
- Antagonist at α_1-adrenergic receptor
  - Similar activity to Prazosin® (prazosin)
- Antagonist at histamine H_1 receptors
  - Similar activity to Benadryl® (diphenhydramine) and hydroxyzine
- Antagonist at muscarinic M_1 receptors
  - Similar activity to Benadryl® (diphenhydramine), Prozac® (fluoxetine), Paxil® (paroxetine), Zyprexa (olanzapine) and Seroquel® (quetiapine).

TONIX PHARMACEUTICALS

Cyclobenzaprine Binding Affinities for Receptor and Transporter

CNS PORTFOLIO

	H_1	5-HT_{2A}	α_{1A}	α_{1B}	M_1	SERT	NET
Cyclobenzaprine (CBP)	1.2	5.4	7.1	8	8.4	29	39
Norcyclobenzaprine (nCBP)	17.8	38	82	71	155	461	12.8

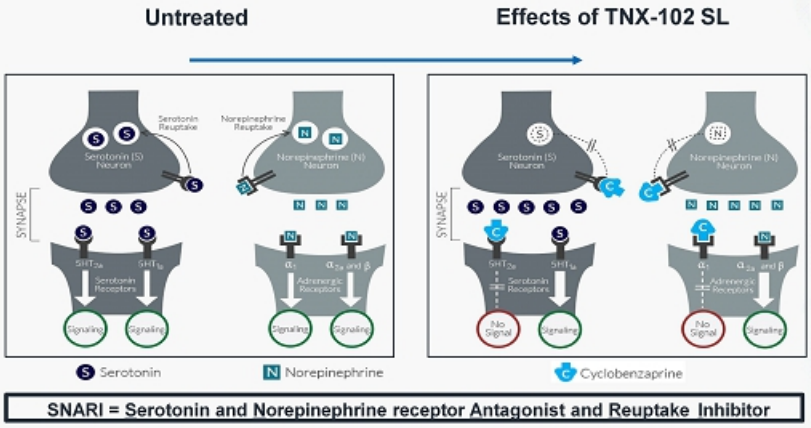
CBP/nCBP Activity: Antagonist | Inhibitor

TONIX PHARMACEUTICALS

Cyclobenzaprine Effects on Nerve Cell Signaling

Cyclobenzaprine is a multi-functional drug – SNARI

- inhibits serotonin and norepinephrine reuptake
- blocks serotonin 5-HT_{2A} and norepinephrine$_{\alpha 1}$ receptors



SNARI = Serotonin and Norepinephrine receptor Antagonist and Reuptake Inhibitor

CNS PORTFOLIO

TONIX PHARMACEUTICALS

TNX-102 SL – No Recognized Abuse Potential in Clinical Studies

Active ingredient is cyclobenzaprine, which is structurally related to tricyclic antidepressants

- Cyclobenzaprine interacts with receptors that regulate sleep quality: 5-HT2A, α1-adrenergic and histamine H1 receptors
- Cyclobenzaprine does NOT interact with the same receptors as traditional hypnotic sleep drugs, benzodiazepines or non- benzodiazepines that are associated with retrograde amnesia
- Cyclobenzaprine-containing product was approved 40 years ago and current labeling (May 2016) indicates no abuse or dependence concern

TNX-102 SL NDA can be filed without drug abuse and dependency assessment studies

- April 2017 meeting minutes from the March 2017 FDA meeting

CNS PORTFOLIO

TONIX PHARMACEUTICALS

TNX-102 SL –Sublingual Formulation is Designed for Bedtime Administration

TNX-102 SL: Proprietary sublingual formulation of cyclobenzaprine (CBP) with transmucosal absorption

- Innovation by design with patent protected CBP/mannitol eutectic
- Rapid systemic exposure
- Increases bioavailability during sleep
- Avoids first-pass metabolism
- Lowers exposure to long-lived active major metabolite, norcyclobenzaprine (norCBP)

CBP undergoes extensive first-pass hepatic metabolism when orally ingested

- Active major metabolite, norCBP1
- Long half-life (~72 hours)
- Less selective for target receptors (5-HT2A, α1-adrenergic, histamine H1)
- More selective for norepinephrine transporter and muscarinic M1

Multi-functional activity suggests potential for other indications

- TNX-102 SL was developed for the management of fibromyalgia (Phase 3)
- Sleep quality is a problem in other conditions

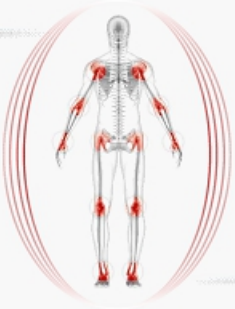
CNS PORTFOLIO

TONIX PHARMACEUTICALS

Chronic Overlapping Pain Conditions (COPC) Believed to Result from Shared Brain Processes

- COPC is a set of disorders that coaggregate; these disorders can include but are not limited to[1,2]:

- Temporomandibular disorder
- Fibromyalgia
- Irritable bowel syndrome
- Vulvodynia
- CFS/ME[3]
- Interstitial cystitis/painful bladder syndrome



- Endometriosis
- Chronic tension-type headache
- Migraine headache
- Chronic lower back pain

- Similar central mechanisms play significant roles in all pain conditions, even those with known peripheral contributions[1,2]

[1]Maixner W, et al. *J Pain*. 2016;17(9 Suppl):T93-T107.
[2]Veasley C, et al. http://www.chronicpainresearch. org/public/CPRA_WhitePaper_2015-FINAL-Digital.pdf. Published May 2015. Accessed July 26, 2021.
[3]CFS/ME – chronic fatigue syndrome/myalgic encephalomyelitis

CNS PORTFOLIO

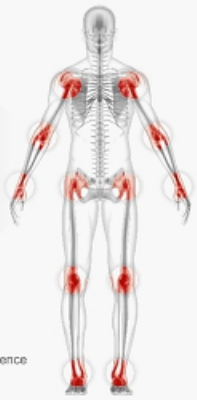
TONIX PHARMACEUTICALS

Role of Infections in Triggering Fibromyalgia or Chronic fatigue (CFS)-Like Illnesses

- 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*[1] which endorses the connection between Long COVID and chronic fatigue syndrome.

Infection initiates an autoreactive process, which affects several functions, including brain and energy metabolism[2-7]

- Infections can trigger any of these conditions in approximately 10% of exposed individuals
- The initial location of the infection determines the subsequent pain syndrome
- Any type of infectious diarrhea will trigger irritable bowel syndrome (IBS) in 10% to 20% of those exposed

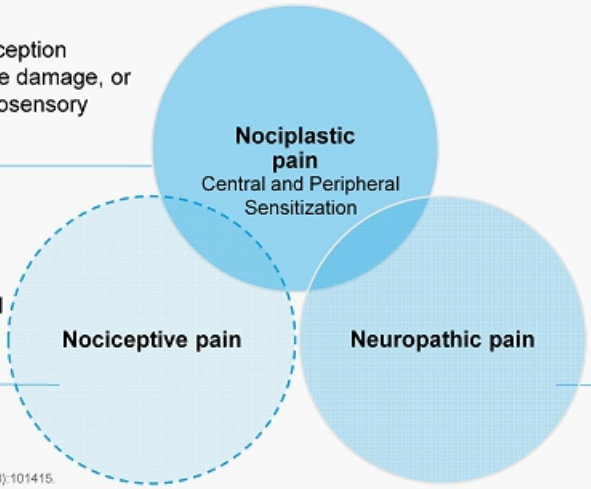


[1]Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID, 200 Independence Ave SW, Washington, DC 20201.
[2]Blomberg J, et al. Front Immunol. 2018;9:229. Published 2018 Feb 15.
[3]Warren JW, et al. Urology. 2008;71(6):1085-1090.
[4]Buskila D, et al. Autoimmun Rev. 2008;8(1):41-43.
[5]Hickie I, et al. BMJ. 2006;333(7568):575.
[6]Parry SD, et al. Am J Gastroenterol. 2003;98(9):1970-1975.
[7]Halvorson HA, et al. Am J Gastroenterol. 2006;101(8):1894-1942.

New Classification for Central Pain: Nociplastic Pain[1]

Nociplastic syndrome includes widespread (or nociplastic) pain, fatigue, sleep disturbances and cognitive dysfunction ("brain fog")

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



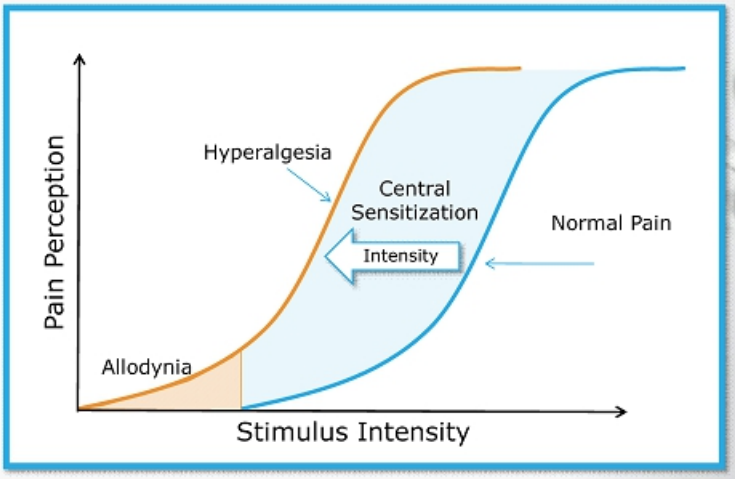
Pain due to the activation of nociceptors that arises from actual or threatened damage to non-neural tissue

Pain caused by a lesion or disease of the somatosensory nervous system

[1]Trouvin AP, et al. *Best Pract Res Clin Rheumatol*. 2019;33(3):101415.

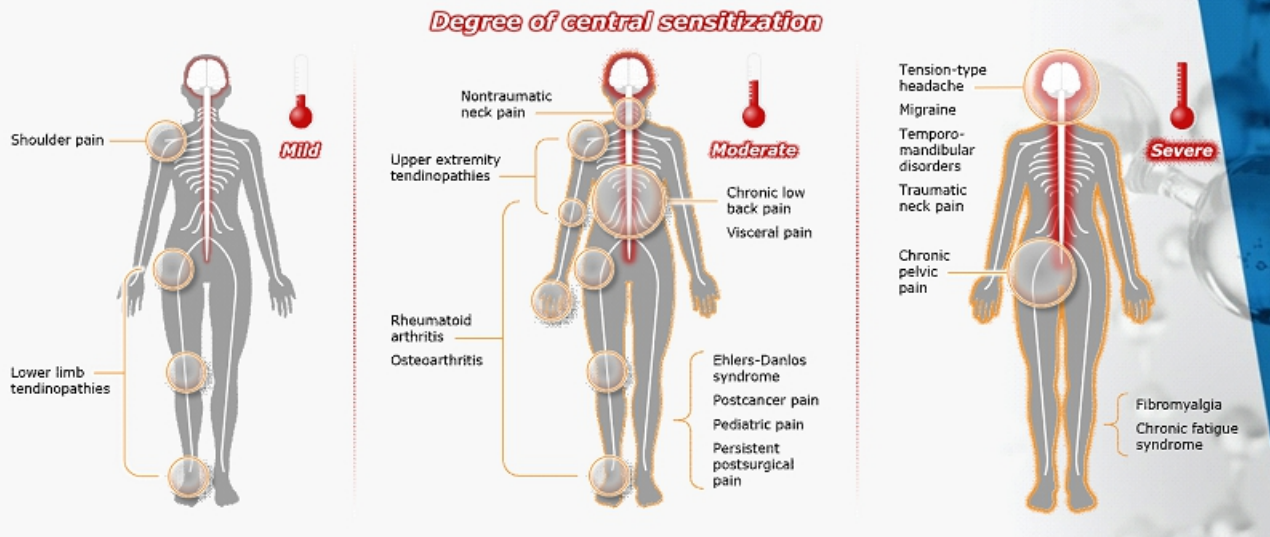
Central Sensitization (CS)
A Feature of Many Nociplastic Pain Syndromes

- CS is caused by amplified neural signaling in CNS pain circuits[1-3]
- Patients with CS perceive higher pain to a slightly noxious stimuli than in non-CS individuals (hyperalgesia)[1]
- Severe CS can lead to hypersensitivity to stimuli that are not typically painful (allodynia)[2]
- CS varies in severity and is observed in syndromes including FM and ME/CFS[1,3]



[1]CFS/ME – chronic fatigue syndrome/myalgic encephalomyelitis
[2]FM - fibromyalgia
[3]Nijs J, et al. *Lancet*. 2021;3(5):e383-e392.

Central Sensitization (CS)
Can Occur in a Range of Diseases and Conditions



Nijs J, et al. *Lancet*. 2021;3(5):e383-e392.

About Fibromyalgia-Type Long COVID

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

Many Long-COVID symptoms overlap with core symptoms of fibromyalgia

and are hallmarks of other chronic pain syndromes like myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

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

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

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

TNX-102 SL: Phase 2 PREVAIL Study Design

PREVAIL Study

Study characteristics:

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

Primary Endpoint:

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

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

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

Placebo once-daily at bedtime

ClinicalTrials.gov Identifier: NCT05472090
"A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL in Patients With Multi-Site Pain Associated With Post-Acute Sequelae of SARS-CoV-2 Infection (PREVAIL)"

14 weeks

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

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

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

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

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

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

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

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

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

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

Large unmet need:

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

Current standard of care:

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

[1]National Center for PTSD. How Common is PTSD in Adults? https://www.ptsd.va.gov/understand/common/common_adults.asp
[2]Wisco et al. *J Clin Psychiatry*. 2014.75(12):1338-46

ASR/ASD Program Status

Status: Expect to start Phase 2 in 1Q 2024

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

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

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

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TNX-102 SL: Phase 2 OASIS Study Design

General study characteristics:

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

Objective:

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

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

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

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

Tonix Medicines: Commercial-Stage Specialty Pharma Subsidiary

- **Tonix Medicines is a wholly-owned subsidiary of Tonix (NASDAQ: TNXP)**
  - Currently marketing two products indicated for the treatment of acute migraine: Zembrace® SymTouch ® and Tosymra®
  - ~16 M in net sales[1]
  - Nascent commercial organization
- **Tonix Medicines is led by James (Jim) Hunter**
  - Veteran pharma executive with a track record for growing early businesses
  - Hunter previously founded Validus with Tonix CEO, Dr. Lederman
- **Tonix Medicines is preparing to launch TNX-102 SL for fibromyalgia**
  - Fibromyalgia care is relatively concentrated to specialized providers
  - We believe prescribing physicians can be targeted effectively by a specialty sales force
  - Evolving landscape in commercial markets favors distribution channels such as specialty pharmacies

[1]Tonix 10-Q for 3Q23

TONIX PHARMACEUTICALS

Two Marketed Proprietary Migraine Drugs
Non-oral Formulations of Sumatriptan

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]

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

Combined retail product sales of $27 million for the 12 months ended September 30, 2023[6]

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

[1]Zembrace SymTouch [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: February 2021 - For more information, talk to your provider and read the Patient Information and Instructions for Use. – Important Safety Information is provided in the appendix
[2]Tosymra [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: Feb 2021. For more information, talk to your provider and read the Patient Information and Instructions for Use. – Important Safety Information is provided in the appendix
[3]Upsher-Smith Laboratories, LLC; Data On File, 2023
[4]Mathew NT, et al. Dose ranging efficacy and safety of subcutaneous sumatriptan in the acute treatment of migraine. US Sumatriptan Research Group. Arch Neurol. 1992;49(12):1271-1276.
[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.
[6]Symphony Health Solutions data as of November 2023

Zembrace and Tosymra Bypass the GI Tract

Bypassing gastrointestinal (GI) tract is *potential advantage for treating acute migraine*

- GI absorption may be inconsistent in migraineurs due to gastric stasis (also called "gastroparesis")[1-4]
- Nausea and vomiting are symptoms of migraine[5] which can complicate oral treatment

Existing intranasal products

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

New intranasal products bringing attention to non-oral route

- Pfizer's Zavzpret® (zavegepant), FDA approved in March, 2023[1] is the first intranasal gepant
- Impel NeuroPharma's Trudhesa® (dihydroergotamine) FDA approved 2021[2]

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

Pipeline

Programs and Strategy for Partnerships

Pipeline Development Strategy

Focusing on government and academic collaborations

- Validates Tonix's scientific expertise and technology
- Reduces internal spend
- Increases number of trials
- Potentially speeds time to market
- Grants, contracts, cost-sharing or "in-kind" arrangements

External Partnerships

Government partners providing direct funding, cost sharing or in-kind support include:

- National Institutes of Health (NIH)
- National Institute of Allergy and Infectious Disease (NIAID)
- National Institute on Drug Abuse (NIDA)
- Department of Defense (DoD)

Academic partners sponsoring clinical trials of Tonix's investigational drug products include:

- Massachusetts General Hospital (MGH)
- University of Washington
- University of North Carolina

Key Partnerships

TNX-1500: ALLOGRAFT REJECTION

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

TNX-1300: COCAINE INTOXICATION

NIH National Institute on Drug Abuse

COLUMBIA UNIVERSITY

TNX-102 SL: ACUTE STRESS DISORDER

U.S. Department of Defense

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

TNX-1800: COVID-19 VACCINE

NIH National Institutes of Health

NIH National Institute of Allergy and Infectious Diseases

TNX-2900: PRADER-WILLI SYNDROME

InsermTransfert

CHU de Toulouse

Aix*Marseille université

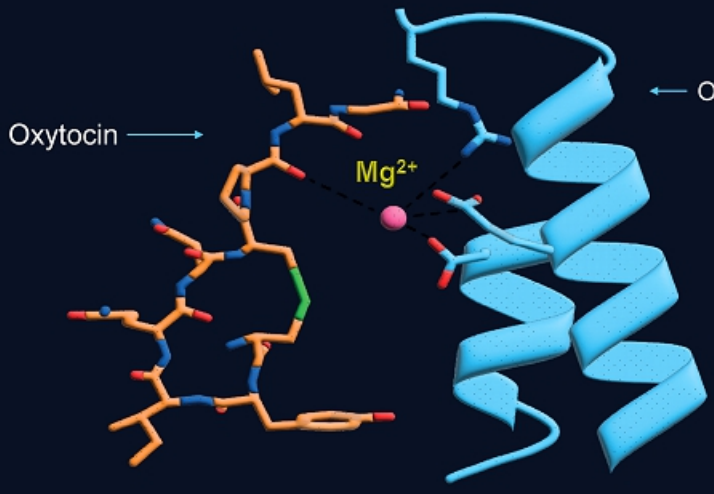
TNX-2900

Intranasal Potentiated Oxytocin with Magnesium

A novel, non-CGRP antagonist approach to treatment

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

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



Key Differentiators

- Targeted intranasal delivery
  - Low systemic exposure

[1]Antoni et al., 1989. *Biochem J.* 257(2):611-4
[2]Meyerowitz et al., 2022. *Nat Struct Mol Biol.* (3):274-281
*TNX-1900 and TNX-2900 have not been approved for any indication.

TNX-2900 for Prader-Willi Syndrome

RARE DISEASE PORTFOLIO

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

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

Current standard of care:

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

Large unmet need:

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

TNX-2900 has been granted FDA Orphan Drug Designation and received IND clearance by FDA for Phase 2 Trial

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

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TNX-1300

Cocaine Esterase

Fast acting antidote for life threatening cocaine intoxication

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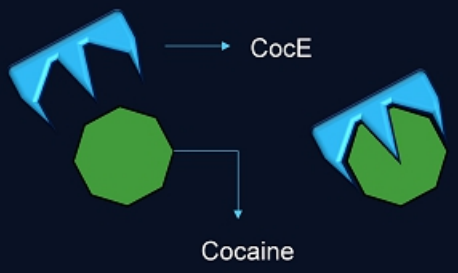
TNX-1300: Recombinant Protein Rapidly Degrades Cocaine in the Bloodstream

Drops plasma exposure by 90% in 2 minutes



FDA Breakthrough Therapy Designation

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

Key Differentiators

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

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

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About Cocaine Intoxication

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

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

Current standard of care:

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

Large unmet need:

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

CNS PORTFOLIO

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

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

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IMMUNOLOGY: KEY CANDIDATES
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TNX-1500
Anti-CD40L Monoclonal Antibody
Next Generation mAb preserves efficacy without risk of thrombosis
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TNX-1500: Next Generation anti-CD40L mAb

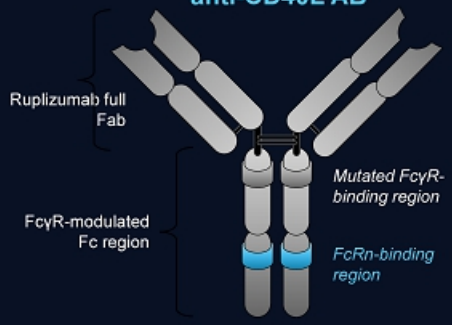
Re-engineered to better modulate the binding of FcγR and mitigate risk of thrombosis

Key Differentiators

Expected to deliver efficacy without compromising safety

- **First Generation:** Development halted due to thromboembolic (TE) complications—blood clots—traced to Fc gamma receptor (FcγR)
- **Second Generation:** Eliminated the FcγR TE complication but potency and half life was reduced, limiting utility
- **Third Generation (TNX-1500):** Re-engineered to better modulate the binding of FcγR.

Selectively Modified anti-CD40L AB



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

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

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TNX-1500 Strategy and Status

IMMUNOLOGY PORTFOLIO

1 Proposed Initial Indication: Prevention of Allograft Rejection

Status: ***Phase 1 enrollment and dosing complete***

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

Next Steps: Initiate Phase 2 study in Kidney Transplant Recipients

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

- Potential to reduce GvHD

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

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

Currently exploring strategic partnerships and out-licensing opportunities

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TNX-1500 Preclinical Data and Publications

Non-human Primate Kidney Allo-Transplantation

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

Non-human Primate Heart Heterotopic Allo-Transplantation

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

Non-Human Primate Kidney Xenograft Transplantation

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

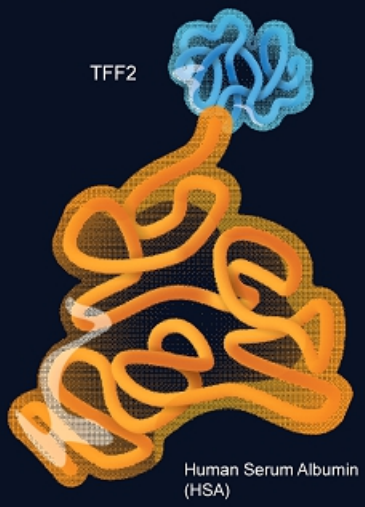
TNX-1700

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

Targeting the toxic tumor micro-environment

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

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



Key Differentiators

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

Preclinical Evidence

- mTNX-1700 (mTFF2-MSA fusion protein) and anti-PD-1 monotherapy each was able to evoke anti-tumor immunity in the MC38 model of colorectal cancer[1]
- mTNX-1700 augmented the anti-tumor efficacy of anti-PD-1 therapy in both the MC38 and the CT26.wt models[1]

*TNX-1700 is in the pre-IND stage of development and has not been approved for any indication.
[1]Daugherty, B. et al. March 6, 2023 Keystone Poster. https://bit.ly/48nlRHM

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About Gastric and Colorectal Cancer

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

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

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

Current standard of care:

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

Large unmet need:

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

IMMUNOLOGY PORTFOLIO

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

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Internal Development & Manufacturing Capabilities

R&D Center (RDC): Frederick, MD

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

Advanced Development Center (ADC): North Dartmouth, MA

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

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

BROAD-SPECTRUM ANTIVIRAL DISCOVERY PROGRAMS

INFECTIOUS DISEASE PORTFOLIO

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

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TNX-801

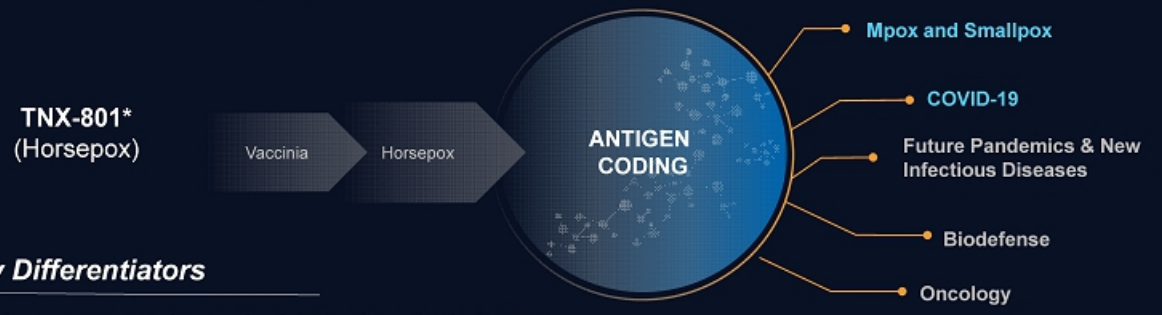
Live Virus Vaccine

Live virus vaccine platform with multitude of potential applications

TONIX PHARMACEUTICALS

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

Cloned version of horsepox[1] purified from cell culture



Key Differentiators

Live virus vaccines are the most established vaccine technology

- Prevents forward transmission
- Effective in eliciting durable or long-term immunity

Economical to manufacture at scale

- Low dose because replication amplifies dose *in vivo*
- Single administration

Standard refrigeration for shipping and storage

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

TONIX PHARMACEUTICALS

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

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

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

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

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

INFECTIOUS DISEASE PORTFOLIO

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

TONIX PHARMACEUTICALS

Management Team

Seth Lederman, MD
Co-Founder, CEO & Chairman

TARGENT · Fusilev (levoleucovorin) for injection · vela

Gregory Sullivan, MD
Chief Medical Officer

Bradley Saenger, CPA
Chief Financial Officer

Shire · VERTEX · Steward · pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank · svb Silicon Valley Bank · American Capital

TONIX PHARMACEUTICALS

Summary of Recently Completed and Upcoming Milestones

Recently Completed - Data Readouts

- Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia – positive topline in confirmatory Phase 3 study reported December 2023
  - Next steps: Pre-NDA meeting with FDA expected 1H 2024

Upcoming - Clinical Trial Initiations

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

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.

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