

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 14, 2023

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada  
(State or Other Jurisdiction  
of Incorporation)

001-36019  
(Commission  
File Number)

26-1434750  
(IRS Employer  
Identification No.)

26 Main Street, Chatham, New Jersey 07928  
(Address of principal executive offices) (Zip Code)

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

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

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

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

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

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

Emerging growth company

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

**Item 7.01 Regulation FD Disclosure.**

On September 14, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced a poster presentation at the Seventh International Cancer Immunotherapy Conference 2023: Translating Science into Survival being held September 20, 2023 to September 23, 2023 ("CICON23") titled *mTFF2-MSA (mTNX-1700) Suppresses Tumor Growth and Increases Survival in Anti-PD-1 Treated CT26.WT Subcutaneous and CT26-Luciferase Orthotopic Syngeneic Colorectal Cancer Models by Targeting MDSCs in BALB/C Mice* (the "Poster"). A copy of the press release that discusses this matter is filed as Exhibit 99.01 hereto and incorporated herein by reference.

The Company updated its investor presentation, which is used to conduct meetings with investors, stockholders and analysts and at investor conferences, and which the Company intends to place on its website, which may contain nonpublic information. A copy of the presentation is filed as Exhibit 99.02 hereto and incorporated herein by reference.

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

**Item 8.01 Other Events.**

On September 14, 2023, the Company announced the presentation of the Poster at the CICON23 conference.

*Forward-Looking Statements*

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

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

**Item 9.01 Financial Statements and Exhibits.**

(d)	<b>Exhibit No.</b>	<b>Description.</b>
	<a href="#">99.01</a>	Press Release of the Company, dated September 14, 2023
	<a href="#">99.02</a>	Corporate Presentation by the Company for September 2023
	104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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**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 14, 2023

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

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## Tonix Pharmaceuticals Announces Poster Presentation Involving TNX-1700 in Preclinical Colorectal Cancer Models at the Seventh International Cancer Immunotherapy Conference 2023

CHATHAM, N.J., September 14, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced a poster presentation at the Seventh International Cancer Immunotherapy Conference 2023 (CICON23): Translating Science into Survival. The Conference is being held September 20-23, 2023, in Milan, Italy. A copy of the poster will be made available on the Tonix Pharmaceuticals website following the presentation at [www.tonixpharma.com](http://www.tonixpharma.com).

### Poster Presentation Details

Title: mTFF2-MSA (mTNX-1700) Suppresses Tumor Growth and Increases Survival in Anti-PD-1 Treated CT26.WT Subcutaneous and CT26-Luciferase Orthotopic Syngeneic Colorectal Cancer Models by Targeting MDSCs in BALB/C Mice

Authors: Bruce L. Daugherty, Rebecca J. Boohaker, Rebecca Johnstone, Karr Stinson, Grace Zhao, Mingfa Zang, Jin Qian, Timothy C. Wan, Seth Lederman

Session Date: September 21, 2023

Session Time: 12:30 p.m. – 2:00 p.m.

### Tonix Pharmaceuticals Holding Corp. \*

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults. Tonix's development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS development portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment of a potentially confirmatory Phase 3 study in the third quarter of 2023, with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 proof-of-concept study has been completed, and topline results were reported in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the  $\mu$ -opioid receptor while maintaining activity in the rat Novel Object Recognition test in vivo and the ability to activate PPAR- $\beta/\delta$  and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment in a Phase 2 proof-of-concept study with topline data expected in the fourth quarter of 2023. TNX-1900 is also being studied in binge eating disorder, pediatric obesity and social anxiety disorder by academic collaborators under investigator-initiated INDs. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the third quarter of 2023. Tonix's rare disease development portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology development portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 was initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals.

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

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. All other marks are property of their respective owners.

This press release and further information about Tonix can be found at [www.tonixpharma.com](http://www.tonixpharma.com).

### Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research

and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the Securities and Exchange Commission (the “SEC”) on March 13, 2023, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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## Cautionary Note on Forward-Looking Statements

Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate” and “intend,” among others. These forward-looking statements are based on Tonix’s current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, the risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by Tonix on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the Securities and Exchange Commission (the “SEC”) on March 13, 2023, and periodic reports and current reports filed with the SEC on or after the date thereof. All of Tonix’s forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.

## Investment Highlights



### MARKETED PRODUCTS

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



### RICH PIPELINE OF THERAPEUTICS CANDIDATES IN DEVELOPMENT

Tonix's core focus is on **central nervous system** disorders, but we also target unmet needs across multiple therapeutic areas including **immunology, infectious disease** and **rare disease**.



### IN-HOUSE CAPABILITIES

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



### STRATEGIC PARTNERSHIPS

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

<sup>1</sup>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

<sup>2</sup>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. © 2023 Tonix Pharmaceuticals Holding Corp.



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## Pipeline: Key Clinical Development Programs

Candidates*	Indication	Status/Next Milestone
TNX-601 ER	Depression	Phase 2 – enrollment complete <sup>1</sup>
TNX-1900 <sup>2</sup>	Prevention of Chronic Migraine	Phase 2 – enrollment complete <sup>3</sup>
TNX-102 SL <sup>4</sup>	Fibromyalgia (FM) Long COVID (PASC <sup>5</sup> )	Mid-Phase 3 – enrollment complete Phase 2 – Topline Reported
TNX-2900 <sup>6</sup>	Prader-Willi Syndrome - <i>FDA Orphan Drug Designation</i>	Phase 2 ready
TNX-1300 <sup>7</sup>	Cocaine Intoxication - <i>FDA Breakthrough Designation</i>	Mid-Phase 2. Targeted 4Q 2023 Start
TNX-1500 <sup>8</sup>	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.

<sup>1</sup>Phase 1 trial for formulation development was completed outside of the U.S.; Other potential indications include PTSD and neurocognitive dysfunction from steroids

<sup>2</sup>Acquired from Trigemina; license agreement with Stanford University. Planned investigator-initiated Binge Eating Disorder (BED) study initiated 3Q 2023.

<sup>3</sup>A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

<sup>4</sup>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.

<sup>5</sup>Post-Acute Sequelae of COVID-19.

<sup>6</sup>Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)

<sup>7</sup>TNX-1300 (double-mutant cocaine esterase) is licensed from Columbia University

<sup>8</sup>anti-CD40L humanized monoclonal antibody – IND cleared

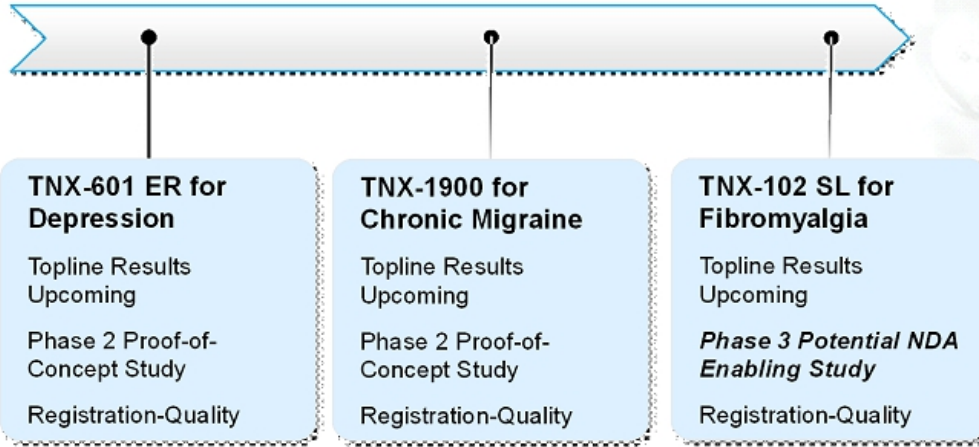
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## Upcoming Expected Topline Results

### Fourth Quarter 2023



## TONIX MEDICINES: MARKETED PRODUCTS



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

### Zembrace® SymTouch® (sumatriptan injection) 3 mg<sup>1</sup>



- 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<sup>3</sup>
- Each may provide migraine **pain relief in as few as 10 minutes** for some patients<sup>1,2,4,5</sup>
- Patents to 2036 (Zembrace) and 2031 (Tosymra)

### Tosymra® (sumatriptan nasal spray) 10 mg<sup>2</sup>



#### Consolidated Product Sales for the 12 months ended March 31<sup>st</sup> 2023

- Factory sales: \$30.4M<sup>3</sup>
- Net sales: \$16.4M<sup>3</sup>

#### Retail Product Sales for the 12 months ended December 31<sup>st</sup> 2022

- Retail sales: ~\$23 M (Zembrace ~\$19.6 M and Tosymra ~\$3.5 M)<sup>4</sup>

#### 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

<sup>1</sup>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.  
<sup>2</sup>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.  
<sup>3</sup>Upsher-Smith Laboratories, LLC; Data On File, 2023

<sup>4</sup>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.

<sup>5</sup>Wenot 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. 2005;28(4):517-526.

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## 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")<sup>1-4</sup>
- Nausea and vomiting are symptoms of migraine<sup>5</sup>

### 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<sup>1</sup> is the first intranasal gepant
- Impel NeuroPharma's Trudhesa® (dihydroergotamine) FDA approved 2021<sup>2</sup>
  - Precision Olfactory Delivery (POD) technology targets vascular-rich upper nasal space

<sup>1</sup>Pfizer Press Release March 10, 2023. - <https://www.pfizer.com/news/press-release/press-release-detail/pfizers-zavzpretm-zavegepant-migraine-nasal-spray>

<sup>2</sup>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/>

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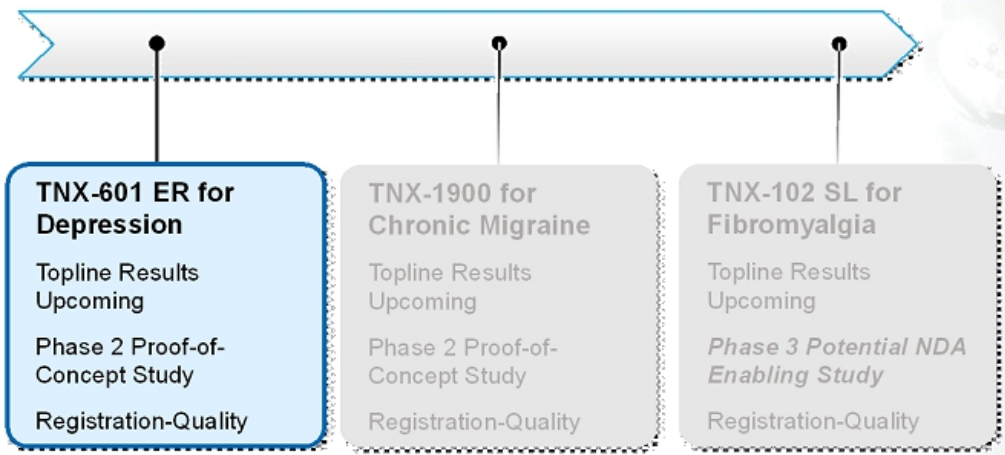


**CNS:  
KEY DEVELOPMENT  
CANDIDATES**

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**Upcoming Expected Topline Results**

**Fourth Quarter  
2023**



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

## PROFILE

- A novel, oral, extended-release once-daily tablet
- Treatment effect of tianeptine sodium immediate release *t.i.d.* in depression is well-established
- Tianeptine restores neuroplasticity in animal models
- PPAR-β/d and PPAR-γ agonist<sup>1</sup>

### 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<sup>2</sup>

## Patents Issued

## DEVELOPMENT PROGRAM

**Market Entry:** Major Depressive Disorder (MDD)

**Additional Indications:** PTSD, Neurocognitive Disorder From Corticosteroids, Alzheimer's Disease<sup>3</sup>

**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.

<sup>1</sup>Sullivan G et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. <https://bit.ly/42e3jnV>

<sup>2</sup>Summary of product characteristics (SmPC), European Medicines Agency, Stablon®. [www.servier.cz/sites/default/files/spc-pil/SPC\\_Stablon\\_1.pdf](http://www.servier.cz/sites/default/files/spc-pil/SPC_Stablon_1.pdf) accessed 7-16-23.

<sup>3</sup>Garola-Aberca et al., 2022. *J Alzheimers Dis.* 88(2):707-720

## TNX-601 ER - Phase 2 UPLIFT\* Study Design

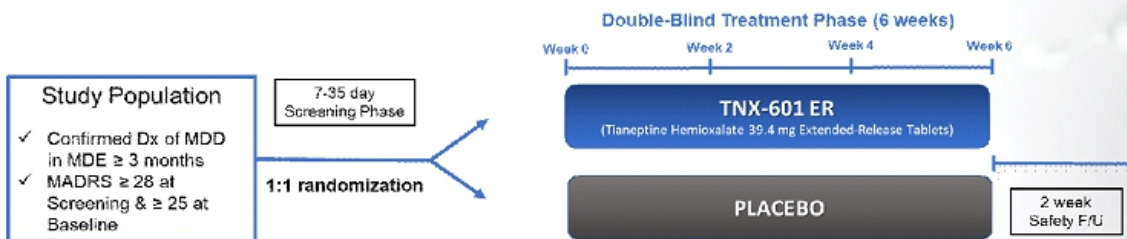


### General study characteristics:

- 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



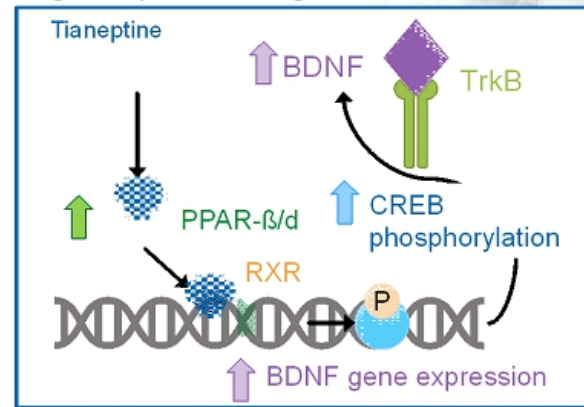
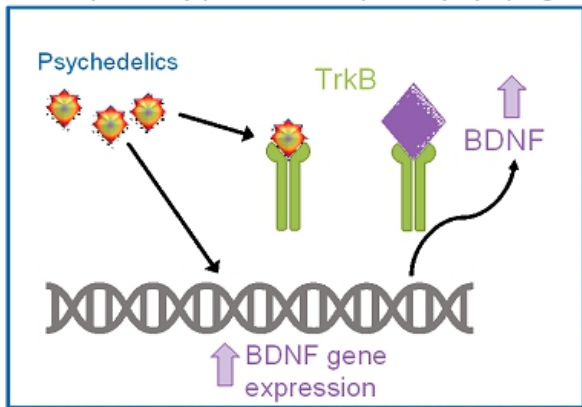
\*ClinicalTrials.gov Identifier: NCT05686408

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

# 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<sup>1</sup>

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



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

<sup>1</sup>de Vos CMH, et al. *Front Psychiatry*. 2021;12:724606

<sup>2</sup>Moliner R, et al. *Nat Neurosci*. 2023;26(6):1032-1041

<sup>3</sup>Ji M.J, et al. *Int J Neuropsychopharmacol*. 2015;19(1):pyv083

<sup>4</sup>Seo MK, et al. *Psychopharmacology (Berl)*. 2016;233(13):2617-2627

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

### Racemic tianeptine:

- Approved in Europe and ex-US
- 1:1 mixture of 2 mirror-image isomers<sup>1,2</sup>
- Weak μ-opioid receptor agonism<sup>2</sup>
  - Risk of abuse or diversion for euphoric effects<sup>3</sup>

	Racemic-Tianeptine	(S)-Tianeptine TNX-4300	(R)-Tianeptine
Activates PPAR-β/d	+	+	-
Neuroplasticity	+	+	-
Novel Object Test <sup>5</sup>	+	+	-
μ-Opioid Receptor	+	-	+
Forced Swim Test <sup>6</sup>	+	-	+
Activates PPAR-?	+	+	+

### (S)-Tianeptine: PPAR-β/d agonist, no opiate liability<sup>4</sup>

- New mechanism of action for treating depression

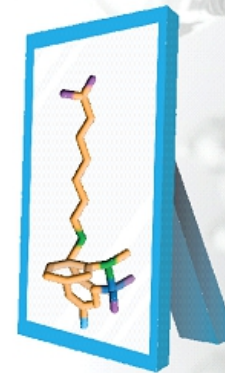
#### (S)-tianeptine



### (R)-Tianeptine: opiate liability<sup>4</sup>

- Weak μ-opioid receptor agonism<sup>4</sup>

#### (R)-tianeptine



<sup>1</sup>Stablon. Summary of product characteristics. Les Laboratoires Servier Industrie; 2014.

<sup>2</sup>PubChem. Accessed November 10, 2022. <https://pubchem.ncbi.nlm.nih.gov/compound/Tianeptine>

<sup>3</sup>Drug Enforcement Administration. May 2019. Accessed November 11, 2022. [https://www.deadiversion.usdoj.gov/drug\\_chem\\_info/tianeptine.pdf](https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf)

<sup>4</sup>Sullivan G et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. <https://bit.ly/42o3jnV>

<sup>5</sup>Rat Novel Object Recognition Test

<sup>6</sup>Mouse Porsolt Forced Swim Test

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# 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<sup>1</sup>
  - PPAR-β/d 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

## DEVELOPMENT PROGRAM

**Market Entry:** Major Depressive Disorder (MDD)

**Additional Indications:** PTSD, Neurocognitive Disorder From Corticosteroids, Alzheimer's Disease<sup>2</sup>

**Status:** Pre-clinical

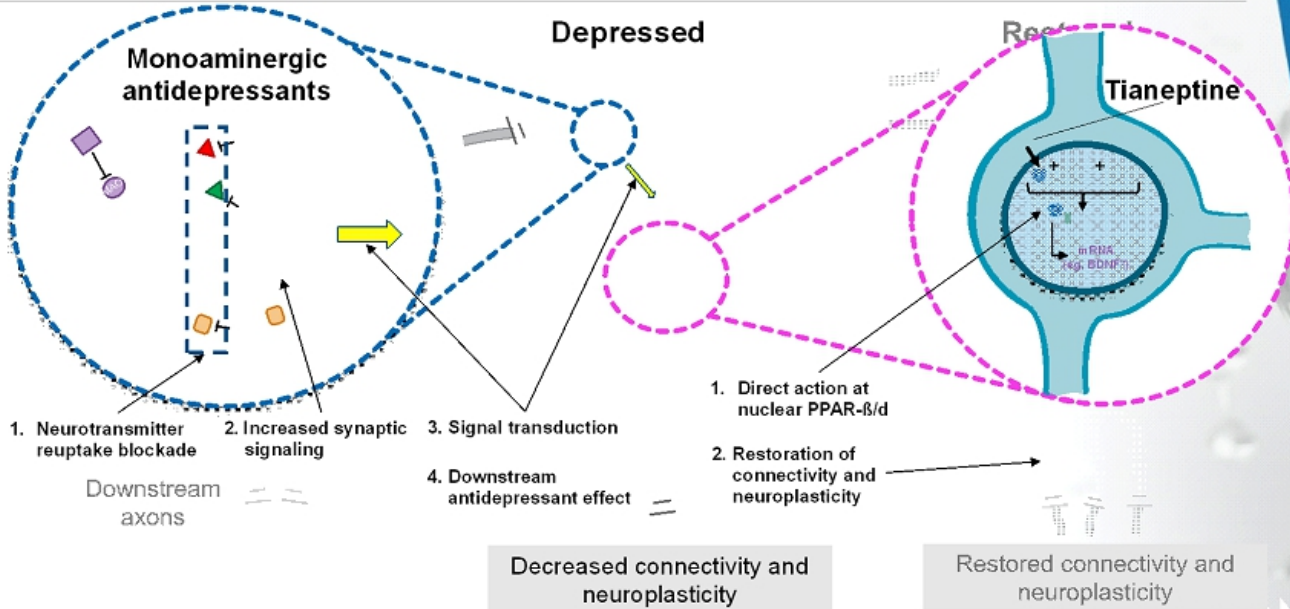
**Next Steps:** Expect IND can be supported by pre-clinical and clinical data from TNX-601 (racemic tianeptine) development

### Patents Issued

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

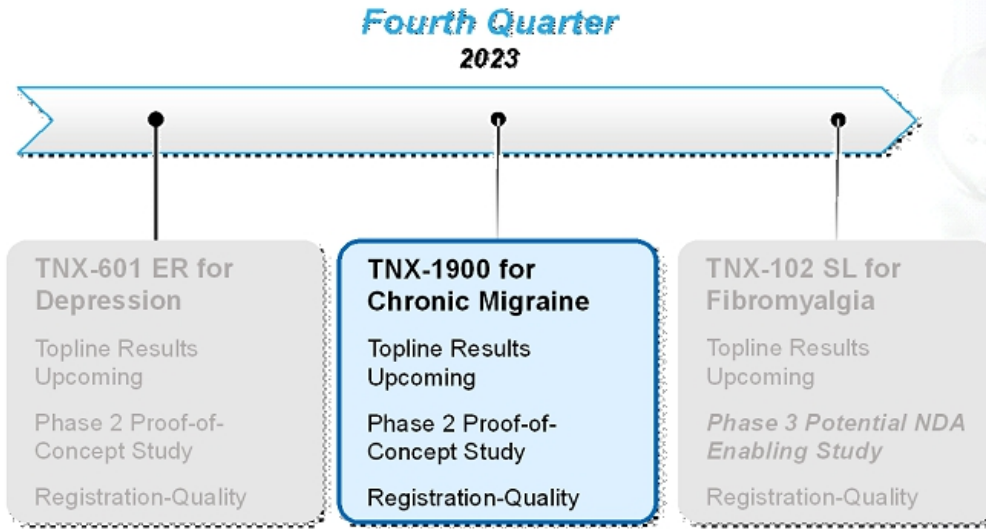
<sup>1</sup>Sullivan G et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. <https://bit.ly/42e3n1V>  
<sup>2</sup>Garcia-Alberca et al., 2022. *J Alzheimers Dis*. 88(2):707-720

## While Monoaminergic Antidepressants Work at the Synapse, (S)-Tianeptine "Cuts in Line" to More Directly Affect Neuroplasticity<sup>1</sup>



<sup>1</sup>Sullivan G et al. Poster presentation at the American Society of Clinical Psychopharmacology, June 2023. <https://bit.ly/42e3n1V>  
<sup>2</sup>BDNF=brain-derived neurotrophic factor.

## Upcoming Expected Topline Results



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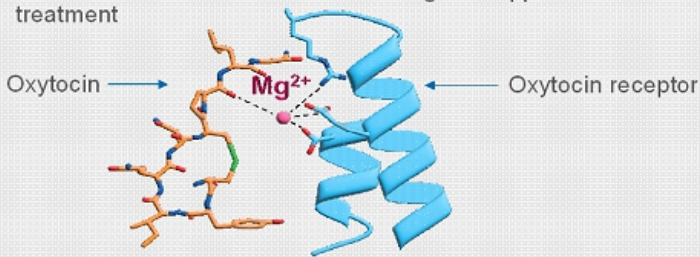
17

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

### PROFILE

- Intranasal OT has potential utility in treating migraine<sup>1</sup>
- Magnesium is known to potentiate the binding of OT to its receptor<sup>2,3</sup>
- 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<sup>4</sup>

**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.

<sup>1</sup>Tzabazis et al., 2017. *Headache*. 57 Suppl 2:84-75

<sup>2</sup>Antoni et al., 1989. *Biochem J*. 257(2):811-4

<sup>3</sup>Meyerowitz et al., 2022. *Nat Struct Mol Biol*. (3):274-281

<sup>4</sup>A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

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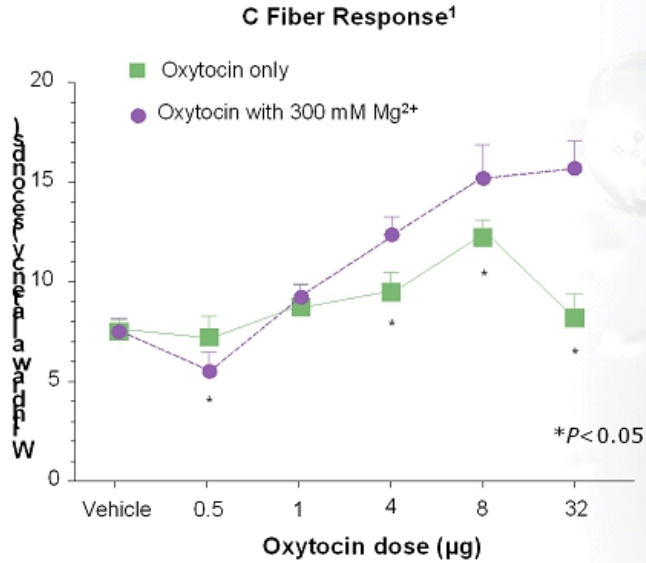
18

# Oxytocin Effects – Addressing the “Inverted U” Dose Response

## Addition of Mg<sup>2+</sup> Augments Oxytocin-Induced Analgesia in Animal Model

- A **nonlinear dose response** decreases efficacy at higher doses
- Addition of **Mg<sup>2+</sup> rescues the efficacy** of oxytocin at high doses

*in vivo* effect of Mg<sup>2+</sup> ion addition with intranasal oxytocin-induced craniofacial analgesia on the withdrawal response time to noxious heat stimulation of the cheek of pre-inflamed rat



<sup>1</sup>Adapted from: Bharadwaj VN, et al. *Pharmaceutics*. 2022;14(5):1105.

## TNX-1900: Phase 2 PREVENTION Study Design

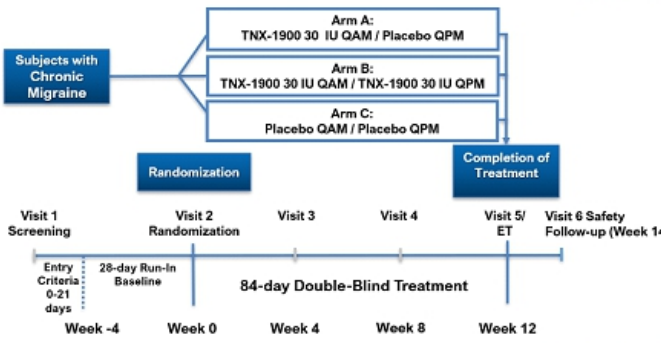


### General study characteristics:

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

### Primary Endpoint:

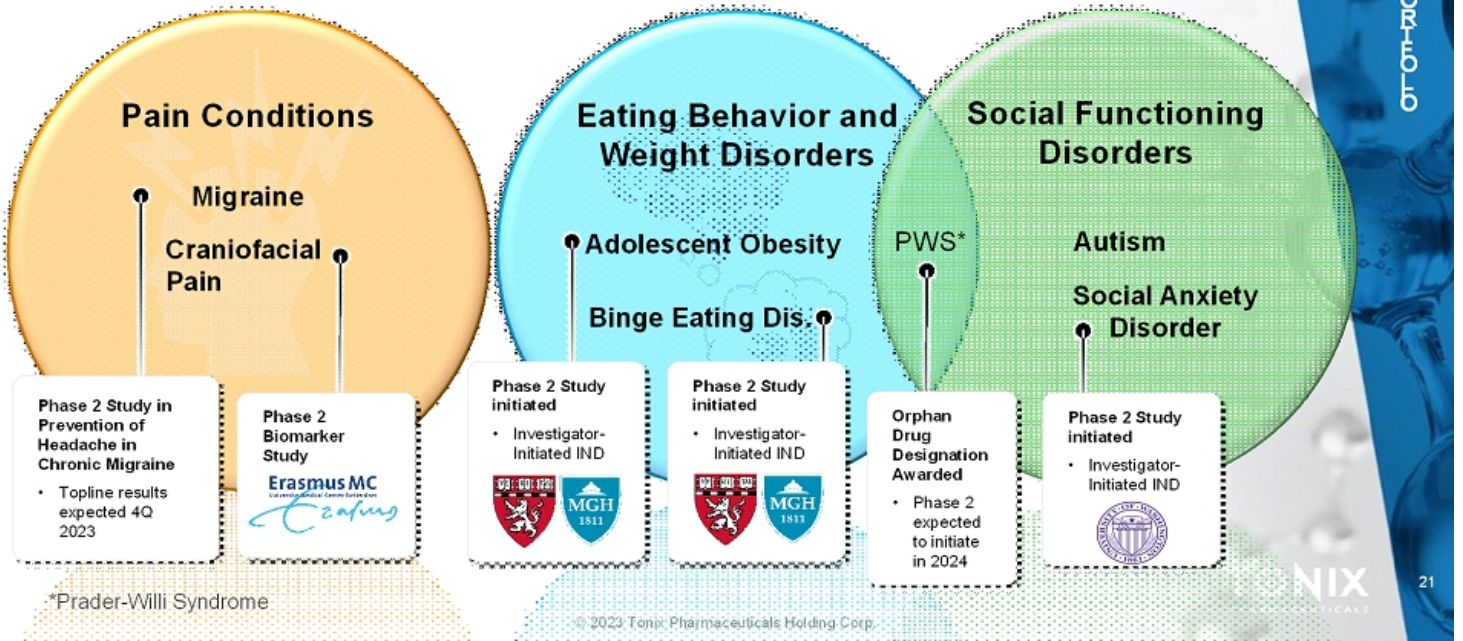
- Mean change in the number of migraine headache days between the 28-day Run-In phase and the last 28-days of the Treatment phase (TNX-1900 vs. placebo)



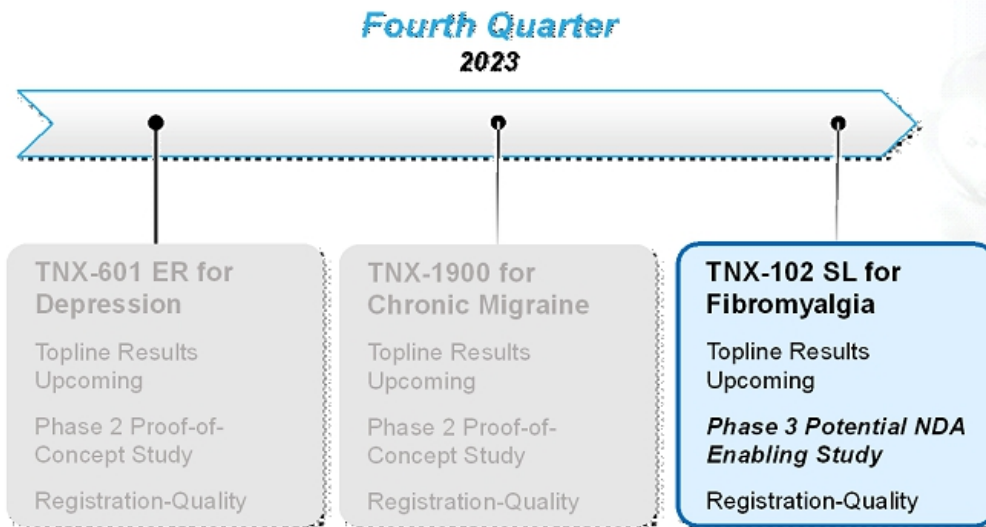
ClinicalTrials.gov Identifier: NCT05679908  
 A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)



## Potential Applications of TNX-1900 and TNX-2900



## Upcoming Expected Topline Results



# 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-HT<sub>2A</sub>, adrenergic- $\alpha$ 1, histaminergic-H<sub>1</sub>, and muscarinic-M<sub>1</sub> 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.

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## 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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## 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., approximately 90% of whom are women<sup>1</sup>
- 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<sup>2</sup>

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.

<sup>1</sup>American Chronic Pain Association ([www.theacpa.org](http://www.theacpa.org), 2019)

<sup>2</sup>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.

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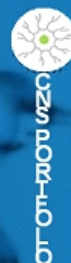


CNS-102-10-10

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# TNX-102 SL: Phase 3 RESILIENT Study Design



## 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

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

**Placebo once-daily at bedtime**

14 weeks

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

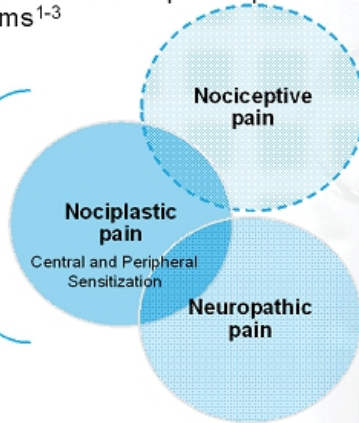
ClinicalTrials.gov Identifier: NCT05273749  
A Phase 3 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With Fibromyalgia (RESILIENT)

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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<sup>1-3</sup>



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

Nociplastic pain<sup>4</sup>: (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

<sup>1</sup>Biede et al., 2021. *J Prim Care Community Health*. 12:21501327211030826  
<sup>2</sup>Moghimi et al., 2021. *Curr Neurol Neurosci Rep*. 21(9):44  
<sup>3</sup>Thaweethai T., et al. 2023. *JAMA*. 2023 329(22):1934-1946  
<sup>4</sup>Trouvin et al., 2019. *Best Pract Res Clin Rheumatol*. 33(3):1014-15

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

## PROFILE

- Occurs in approximately 19% of recovered COVID-19 patients<sup>1</sup>
- As many as 40% of Long COVID patients experience multi-site pain, a hallmark of fibromyalgia<sup>2,3</sup>
- 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<sup>4</sup> 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 1<sup>st</sup> Quarter 2024

### Patents Issued

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

<sup>1</sup>June 22, 2022- CDC - [https://www.cdc.gov/nchs/pressroom/nchs\\_press\\_releases/2022/20220622.htm](https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm)

<sup>4</sup>Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID.



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



### Study characteristics:

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

### Primary Endpoint:

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

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

\*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





## PREVAIL Topline Results<sup>1</sup>

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<sup>2</sup>
- 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<sup>3-5</sup> – including Tonix's studies in fibromyalgia – make PROMIS Fatigue a solid candidate for the primary endpoint of future Long COVID registrational studies.

<sup>1</sup>Tonix Press Release, September 5, 2023 - <https://bit.ly/3Z8FQHQ>

<sup>2</sup>Walker S, et al. *BMJ Open* 2023;13:e069217. doi:10.1136/bmjopen-2022-069217

<sup>3</sup>Cook, K.F., et al. 2016. *Journal of Clinical Epidemiology*, 73, 89-102

<sup>4</sup>Cella, D., et al. 2016. *Journal of Clinical Epidemiology*, 73, 128-134

<sup>5</sup>Lai, J.S., et al. 2011. *Archives of Physical Medicine and Rehabilitation*, 92(10 Supplement), S20-S27.

## PREVAIL Next Steps

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

- Expected date of End of Phase 2 meeting is 1<sup>st</sup> 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 4<sup>th</sup> Quarter 2023





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## TNX-1500\*



### Next Generation -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 (Fc $\gamma$ R)

**Second Generation:** Eliminated the Fc $\gamma$ R TE complication but potency and half life was reduced, limiting utility

**Third Generation (TNX-1500):** Re-engineered to better modulate the binding of Fc $\gamma$ R.

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

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### Prevention of Allograft Rejection

Status: Phase 1 currently enrolling

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

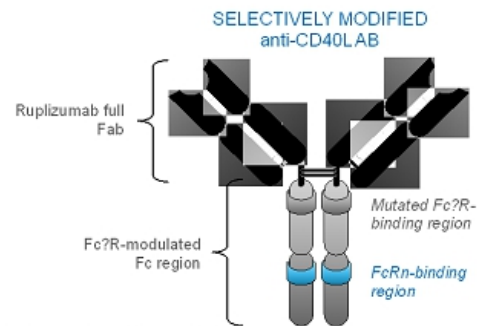
**Next Steps:** Initiate Phase 2 study in Kidney Transplant Recipients

### Autoimmune Diseases

Status: Potential future indications include:

**Sjögren's Syndrome, Systemic Lupus Erythematosus**

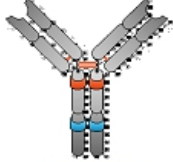
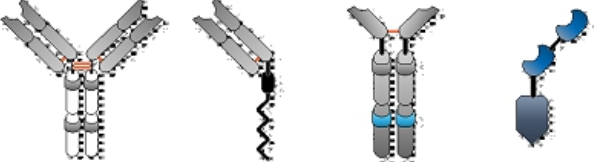
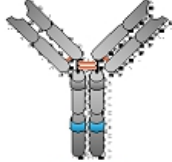
- These indications require large studies, but represent large target markets



Contains the full ruplizumab Fab and the engineered Fc region that modulates Fc $\gamma$ R-binding, while preserving FcRn function.

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## Third-Generation a-CD40L Engineered to Decrease Risk of Thrombosis

First-generation anti-CD40L mAbs	Second-generation anti-CD40L proteins	Third-generation anti-CD40L mAbs*
 <p><b>Ruplizumab</b></p>	 <p><i>Aglycosyl Ruplizumab</i>    <i>Dapirolizumab</i>    <i>Letolizumab</i>    <i>Dazodalibep</i></p>	 <p><b>TNX-1500</b></p>
<p>Constant fragment (Fc) domain interacted with FcγRIIA (CD32A), which suggested a mechanism for the increased risk of thrombosis.<sup>1,2</sup></p>	<p>Second-generation anti-CD40L proteins exhibited dramatically reduced binding to FcγRIIA<sup>3-6</sup> but had other issues, including decreased efficacy, shortened half-life, or engendering of anti-drug antibodies (ADAs).<sup>7-9</sup></p>	<p>TNX-1500 is engineered to target CD40L therapeutically while reducing FcγRIIA binding and thereby lowering the potential for thrombosis.<sup>1-9</sup></p>

\*Sanofi's frexalimab (formerly SAR441344) and Eledon's tegoprubart (formerly AT-1501) also are Fc modified

<sup>1</sup>Inwald et al., 2003. *Circ Res*. 92(9):1041-1048

<sup>2</sup>Robles-Camilo et al., 2010. *J Immunol*. 185(3):1577-1583

<sup>3</sup>Shock et al., 2015. *Arthritis Res Ther*. 17(1):234

<sup>4</sup>Xie et al., 2014. *J Immunol*. 192(9):4083-4092

<sup>5</sup>Ferrant et al., 2004. *Int Immunol*. 16(11):1583-1594

<sup>6</sup>Karnell et al., 2019. *Sci Transl Med*. 11(489):eaar6584

<sup>7</sup>ClinicalTrials.gov identifier: NCT02273960. Updated July 16, 2019. Accessed June 1, 2021. <https://clinicaltrials.gov/ct2/show/results/NCT02273960?view=results>

<sup>8</sup>Waters, 2018. *Biocentury*.

<sup>9</sup>Company data

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## 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.<sup>1,2</sup>

<sup>1</sup>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>

<sup>2</sup>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>

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## 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<sup>1,2</sup>
- Frexalimab, f.k.a. SAR441344 (Fc-modified)

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

- Two Positive Phase 2 studies reported<sup>3,4</sup>
- 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<sup>5</sup>
- Dapirolizumab pegol (pegylated Fab)

<sup>1</sup>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/2023/2023-05-31-05-00-00-2673991](http://www.sanofi.com/en/media-room/press-releases/2023/2023-05-31-05-00-00-2673991) (accessed August 11 2023)

<sup>2</sup>Carvalho, T. *Nature Medicine (News)* (2023), 29: 1882

<sup>3</sup>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)

<sup>4</sup>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

<sup>5</sup><https://www.ucb.com/our-science/pipeline>

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



### Potential New Cancer Treatment

- TNX-1700 (rTFF2) has effects on cancer by altering the tumor micro-environment
- Mechanism of action: suppresses myeloid-derived suppressor cells and activates anti-cancer CD8+ T cells
- Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies (mAbs)

### Preclinical Evidence for Inhibiting Growth of Cancer Cells

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

**Market Entry:** Immuno-oncology, combination therapy with PD1 blockers for gastric and colorectal cancer

**Status:** Preclinical

**Next Steps:** Animal studies ongoing

**Differentiator:** No product yet identified consistently augments PD1 effects on cold tumors

### Licensed from Columbia University

- Developing in partnership under sponsored research agreement

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

### Patents Filed

<sup>1</sup>Daugherty, B. et al. March 6, 2023 Keystone Poster, [www.tonixpharma.com/wp-content/uploads/2023/03/mTFF2-MSA\\_mTNX-1700\\_Suppresses-Tumor-Growth-and-Increases-Survival-in-an-Anti-PD-1-Treatd-MC38-Colorectal-Cancer-Model-by-Targeting-MDSCs.pdf](http://www.tonixpharma.com/wp-content/uploads/2023/03/mTFF2-MSA_mTNX-1700_Suppresses-Tumor-Growth-and-Increases-Survival-in-an-Anti-PD-1-Treatd-MC38-Colorectal-Cancer-Model-by-Targeting-MDSCs.pdf)



## 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.

\*Noyce et al., 2018. PLoS One. 13(1):e0189453

### Mpox and Smallpox Vaccine

Status: Preclinical

- TNX-801 is a cloned version of horsepox<sup>1</sup> (without any DNA insert) purified from cell culture

Milestone: Successful completion of pre-IND meeting

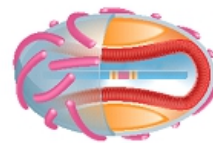
Next Steps: Preparation of IND submission

### Vaccine for Future Emerging Infectious Diseases

Example: TNX-1850 for COVID-19

Status: Model System

TNX-801\*  
schPXV (Horsepox)  
212,811 bp





## 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

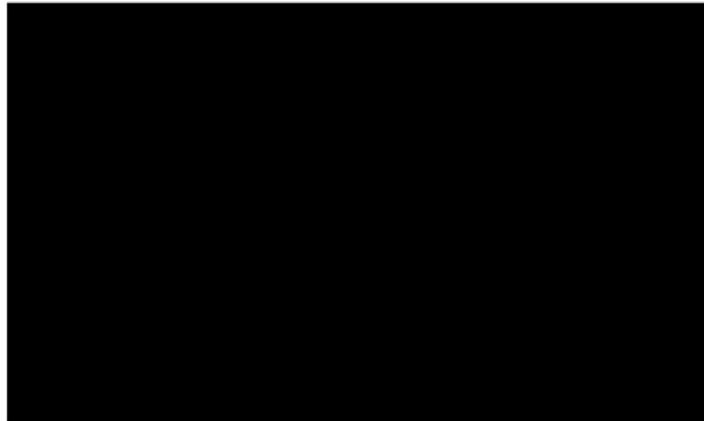
- **Function:** Development and clinical scale manufacturing of biologics
- **Description:** ~45,000 square feet, BSL-2
- **Status:** Operational



## Broad Spectrum Antivirals

### New DoD approach<sup>1</sup> raises importance of broad-spectrum medical counter measures

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



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



## DTRA RFP for Broad Spectrum Antivirals Through Medical CBRN

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

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

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

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## Broad-Spectrum Antiviral Discovery Programs

### Host-directed antiviral discovery programs

#### CD45 targeted therapeutics

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

#### Cathepsin inhibitors

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

### Virus-directed antivirals discovery program

#### Viral glycan-targeted engineered biologics

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

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**TEAM,  
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## Key Development Partners



MASSACHUSETTS  
GENERAL HOSPITAL



HARVARD  
MEDICAL SCHOOL

COLUMBIA  
UNIVERSITY



**TNX-1500: ALLOGRAFT REJECTION**

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



STANFORD  
UNIVERSITY



UNIVERSITÉ  
DE GENÈVE



UNIVERSITY OF  
ALBERTA



SR  
SOUTHERN  
RESEARCH

**TNX-1900: MIGRAINE & OTHER INDICATIONS**

**TNX-801: SMALLPOX AND MONKEYPOX VACCINE  
TNX-1850: COVID-19 VACCINE**



Inserm Transfert  
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CHU  
de Toulouse



Aix-Marseille  
université

KANSAS STATE  
UNIVERSITY

**TNX-2900: PRADER-WILLI SYNDROME**

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

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## Upcoming: Expected Topline Clinical Data and Trial Initiations 2023

### 4<sup>th</sup> Quarter

- Phase 2 PREVENTION study of TNX-1900 for chronic migraine
  - Affects approximately 3-7 M adults in the U.S<sup>1</sup>
- 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)<sup>2</sup>
- Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia
  - Affects approximately 6-12 M adults in the U.S<sup>3</sup>

### 3<sup>rd</sup> Quarter Clinical Trial Initiations

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

### 4<sup>th</sup> Quarter Clinical Trial Initiations

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

<sup>1</sup>Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalgia, 2010, 30: 599-609

<sup>2</sup>CDC - [https://www.cdc.gov/mmwr/volumes/72/wr/mm7224a1.htm?s\\_cid=mm7224a1\\_w](https://www.cdc.gov/mmwr/volumes/72/wr/mm7224a1.htm?s_cid=mm7224a1_w)

<sup>3</sup>American Chronic Pain Association (www.theacpa.org, 2019)

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.upsheer-smith.com](http://www.upsheer-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-ef1bd8aea867d>

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

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

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



## Tosymra® IMPORTANT SAFETY INFORMATION (1 of 2)

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

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

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

Do not use Tosymra if you have:

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

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



## Tosymra® IMPORTANT SAFETY INFORMATION (2 of 2)

**Tosymra may cause serious side effects including:**

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

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

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

This is the most important information to know about Tosymra but is not comprehensive. For more information, talk to your provider and read the [Patient Information and Instructions for Use](#). You can also visit [www.upsher-smith.com](http://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](http://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.