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): May 21, 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.

On May 21, 2024, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that EVERSANA® Life Science Services, LLC ("Eversana") completed the initial phase of an assessment of the U.S. market opportunity for the Company's Tonmya™ product candidate (also known as TNX-102 SL, cyclobenzaprine HCl sublingual tablets). A copy of the press release that discusses this matter is filed as Exhibit 99.01 and 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 May 21, 2024, the Company announced Eversana completed the initial phase of an assessment of the U.S. market opportunity for Tonmya. Key findings from Eversana's assessment include the following:

- Approximately 2.7 million adults in the U.S. are currently diagnosed and treated for fibromyalgia, 90% of which are female.
- Percentage of fibromyalgia patients who were prescribed certain drugs:
  - FDA-approved fibromyalgia drug prescriptions:
    i. duloxetine (generic Cymbalta®:) 23%), pregabalin (generic Lyrica®): 13%), and Savella® (milnacipran): 1%
  - Off-label drug prescriptions:

i. Gabapentin: (26%), hydroxycodone: 20%, cyclobenzaprine: 18%, oxycodone: 19%, tramadol: 13%, meloxicam: 12%, and amitriptyline: 6%

- Off-label opioids prescriptions:

i. Hydroxycodone: 20%, oxycodone: 19%, and tramadol: 13%

- Most physicians who prescribe drugs for patients suffering from fibromyalgia are rheumatologists, pain medicine specialists, primary care physicians, neurologists, and psychiatrists.
- 85% of fibromyalgia patients fail first-line therapy due to efficacy and tolerability issues; 79% are on multiple therapies.
- Median interest in Tonmya as a new treatment option among physicians interviewed of 4.0 on a 5-point scale; physicians interviewed indicated intended use in 40% of their fibromyalgia patients, assuming no market access barriers.

Forward- Looking Statements

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

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

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press Release, dated May 21, 2024
99.02	Corporate Presentation by the Company for May 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: May 21, 2024

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

Exhibit 99.01

Tonix Pharmaceuticals Announces Key Findings from Initial Phase of EVERSANA Market Opportunity Analysis for Tonmya™ for the Management of Fibromyalgia

Tonmya is a potential new first-line, centrally acting non-opioid analgesic for the management of fibromyalgia, supported by statistically significant results from two Phase 3 trials

Primary physician research found high level of interest in Tonmya as a potential new treatment option for fibromyalgia

Significant dissatisfaction reported with drugs currently approved by FDA for the treatment of fibromyalgia

Analysis of claims data revealed that addictive opioids are prescribed more frequently than currently approved drugs following fibromyalgia diagnosis

New Drug Application (NDA) submission to the FDA on track for the second half of 2024

CHATHAM, N.J., May 21, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, announced today that EVERSANA® Life Science Services, LLC, a leading provider of commercialization services to the global life sciences industry, completed the initial phase of an assessment of the U.S market opportunity for Tonmya™ (also known as TNX-102 SL, cyclobenzaprine HCl sublingual tablets), a potential new first line therapy for the management of fibromyalgia. Tonix previously announced that EVERSANA was selected to support the launch strategy and commercial planning of Tonmya. Specifically, EVERSANA is working with Tonix to assess the fibromyalgia landscape and help plan an efficient go-to-market (GTM) strategy.

“The primary research and analysis conducted by EVERSANA provides valuable insights and informs the vision for the commercialization of Tonmya,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “We are excited to refine our business strategy for the anticipated launch of Tonmya in 2025. It has been approximately fifteen years since patients suffering with fibromyalgia have been provided a new therapeutic option. The market research conducted by EVERSANA with physicians indicates a continued high unmet need, with the need ranked > 4.0 on a 5-point scale.”

Dr. Lederman continued, “We were surprised to learn that opioids dominate the fibromyalgia prescription market, despite the well-known risks of dependency. Opioids are prescribed to more patients following fibromyalgia diagnosis than all the FDA-approved fibromyalgia drugs combined. If approved, we believe that Tonmya can provide a non-opioid, centrally-acting solution for fibromyalgia patients. This is corroborated by EVERSANA’s primary market research in which physicians indicated median interest of 4.0 on a 5-point scale and intended use of Tomya in 40% of their fibromyalgia patients, upon approval.[1] We look forward to submitting the NDA for Tonmya in the second half of this year and expect an FDA decision on approval in 2025.”

EVERSANA’s analysis of the market size was based on medical claims databases and epidemiological studies on prevalence and diagnosis[2]. Primary research with physicians was conducted to test the potential adoption of Tonmya based on its activity and tolerability.

Key findings from claims data analyses[2]:

- ~2.7 million adults in the U.S. currently diagnosed and treated for fibromyalgia.
  - ~90 percent of patients diagnosed with fibromyalgia are female.
- Percentage of fibromyalgia patients who were prescribed certain drugs[3]:
  - FDA-approved fibromyalgia drug prescriptions:
    i. Duloxetine (generic Cymbalta®): 23%, pregabalin (generic Lyrica®): 13%, and Savella® (milnacipran): 1%
  - Off-label drug prescriptions:
    i. Gabapentin: 26%, hydroxycodone: 20%, cyclobenzaprine: 18%, oxycodone: 19%, tramadol: 13%, meloxicam: 12%, and amitriptyline: 6%
  - Off-label opioids prescriptions:
    i. Hydroxycodone: 20%, oxycodone: 19%, and tramadol: 13%
- Targeted prescriber strategy for launch.
  - High prescribers are rheumatologists, pain medicine specialists, primary care physicians, neurologists, and psychiatrists.
- ~50 percent of diagnosed fibromyalgia patients are covered by Medicare.
  - Medicare population stands to benefit from a decrease in out-of-pocket prescription drug liability to $2,000 per year when the changes from the Inflation Reduction Act are enacted in 2025.

Key findings from primary physician research[4]:

- High level of dissatisfaction with currently prescribed drugs.
  - Physicians interviewed estimate that 85% of their patients fail first-line therapy due to efficacy and tolerability issues and 79% of their patients are on multiple therapies.
  - Prescribers indicate high unmet need in fibromyalgia, ranked >4.0 on a 5-point scale.
- High level of interest in Tonmya from physicians interviewed as a potential new treatment option based on favorable activity and tolerability profile observed in Tonmya fibromyalgia clinical studies.
  - Median interest in Tonmya of 4 on a 5-point scale.
  - Physicians indicated intended use of Tonmya in 40% of their fibromyalgia patients.[1]

Tonmya is a centrally acting, non-opioid medication. As previously announced, Tonix's second statistically significant Phase 3 study, RESILIENT, met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.00005) in participants with fibromyalgia. Statistically significant and clinically meaningful results (p=0.001 or better) were also seen in all key secondary endpoints related to improving sleep quality, reducing fatigue, and improving overall fibromyalgia symptoms and function.

Tonix plans to submit an NDA to the U.S. Food and Drug Administration (FDA) in the second half of 2024 for Tonmya for the management of fibromyalgia and has scheduled a Type B pre-NDA meeting with FDA for the second quarter of 2024.

[1] *40% was the median preference share among physicians interviewed, assuming no market access barriers.*

[2] *EVERSANA analysis of claims database, May 2024; commissioned by Tonix*

[3] *Note: the total number of patients is greater than 100% because of switching between medications and polypharmacy.*

[4] *EVERSANA primary physician research, May 2024; commissioned by Tonix*

About Tonmya* (also known as TNX-102 SL)

Tonmya is a centrally acting, non-opioid, non-addictive, bedtime medication. The tablet is a patented sublingual formulation of cyclobenzaprine hydrochloride developed for the management of fibromyalgia. In December 2023, the company announced highly statistically significant and clinically meaningful topline results in RESILIENT, a second positive Phase 3 clinical trial of Tonmya for the management of fibromyalgia. In the study, Tonmya met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.00005) in participants with fibromyalgia. Statistically significant and clinically meaningful results were also seen in all key secondary endpoints related to improving sleep quality, reducing fatigue and improving overall fibromyalgia symptoms and function. RELIEF, the first positive Phase 3 trial of Tonmya in fibromyalgia, was completed in December 2020. It met its pre-specified primary endpoint of daily pain reduction compared to placebo (p=0.010) and showed activity in key secondary endpoints.

*Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration (FDA) as the tradename for TNX-102 SL for the management of fibromyalgia. Tonmya has not been approved for any indication.

About EVERSANA®

EVERSANA® is a leading independent provider of global services to the life sciences industry. The company's integrated solutions are rooted in the patient experience and span all stages of the product life cycle to deliver long-term, sustainable value for patients, prescribers, channel partners and payers. The company serves more than 650 organizations, including innovative start-ups and established pharmaceutical companies, to advance life sciences solutions for a healthier world. To learn more about EVERSANA, visit eversana.com or connect through LinkedIn and X.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for Tonmya, a product candidate for which two positive Phase 3 studies have been completed for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction as well as fibromyalgia-type Long COVID. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase) a biologic designed to treat cocaine intoxication with Breakthrough Therapy designation. Tonix's immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

*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. All other marks are property of their respective owners.

This press release and further information about Tonix can be found atwww.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 commercialize 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, 2023, as filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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Exhibit 99.02

TONIX PHARMACEUTICALS

Corporate Presentation

Abbreviated

Focus on: Tonmya™* (TNX-102 SL) in Development for the Management of Fibromyalgia

May 2024

NASDAQ: TNXP

*Tonmya is conditionally accepted by FDA as the tradename for TNX-102 SL for the management of fibromyalgia

Version P0567 May 21, 2024 (Doc 1434)

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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, 2023, as filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, 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.

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Who We Are

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

With a Focus on:

Filing a New Drug Application (NDA) with the US Food and Drug Administration (FDA) for Tonmya™ (TNX-102 SL) for the management of Fibromyalgia (FM)

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Key Clinical Programs

Molecule*	Indication	Phase 1	Phase 2	Phase 3	NDA Submission
Tonmya™ TNX-102 SL Cyclobenzaprine HCl Protectic® Sublingual Tablets	Fibromyalgia	*Statistically Significant Phase 3 Topline Results Reported 4Q'23*			***Submission expected 2H'24***
	Long COVID	*Phase 2 Topline Results Reported 3Q'23*			
	Acute Stress Disorder	*Phase 2 Study** Start Expected 2Q'24*			
TNX-1300 Cocaine Esterase *NIDA Funded*	Cocaine Intoxication	*Phase 2 Study Start Expected 2Q'24*			
TNX-2900 Intranasal Potentiated Oxytocin *FDA Orphan Drug and Rare Pediatric Disease Designation*	Prader-Willi Syndrome	*Phase 2 Ready*			
TNX-1500 Anti-CD40L mAb	Organ Transplant Rejection/ Autoimmune Conditions	*Phase 1 Study Ongoing*	*Clinical Stage complete*		

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

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Tonmya™
(TNX-102 SL, Cyclobenzaprine HCl Sublingual Tablets)

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

Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration (FDA) as the tradename for TNX-102 SL for the management of fibromyalgia. Tonmya has not been approved for any indication.

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About Fibromyalgia

*Fibromyalgia is a **chronic pain disorder** resulting from amplified sensory and pain signaling within the CNS[1]*

*Fibromyalgia is a **syndrome** comprised of the **symptoms**: chronic widespread pain, **nonrestorative sleep**, and fatigue*

Fibromyalgia is considered a **chronic overlapping pain condition (COPC)**
*- the **only COPC** with any **FDA-approved drugs**[3]*

Fibromyalgia is the prototypic nociplastic syndrome

[1]American Chronic Pain Association (www.theacpa.org, 2019)
[3]CFS/ME = chronic fatigue syndrome/myalgic encephalomyelitis
[3]The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica®); Duloxetine (Cymbalta®); Milnacipran (Savella®)

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Fibromyalgia is a Large, Underserved and Dissatisfied Population*

- **~10 million U.S. adults are affected – predominantly women[1,2]**
  - Debilitating and life altering condition
  - Significant economic impact
- **Patients are dissatisfied, despite three FDA approved drugs[3,4]**
  - 85% of patients fail first-line therapy[5]: efficacy variability, tolerability issues especially when used long-term and lack of broad-spectrum activity
  - Typical for patients to rotate between drugs and be on multiple drugs at the same time; 79% of FM patients are on multiple therapies[5]
- **~2.7 million diagnosed FM patients see their physician each year[6]**
  - >22 million prescriptions are issued for the treatment of fibromyalgia (on- and off-label usage) each year[7,8]

**This slide and others contain market information and analyses regarding fibromyalgia prepared for Tonix by EVERSANA*

[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 A, et al. *Arthritis Care Res (Hoboken)*. 2013 65(5):786-92. doi: 10.1002; diagnosed prevalence rate was 1.1% of adult population or 50% of the prevalent population
[3]Robinson RL, et al. *Pain Med*. 2012 13(10):1366-76. doi: 10.1111; 85% received drug treatment
[4]The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)
[5]EVERSANA primary physician research, May 2024; commissioned by Tonix
[6]EVERSANA analysis of claims database, May 2024; commissioned by Tonix
[7]Product sales derived from IMS MIDAS; IMS NDTI used to factor usage for fibromyalgia; data accessed April 2015.
[8]Market research by Frost & Sullivan, commissioned by Tonix, 2011

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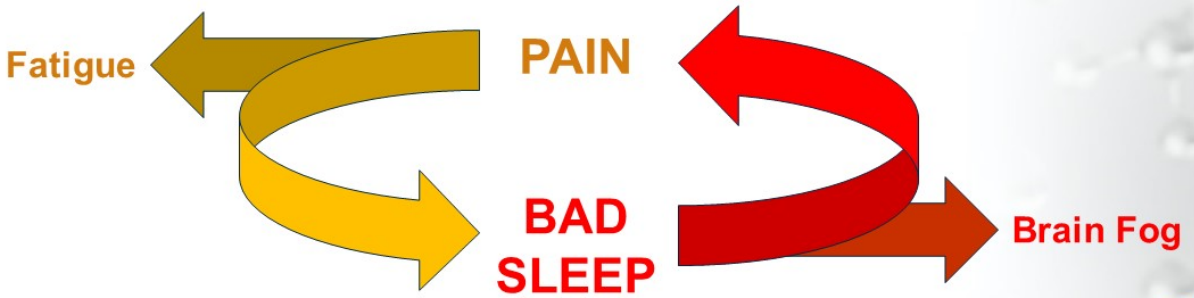
Poor Sleep and Pain have Bi-directional Reinforcing Effects[1]

- **Poor sleep and pain form a vicious cycle in driving fibromyalgia decompensation**
  - Can't sleep → worse pain / In pain → can't sleep
  - Poor sleep and pain contribute to persistence, chronicity and severity
  - Syndrome includes symptoms of fatigue and brain fog
- **Treating sleep disturbance in fibromyalgia has the potential to break the vicious cycle**
  - Potential to remove an obstacle to recovery
  - Using the right medicine is important – some sedative/hypnotics don't work[1,2]



[1]Moldofsky H, et al. *J Rheumatol*. 1996;23:529–533.
[2]Grönbald M, et al. *Clin Rheumatol*. 1993;12(2):186–191

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Tonmya™ (TNX-102 SL, Cyclobenzaprine HCl Sublingual Tablets)[1]

- **Non-opioid analgesic designed for long-term daily bedtime use in fibromyalgia patients**
  - Targets non-restorative sleep
  - Potent binding and antagonist activities at four post-synaptic receptors
    - serotonin-5-HT2A
    - α1-adrenergic
    - histaminergic-H1
    - muscarinic-M1
  - No recognized risk for abuse

- **Improves sleep quality, does not increase sleep quantity:**
  - Not a traditional hypnotic or sedative

- **Proprietary, sublingual transmucosal formulation of cyclobenzaprine designed to optimize delivery and absorption**
  - Protectic® formulation based on eutectic composition of matter
    - Rapid absorption
    - Decrease in major metabolite by bypassing first-pass hepatic metabolism

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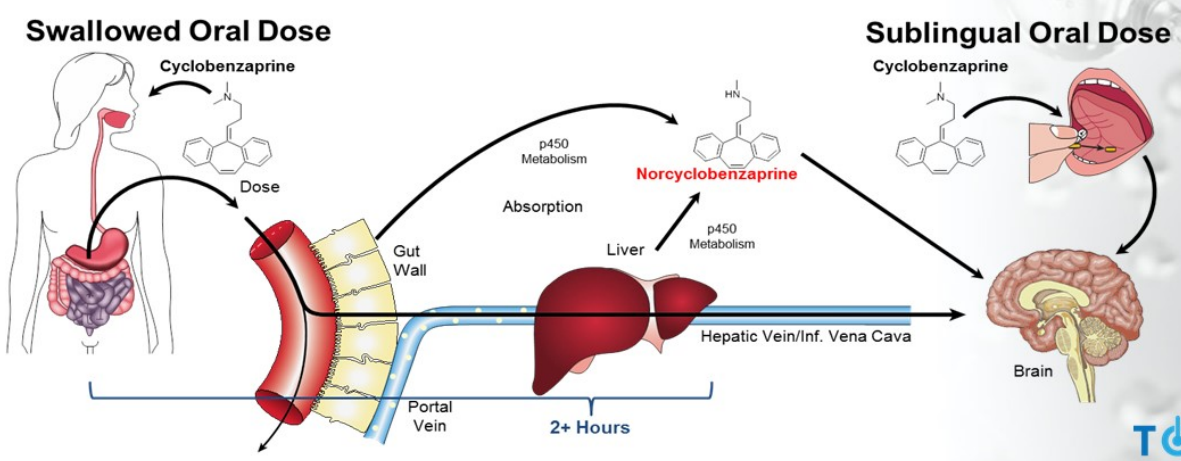
TNX-102 SL: Sublingual Administration and Transmucosal Delivery

- 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)



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Fibromyalgia Program Status

Tonmya™*
(TNX-102 SL)
Cyclobenzaprine Protectic®
Sublingual Tablets

Fibromyalgia

Statistically Significant 2nd Phase 3 Topline Results Reported 4Q'23

- **First pivotal Phase 3 study (*RELIEF*) reported – December 2020**[1]
- **Second Phase 3 study (*RALLY*) missed primary endpoint – July 2021**
- **Confirmatory pivotal Phase 3 study (*RESILIENT*) reported – December 2023**

Next Steps:

- **Type B Pre-NDA meeting scheduled with FDA in 2Q'24**
- **NDA filing expected 2H'24**
- **FDA decision on NDA approval expected 2H'25**

*Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration (FDA) as the tradename for TNX-102 SL for the management of fibromyalgia. Tonmya has not been approved for any indication.

[1]Lederman S, et al. *Arthritis Care Res (Hoboken)*. 2023 Nov;75(11):2359-2368. doi: 10.1002

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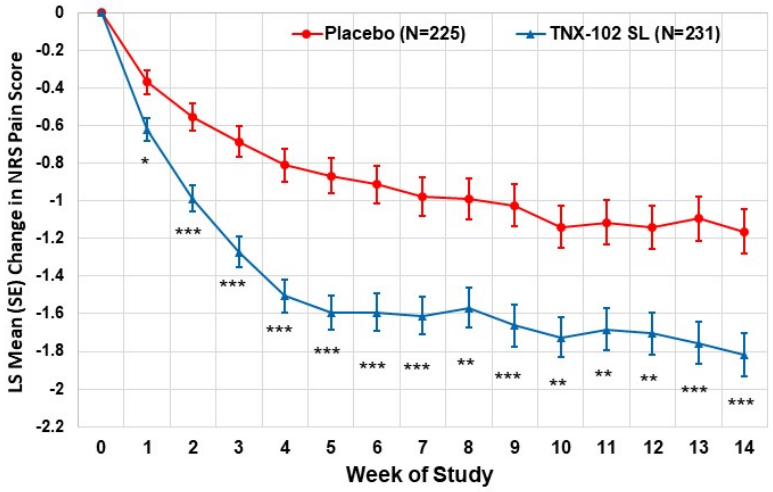
RESILIENT Primary Outcome Measure
Reduction in Widespread Pain

RESILIENT Study

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 Summary of Endpoints

RESILIENT Study

CNS PORTFOLIO

Endpoint	P-value	Effect Size (ES)
Primary Endpoint		
Daily Diary Pain ratings	***p* = 0.00005****	ES = 0.38
Key Secondary Endpoints*		
Patient Global Impression of Change (PGIC), responders	*p* = 0.00013**	--
Fibromyalgia Impact Questionnaire – Symptoms domain	*p* = 0.000002**	ES = 0.44
Fibromyalgia Impact Questionnaire – Function domain	*p* = 0.001**	ES = 0.30
PROMIS Sleep Disturbance instrument	*p* = 0.0000001**	ES = 0.50
PROMIS Fatigue instrument	*p* = 0.00009**	ES = 0.37
Diary Sleep Quality ratings	*p* = 0.0007**	ES = 0.32

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

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RESILIENT – Cognitive Dysfunction or "Brain Fog"

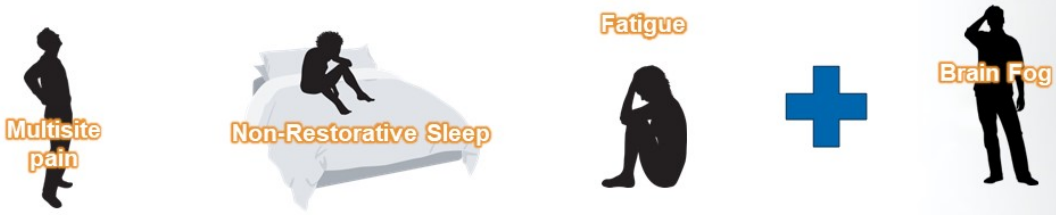
RESILIENT Study

CNS PORTFOLIO

Brain Fog assessed by the FIQ-R[1] item on memory

- Patients rated their level of memory problems
- 11-pt scale going from "Good Memory" to "Very Poor Memory"
- Prespecified endpoint, but not in the "waterfall" with the key secondary endpoints

- TNX-102 SL patients vs PBO change from baseline LS mean (SE) difference of −0.8 (0.23)
- *p* = 0.001 (not corrected for multiple comparisons)
- Cohen's *d* effect size = 0.31



[1]FIQ-R = Fibromyalgia Impact Questionnaire - Revised

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Tonmya™ Showed Broad-Spectrum Activity and was Well Tolerated

		Lyrica®	Cymbalta® Savella®	Tonmya™
Activity	Pain	**YES**	**YES**	**YES**
	Sleep	**YES**	**-**	**YES**
	Fatigue	**-**	**YES**	**YES**
Systemic Tolerability Issues	Insomnia	**-**	**+**	**-**
	Fatigue	**+**	**-**	**-**
	Weight	**+**	**-**	**-**
	Blood Pressure	**-**	**+**	**-**
	Sexual function	**-**	**+**	**-**
	GI issues	**-**	**+**	**-**

- Tonmya showed activity in all three measures of pain, sleep, and fatigue
- Tonmya is not associated with any of the commonly reported side effects of the FDA-approved medications for fibromyalgia

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Safety and Tolerability

- **Completion Rate (safety population): TNX-102 SL: 81.0% and Placebo: 79.2%**
- **No new safety signals observed**
- **Only systemic adverse events (AEs) at rate ≥ 3.0% (TNX-102 SL v. Placebo)**
  - COVID-19 (4.3% v. 3.1%), somnolence (3.0% v. 1.3%), and headache (3.0% v. 1.8%)
- **As previously observed TNX-102 SL associated with administration site reactions**
  - Hypoaesthesia oral (23.8% v. 0.4%), product taste abnormal (11.7% v. 0.9%), paraesthesia oral (6.9% v. 0.9%), and tongue discomfort (6.9% v. 0%)
- **No effect on weight or blood pressure (BP)**
  - Weight: Week 14 change from baseline for TNX-102 SL of +0.04 lbs.; and for Placebo of +0.44 lbs.
  - Systolic BP: Week 14 change from baseline for TNX-102 SL of +0.7 mmHg; and for Placebo of +0.5 mmHg
  - Diastolic BP: Week 14 change from baseline for TNX-102 SL of +1.1 mmHg; and for Placebo of +0.2 mmHg
- **No sexual dysfunction AEs and improved female sexual functioning**
  - No reported AEs of any type of sexual dysfunction
  - Improvement in female sexual function using Changes in Sexual Functioning Questionnaire (p=0.010)

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CNS PORTFOLIO

RESILIENT Safety Summary

RESILIENT Study

CNS PORTFOLIO

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
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%)
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%)

*Safety Population

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~50% of U.S. Fibromyalgia Patients are on Medicare: Prescription Coverage in Medicare Stands to Benefit from Changes in IRA

CNS PORTFOLIO

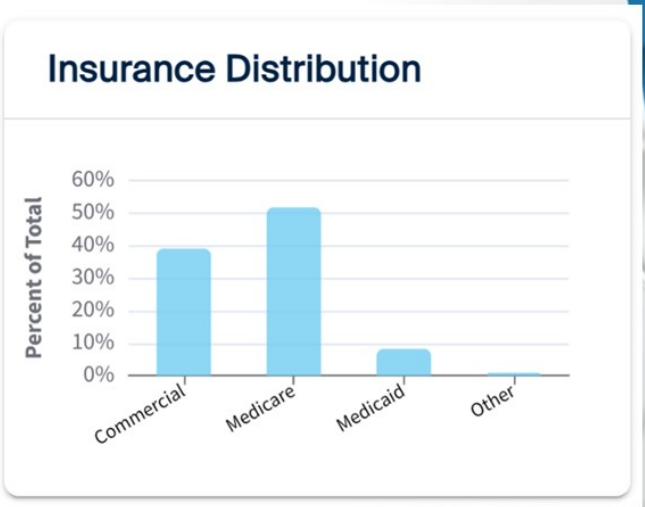
Approximately 50% of fibromyalgia patients are on Medicare

- EVERSANA analysis of claims database consisting of 2.2M patients, for which 1.2M claims were submitted throughout March 2002-March 2023[1]

Beneficial Changes in 2025 to Medicare Part D through Inflation Reduction Act (IRA)[2]

- Medicare prescription payment plan to offer enrollees the option to pay out-of-pocket prescription drug costs in the form of capped monthly installment payments instead of all at once at the pharmacy
- Annual out-of-pocket costs will be capped at $2,000 in year 2025
- Will replace the existing Coverage Gap Discount Program, which sunsets as of January 1, 2025

Fibromyalgia Patients by Coverage[1]



[1] EVERSANA analysis of claims database, May 2024; commissioned by Tonix
[2] Source: Final CY 2025 Part D Redesign Program Instructions Fact Sheet | CMS

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Prescribers Interviewed are Broadly Dissatisfied with Available Fibromyalgia Medications: Results of Primary Research[1]

Perspectives on FM Therapies from Prescribers Interviewed		
Drug	**Positives**	**Negatives**
Duloxetine *(Cymbalta, generic)*	• Relatively high efficacy (compared to alternatives) • Can be titrated slowly from 20mg to 120mg	• Tolerability issues: worsening depression, insomnia • Seldom used as a monotherapy; often requires adjunct
Pregabalin *(Lyrica, generic)*	• Relatively high efficacy (compared to alternatives) • Can often be safely combined with other medications	• Suboptimal for long-term use (e.g., weight gain) • Schedule V status makes some HCPs more cautious to Rx
Savella *(milnacipran)*	• Offers another option if patient fails Cymbalta or Lyrica	• Subpar efficacy does not counterbalance tolerability issues • High cost and access constraints (~$50/month)
Cyclobenzaprine *(Flexeril, generic; oral formulation, off-label)*	• Active for initiating and sustaining sleep; can be titrated up • Active for pain driven by stiffness and muscle spasms	• Mixed perspectives on pain benefit independent of sleep • Suboptimal long-term results as efficacy wanes

85% of patients (avg) fail first line therapy

79% of FM patients (avg) are on multiple therapies

[1] EVERSANA primary physician research, May 2024; commissioned by Tonix

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Opportunity for a New, Unique Fibromyalgia Treatment Option: Results of Primary Research from EVERSANA[1,2]

FM Landscape	• Prescribers indicate a **very high unmet need** in FM (ranked ≥4.0 on a 5-point scale) • Prescribers report there is **no standard of care in FM**, employ an **individualized approach** based on symptomology • No new treatments approved since 2009 • Prescribers report minimal promotional activities by any pharmaceutical company • Highly concentrated prescriber base with 50% of patients treated by ~16k physicians
Physician Primary Market Research	• **Physicians reacted positively to Tonmya's efficacy and safety profile (based on Phase 3 Study results)** • Median interest = 4.0 on a 5-point scale • Driving attributes included **strong efficacy, safety and tolerability** • Unique & differentiating efficacy features included improvements in **sleep and fatigue**
Anticipated Use	• **Physicians indicated intended use in 40% of their FM patients** • Majority of respondents indicated Tonmya would be their first choice, if accessible • Physicians surveyed indicated they are well-equipped to deal with access restrictions including prior authorizations and step-edits

[1] EVERSANA primary physician research, May 2024; commissioned by Tonix
[2] EVERSANA analysis of claims database, May 2024; commissioned by Tonix

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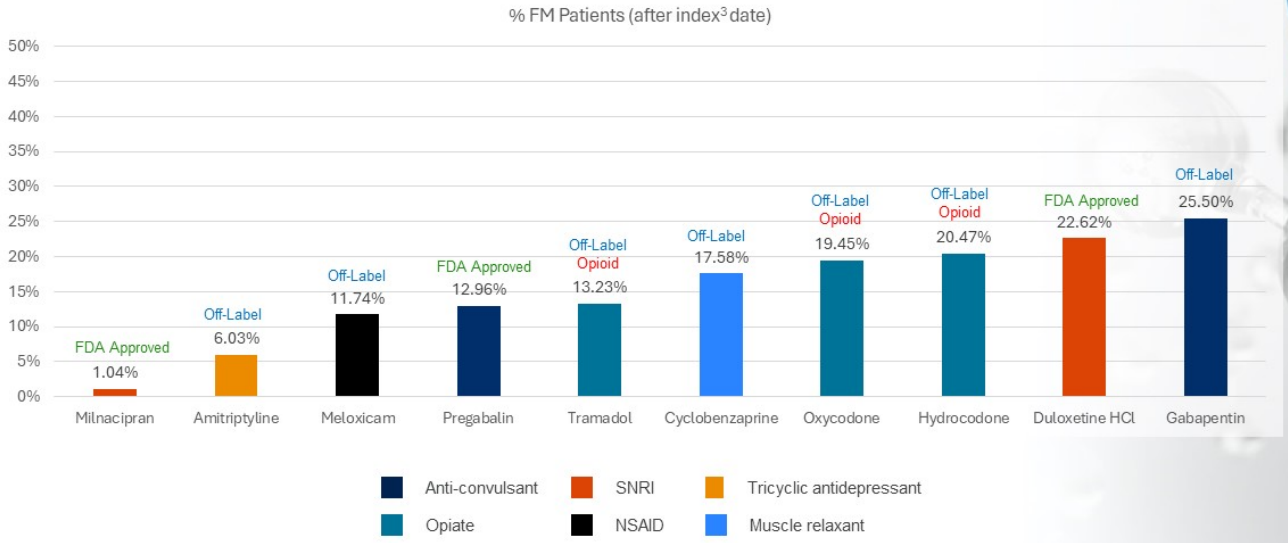
Many Fibromyalgia Patients are Prescribed Off-Label Drugs; ~53% FM Patients Prescribed Opioids Off-Label[1,2]



[1] 2022-2023
[2] EVERSANA analysis of claims database, May 2024; commissioned by Tonix
[3] Index date refers to date when ICD10 code was entered into database

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Planning for Tonmya™ Launch and Marketing

Several companies that successfully developed CNS drugs have launched them

- Big Pharma wants the commercial launch de-risked before acquisition (*e.g.*, Nurtec®)

Company		Product	Indication	FDA Approval	Exit
Axsome	AXSM	Auvelity®	Depression	8/2022	
Biohaven	BHVN	Nurtec®	Migraine	2/2020	Sold to PFE for $12 B in Oct 2022
IntraCellular	ITCI	Caplyta®	Schizophrenia	12/2019	
Supernus	SUPN	Oxtella-XR®	Seizures	1/2019	
Neurocrine	NBIX	Ingrezza®	Tardive Dyskinesia	4/2017	
Acadia	ACAD	Nuplazid®	Parkinson's psychosis	4/2016	

To prepare for the launch of Tonmya, Tonix acquired two marketed Rx drugs: Zembrace® and Tosymra®

- Both are indicated for the acute treatment of migraine

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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

Tonix Medicines Commercial Subsidiary
- Complete commercialization capability
  - Manage supply chain and contract manufacturer
  - Distribution
  - Trade, Managed Care & Government contracting
- Team of professionals including Sales & Marketing personnel

[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]Tonix Medicines, Inc.; 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.

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

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CNS-Focused Biopharma with Preclinical, Clinical and Commercial Stage Products

Tonmya™ for Fibromyalgia: Preparing New Drug Application (NDA)
- Two Phase 3 trials completed with statistical significance on primary endpoint
- 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

*Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration (FDA) as the tradename for TNX-102 SL for the management of fibromyalgia

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Additional Potential Indications for Tonmya™ (TNX-102 SL)

CNS PORTFOLIO

Fibromyalgia-Type Long COVID

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

Next Steps: Meet with FDA

Acute Stress Reaction/ Acute Stress Disorder

- Phase 2 ready investigator-initiated study
- Department of Defense funded
- UNC will perform study
- Received IND clearance from FDA

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

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Additional Programs and Pipeline 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

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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

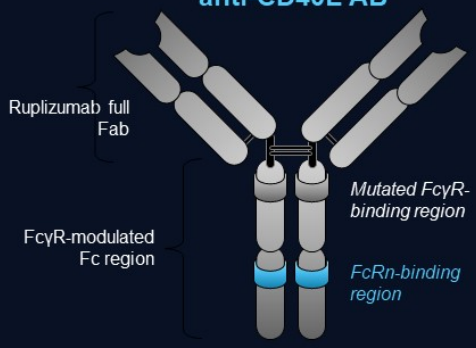
Clinical Stage of Phase 1 study completed

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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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)
  - TNX-1800 selected for Project NextGen
- National Institute on Drug Abuse (NIDA)
  - TNX-1300 for cocaine intoxication; Phase 2 study funding
- Department of Defense (DoD)
  - TNX-102 SL for ASD; Phase 2 study funding

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

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

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TNX-801

Live Virus Vaccine

Live virus vaccine platform with multitude of potential applications

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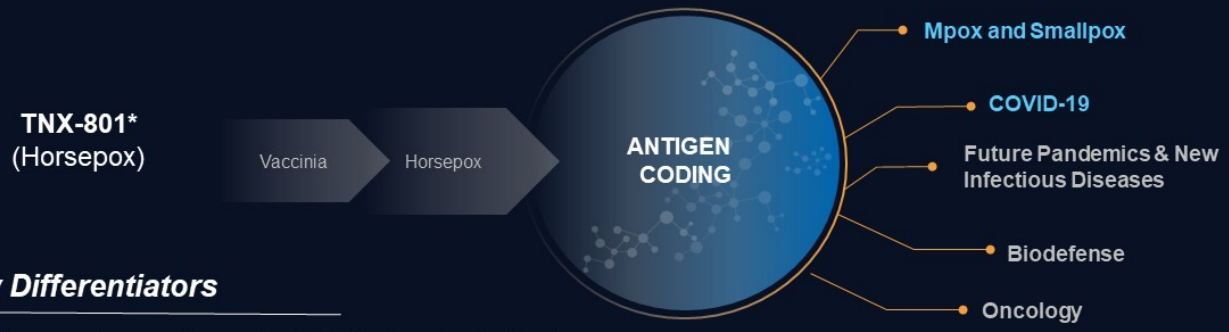
TNX-801: Recombinant Pox Vaccine (RPV) Platform Using Live Virus Technology

Cloned version of horsepox[1] purified from cell culture



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.

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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***

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

[1]Awasthi, M. et al. *Viruses*. 2023. 15(10):2131.
[2]Awasthi, M. et al. *Vaccines (Basel)*. 2023. 11(11):1682.

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INFECTIOUS DISEASE PORTFOLIO

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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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

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TEAM, NETWORK, & UPCOMING MILESTONES

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Management Team

Seth Lederman, MD
Co-Founder, CEO & Chairman

TARGENT | Fusilev (levoleucovorin) for injection | vela

Gregory Sullivan, MD
Chief Medical Officer

Columbia University Department of Psychiatry | New York State Psychiatric Institute

Bradley Saenger, CPA
Chief Financial Officer

Shire | VERTEX | Steward | pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank | svb Silicon Valley Bank | American Capital

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Milestones: Recently Completed and Upcoming

Tonmya™ Milestones

☑ 4th Quarter 2023	Statistically significant topline results of Phase 3 RESILIENT study for Tonmya™ for the management of fibromyalgia
❑ 2nd Quarter 2024	Type B Pre-NDA meeting with FDA for Tonmya™ for fibromyalgia scheduled
❑ 2nd Half 2024	Submit NDA to FDA for Tonmya™ for fibromyalgia

Other Key Program Milestones

❑ 2nd Quarter 2024	Initiate Phase 2 study of TNX-102 SL for acute stress disorder
❑ 2nd Quarter 2024	Initiate Phase 2 study of TNX-1300 for the treatment of cocaine intoxication

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THANK YOU

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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.

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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.

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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.

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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.

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