TNX-102 SL (SUBLINGUAL CYCLOBENZAPRINE HCL): A CENTRALLY ACTING NON-OPIOID ANALGESIC FOR THE TREATMENT OF FIBROMYALGIA

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DISCLAIMERS

- This presentation is being conducted as part of a non-promotional proactive scientific exchange.
- These materials may include information that is not part of the FDA-approved labeling.
- Please see the TONMYA (cyclobenzaprine HCl sublingual) full prescribing Information available at Tonmya-Prescribing-Information.pdf

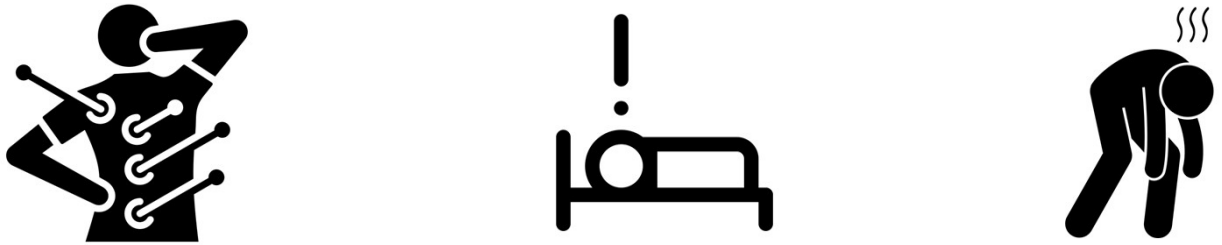
OVERVIEW

- Background: Unmet needs in Fibromyalgia (FM) and rationale for new non-opioid options
- TNX-102 SL (cyclobenzaprine HCl sublingual tablets): Mechanism of action and pharmacology
- Clinical evidence in FM: RESILIENT Phase 3 Results (pain, sleep function; trial rigor)
- Safety and tolerability: Differentiation in real-world care
- Conclusions and Q&A

BACKGROUND

DEFINITION OF FIBROMYALGIA (FM)

- FM is a **chronic pain disorder** resulting from amplified sensory and pain signaling within the CNS—now recognized as **nociplastic pain**[1-4]
- FM is a **syndrome** marked by chronic widespread pain, nonrestorative sleep, and fatigue



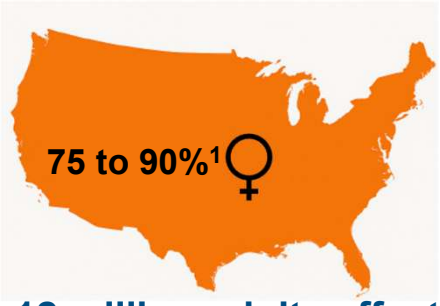
FM is considered a **chronic overlapping pain condition (COPC)**[5,a]

FM is the prototypic nociplastic syndrome

[a]Fibromyalgia is the only COPC with any FDA-approved drugs. The three drugs with prior FDA approval for the treatment of fibromyalgia are pregabalin (Lyrica®), duloxetine (Cymbalta®), and milnacipran (Savella®)

1. Trouvin AP, et al. *Best Pract Res Clin Rheumatol*. 2019;33(3):101415. 2. Fitzcharles MA, et al. *Lancet* 2021;397:2098-110. 3. Kaplan CM, et al. *Nat Rev Neurol.* 2024 20(6):347-363. 4. Clauw DJ. *Ann Rheum Dis.* 2024;83(11):1421-7. 5. Maixner W, et al. *J Pain*. 2016;17(9 Suppl):T93-T107.

FIBROMYALGIA EPIDEMIOLOGY



6–12 million adults affected[2]
2.8 million diagnosed[3]
2.3 million treated currently[4]

Global prevalence 1.8%[5]

2.6% EU[5]
2.4% US[5]
1.6% Asia[5]

Diagnosed age 20-50
Peak prevalence age 50-59[6]

Common Comorbidities

- Depression 54%[7]
- Anxiety Disorders 56%[7]
- Irritable Bowel Syndrome[4]
- Type 2 Diabetes[4,6]
- Migraine[6]
- Hypertension[6]

1. Arout CA, et al. *J Womens Health (Larchmt)*. 2018;27(8):1035-44. 2. Clauw DJ. *JAMA*. 2014;311(15):1547-55. 3. Vincent A, et al. *Arthritis Care Res (Hoboken)*. 2013;65(5):786-92. 4. Robinson RL. et al. *Pain Medicine*, 2012; 13:1366-1376. 5. Heidari F, et al. *Rheumatol Int*. 2017;37(9):1527-39. 6. Walitt B, et al. *PLoS One*. 2015;10(9):e0138024. 7. Aaron RV, et al. *JAMA Netw Open*. 2025;8(3):e250268.

UNMET NEEDS IN THE TREATMENT OF FIBROMYALGIA

Treatment persistence

- High rates of discontinuation, switching, and augmentation[1]
- Currently approved medications may have side effects that limit long-term use[2]

Medication burden

- Average of 2-3 medications used simultaneously[1]
- Typical patient has tried 6 different medications[3]
- Substantial off-label use of narcotic painkillers and prescription sleep aids[3]

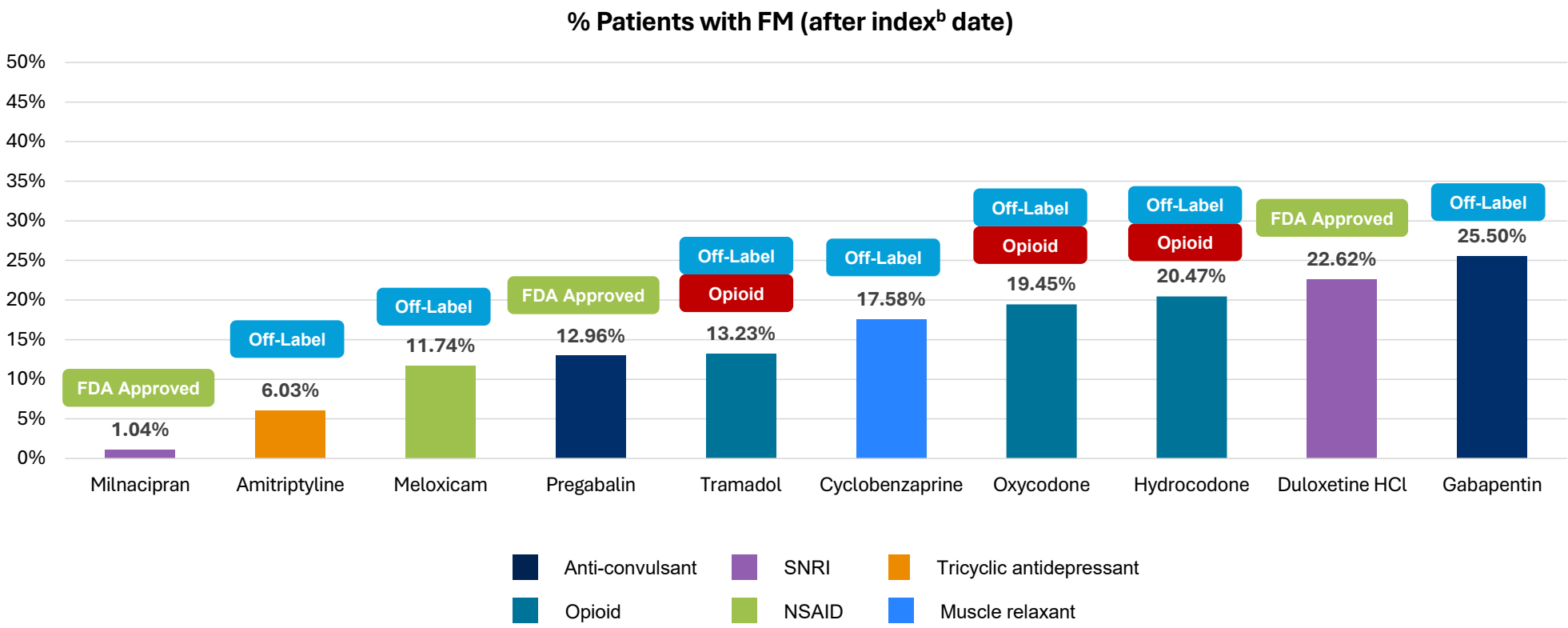
Therapeutic landscape

- No new product approvals since 2009[4]
- Unmet need for non-opioid analgesics addressing nociplastic pain

Treatment objective: *Provide broad efficacy while avoiding intolerable side effect burden*

1. Robinson RL et al, *Pain Medicine* 2012;13:1366.. 2. Nuesch et al, *Ann Rheum Dis* 2013;72:955-62. 3. "Patient Trends: Fibromyalgia", Decision Resources, 2011. 4. Griffin SC, et al. *Sleep Med.* 2021;86:32-9.

SUBSTANTIAL OPIOID USE IN FIBROMYALGIA[a,b]



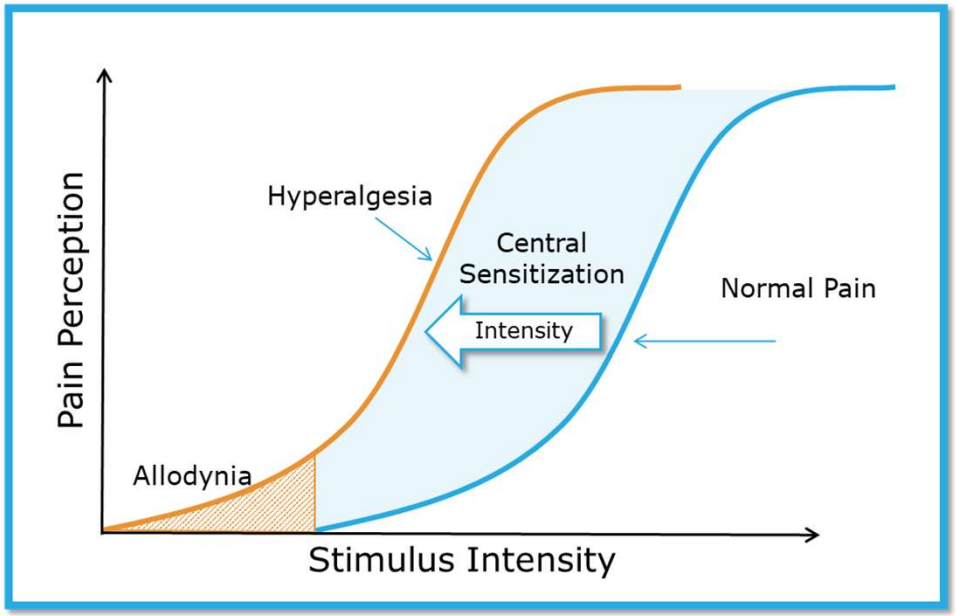
FDA, Food and Drug Administration; FM, fibromyalgia; NSAID, nonsteroidal anti-inflammatory drug; SNRI, serotonin-norepinephrine reuptake inhibitor.
[a]2022-2023. [b]Date when ICD10 code was entered into database. EVERSANA analysis of claims database, May 2024; commissioned by Tonix
[b]Note: listed prescription rates are rates in period after index date of entry of fibromyalgia diagnostic code; these do not necessarily represent rates of use of the listed medication *specifically* prescribed for fibromyalgia or its associated symptoms

FOUNDATIONAL INSIGHT FOR TNX-102 SL

FM IS DRIVEN BY CENTRAL VS PERIPHERAL MECHANISMS

- FM is characterized by nociplastic pain, reflecting altered nociceptive processing in the CNS[1,2]
- Symptoms are typically out of proportion to identifiable tissue injury or inflammation[3,4]
- Central sensitization (amplified CNS signaling) contributes to pain hypersensitivity[3,5]
- Effective therapies must address central mechanisms, not just peripheral pain signaling[1,2]

Central Sensitization

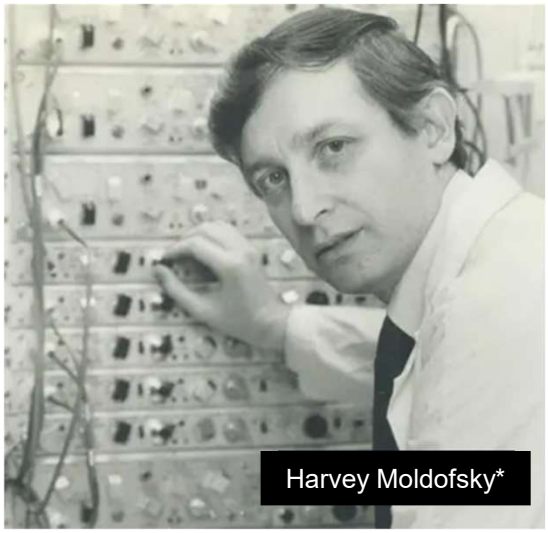


FM, fibromyalgia.

[1]Kosek E, et al. *Pain.* 2016;157:1382-6. [2]Clauw DJ. *Ann Rheum Dis.* 2024;0:1-7. [3]Nijs J, et al. *Lancet Rheumatol.* 2021;3:e383-92. [4]Clauw DJ. JAMA. 2014;311:1547-55.

CYCLOBENZAPRINE IN THE TREATMENT OF FIBROMYALGIA

- **Non-restorative sleep[1,2]**
  - Harvey Moldofsky (pictured) recognized non-restorative sleep in fibromyalgia in 1970s
    - As a core symptom
    - As a potential causative or potentiating factor
- **Oral, immediate-release (IR) cyclobenzaprine[3-9]**
  - Potentially one of the earliest drugs studied in fibromyalgia as an orally-administered agent
  - Studies showed equivocal effects and tolerability issues (somnolence and "hangover" effect) at "muscle spasm" doses

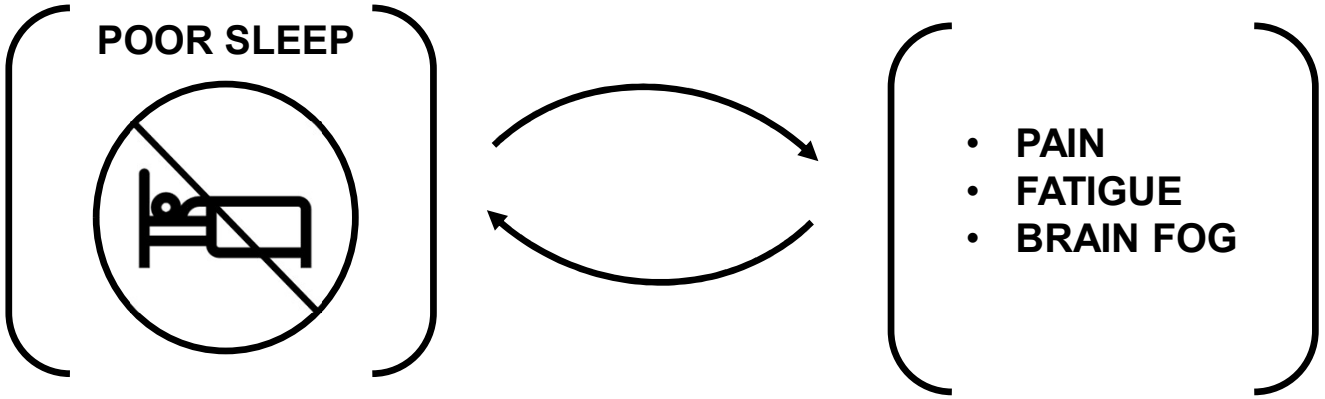

Harvey Moldofsky*

- ***Very low-dose* oral, IR cyclobenzaprine[10-11]**
  - Targeted non-restorative sleep
  - Primitive oral, swallowed formulation – improved sleep, reduced pain and tenderness and improved depression – suggestion of potential benefit in fibromyalgia
- **Bedtime, sublingually-administered TNX-102 SL targeting non-restorative sleep[12]**
  - Dynamic pharmacokinetic profile, rapid absorption, and decrease in major metabolite (nCBP)
  - Two studies (Phase 2 and Phase 3) at 2.8 mg; three Phase 3 studies at 5.6 mg

*[1]Moldofsky H et al. *Psychosom Med.* 1975. 37:341-51. *[2]Moldofsky H and Scarisbrick P. *Psychosom Med.* 1976. 38:35-44. [3]Bennett RM, et al. *Arthritis Rheum* 1988. 31:1535–42. [4]Quimby LG, et al. *J Rheumatol Suppl,* 1989 Nov;19:140-3.[5]Reynolds WJ, et al. *J Rheumatol.* 1991.18:452–4. [6]Santandrea S, et al. *J Int Med Res.* 1993.21:74–80. [7]Cantini F, et al. *Minerva Med.* 1994. 85:97–100. [8]Carette S, et al. *Arthritis Rheum.* 1994. 37:32–40. [9]Tofferi JK, et al. *Arthritis Rheum.* 2004. 51:9–13.*1.* [10]Iglehart IW. 2003; US Patent 6,541,523. *[11]Moldofsky et al. *J Rheumatol.* 2011. 38:2653-2663. [12]Lederman S et al. *Arthritis Care Res.* 2023. 75:2359-2368.

SLEEP DISRUPTION IS A CORE DRIVER OF FIBROMYALGIA (FM) SYMPTOM SEVERITY

- Non-restorative sleep is a common and well-recognized feature of FM[1,2]
- Non-restorative sleep amplifies pain sensitivity and symptom severity[2]
- Poor sleep contributes to fatigue and cognitive symptoms, not just pain[2]
- Improving sleep quality is associated with better daytime function and overall symptom burden[2]

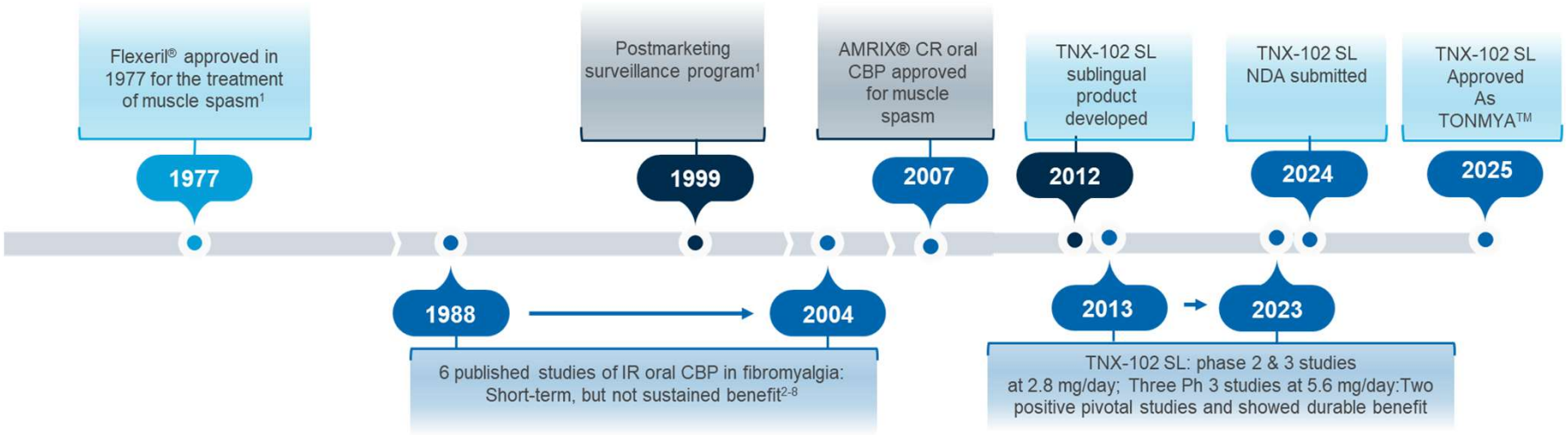


[1]Moldofsky H, et al. *J Rheumatol*. 1996;23:529-33. [2]Clauw DJ. *JAMA*. 2014;311(15):1547-55.

THE SCIENTIFIC RATIONALE FOR TNX-102 SL

WHY CYCLOBENZAPRINE, WHY BEDTIME, WHY SUBLINGUAL (TNX-102 SL)

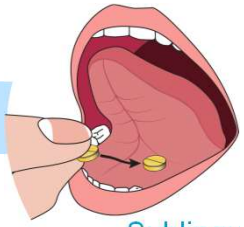
- Selected for sleep/arousal CNS effects and extensive clinical experience
- Low-dose bedtime sublingual dosing pursued to optimize benefit and tolerability
- **Key point:** Sublingual delivery results in a different parent–metabolite balance from that of oral immediate-release cyclobenzaprine administration



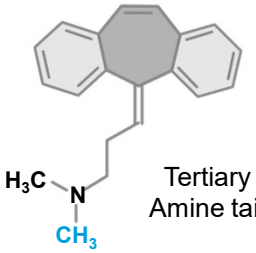
[1]1999 Merck OTC AdCom Briefing Package. [2]Bennett RM, et al. *Arthritis Rheum* 1988; 31:1535–42. [3]Quimby LG, et al. *J Rheumatol Suppl.* 1989; Nov 19:140–3. [4]Reynolds WJ, et al. *J Rheumatol.* 1991; 18:452–4. [5]Santandrea S, et al. *J Int Med Res.* 1993; 21:74–80. [6]Cantini F, et al. *Minerva Med.* 1994; 85:97–100. [7]Carette S, et al. *Arthritis Rheum.* 1994; 37:32–40. [8]Tofferi JK, et al. *Arthritis Rheum.* 2004; 51:9–13.

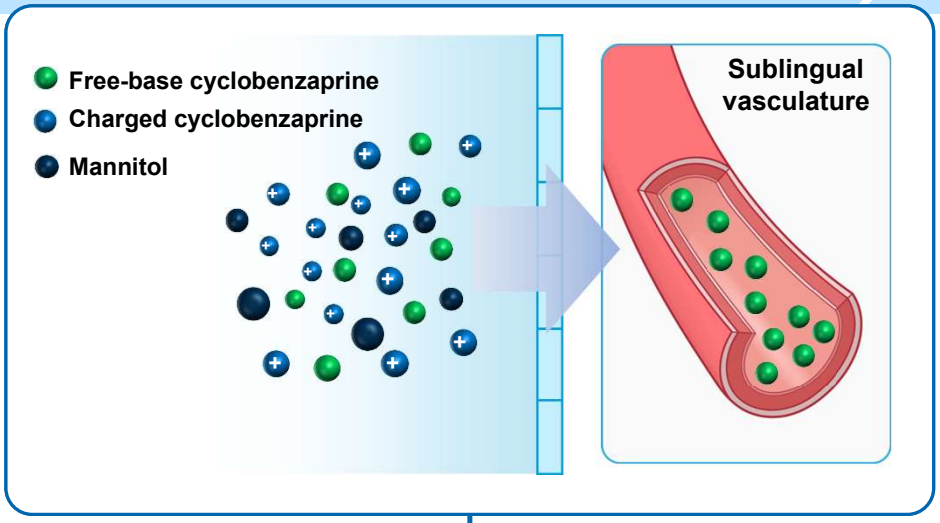
SUBLINGUAL DELIVERY AND PHARMACOLOGIC BENEFITS

TNX-102 SL BYPASSES FIRST-PASS METABOLISM

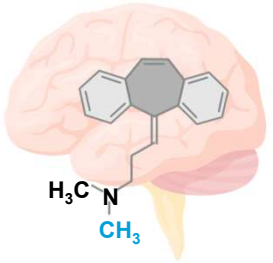


Sublingual administration





The base drives formation of free-base **CBP**, which enters the circulatory system across the mucosal membrane (transmucosal absorption), with 154% relative bioavailability over oral immediate-release cyclobenzaprine[1]

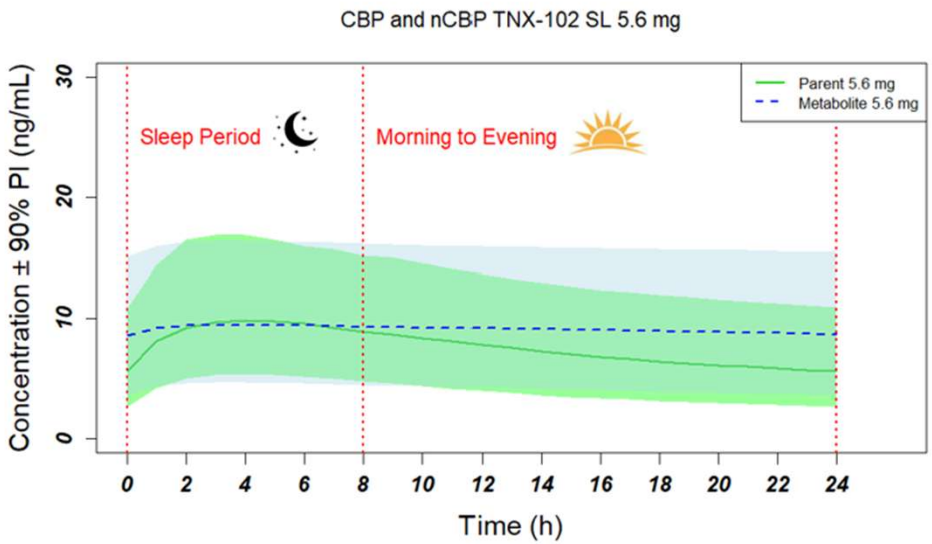


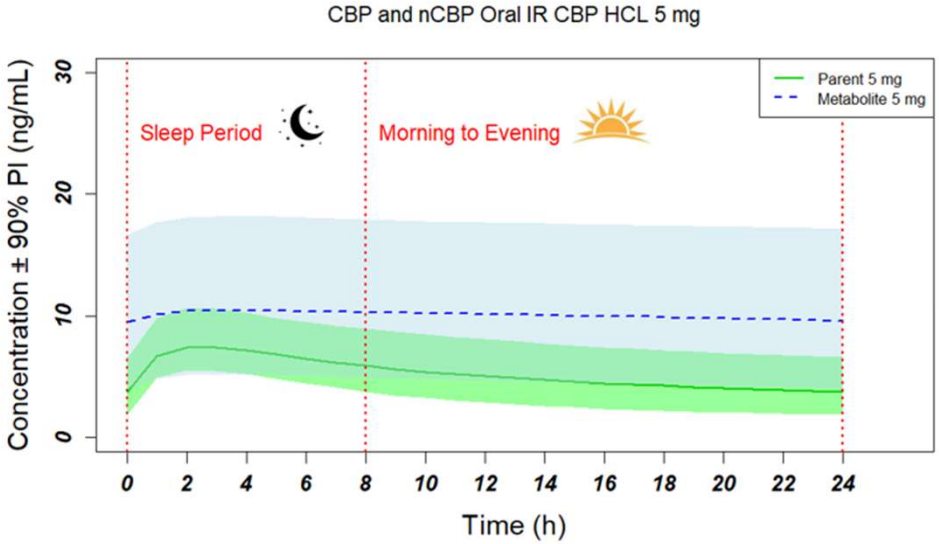
Sublingually administered TNX-102 SL is transmucosally absorbed, leading to more rapid **CBP** absorption, greater relative bioavailability versus IR, and, due to largely bypassing “first-pass” hepatic metabolism, reduced metabolism to **nCBP,** which reduces **nCBP** exposure in brain

[1]Daugherty BL, et al. Single-Dose Pharmacokinetic Assessment of TNX-102 SL (Cyclobenzaprine HCl Sublingual Tablets): Results from Randomized, Open-Label Studies in Healthy Volunteers. Clinical Pharmacology in Drug Development, 2026 *In Press*.

TNX-102 SL PRODUCES DISTINCT MULTI-DOSE PROFILE VS ORAL IR CYCLOBENZAPRINE

Population PK simulated steady-state concentration-time profiles (median and 90% prediction intervals) for CBP and nCBP following once-daily dosing of TNX-102 SL 5.6 mg or oral IR CBP 5 mg





Repeated oral CBP dosing leads to sustained higher nCBP exposure, whereas TNX-102 SL favors parent-drug exposure during sleep with lower daytime nCBP.

CBP, cyclobenzaprine; h, hours; IR, immediate-release; nCBP, norcyclobenzaprine; PK, pharmacokinetic; SL, sublingual.

TNX-102 SL
DIFFERENT PHARMACOLOGY, NOT JUST A REFORMULATION

- Sublingual delivery reshapes parent–metabolite exposure[1,2]
  - Shifts effects toward the parent drug during sleep[1]
  - Limits daytime exposure to the longer-acting *active* metabolite[1]

ORAL CBP
- Extensive first-pass metabolism
- ↑ Norcyclobenzaprine exposure
- Longer daytime persistence

VS

TNX-102 SL
- Largely bypasses first-pass metabolism
- ↓ Norcyclobenzaprine exposure
- Nighttime-focused profile

- Low-dose approach increases specificity to neuroreceptors with high cyclobenzaprine binding and antagonist activity (5-HT_{2A}, α_1, H_1, M_1)
  - Analogy: Low-dose doxepin shows how exposure can redefine clinical use[3]

[1]Lederman S, et al. *Arthritis Care Res (Hoboken)*. 2023;75(11):2359–68. Lederman S, et al. *Pain Med*. 2026;27(1):86-94; US Food and Drug Administration. [3]Silenor (doxepin HCl) NDA 22-036 Medical Review. 2009.

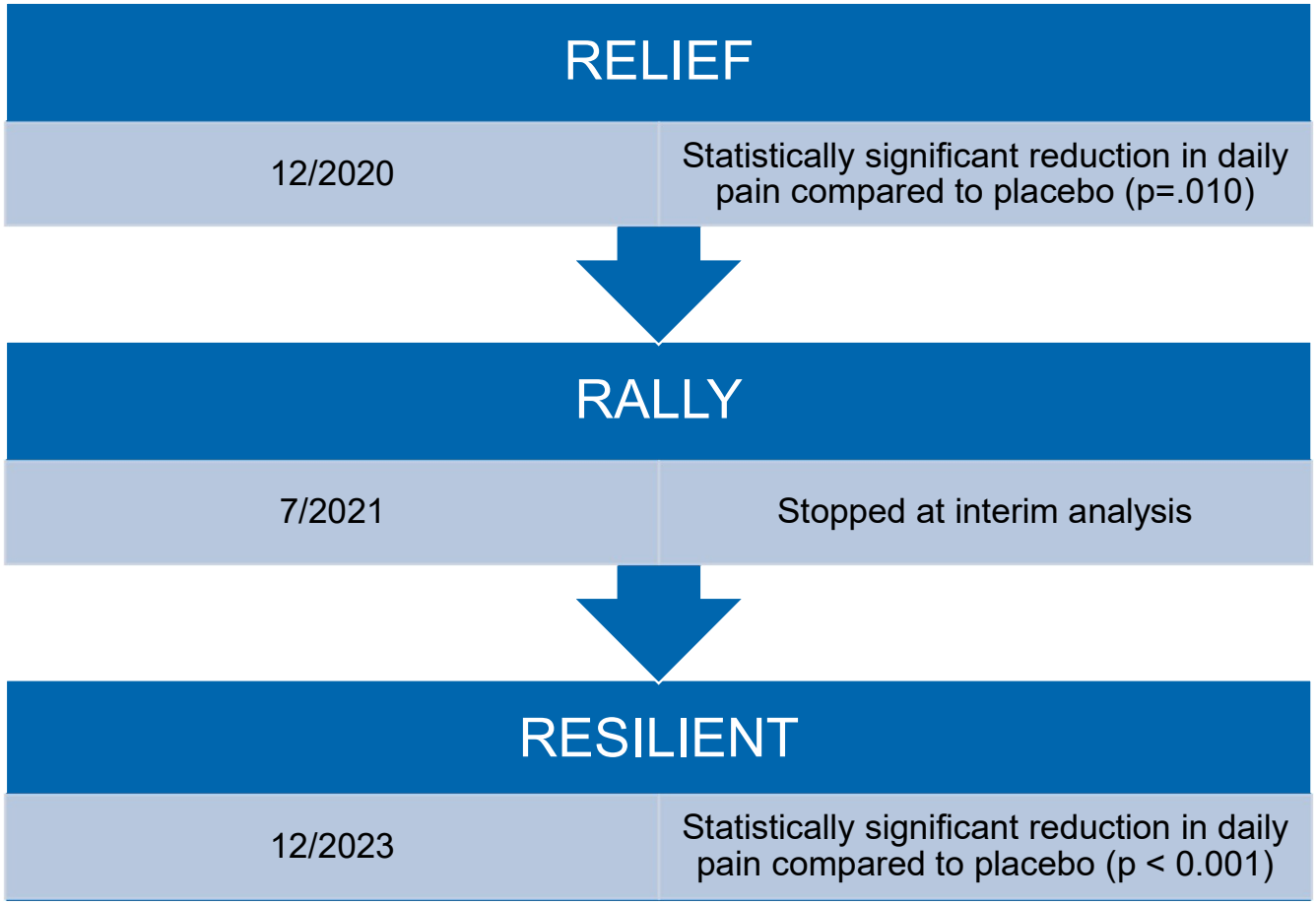
CLINICAL DEVELOPMENT OF TNX-102 SL

A DATA-DRIVEN CLINICAL DEVELOPMENT PROGRAM

- Early studies with TNX-102 SL 2.8 mg demonstrated signal and informed treatment optimization[1]
- Iterative, data-driven refinement advanced to 5.6 mg in Phase 3[1,2]
- Continuous FDA engagement guided trial design and program evolution
- RALLY, RELIEF and confirmatory RESILIENT evaluated pain, sleep, fatigue, global improvement, and function[1,2]

[1]Lederman S, et al. *Arthritis Care Res (Hoboken)*. 2023;75(11):2359–68. [2]Lederman S, et al. *Pain Med*. 2026; Jan 1;27(1):86-94.

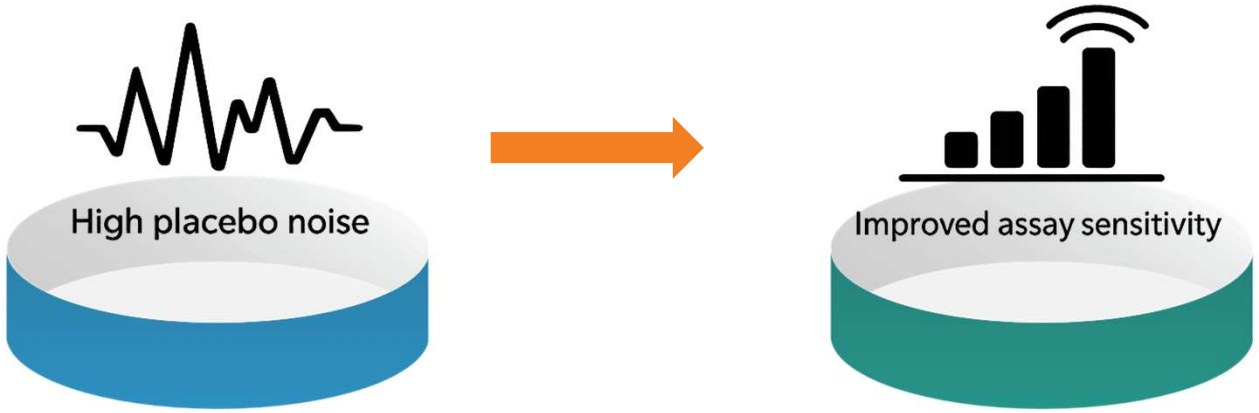
TNX-102 SL (5.6 MG) IN FIBROMYALGIA
PIVOTAL CLINICAL TRIAL RESULT SUMMARY



1. Lederman S, et al. *Arthritis Care Res (Hoboken)*. 2023;75(11):2359-68. 2. Lederman S, et al. *Pain Med.* 2025;pnaf089. RALLY: NCT03508700 clinicaltrials.gov.

REDUCING PLACEBO RESPONSE IN FM TRIALS

- High placebo response is a well-recognized challenge in fibromyalgia trials[1,2]
- RESILIENT trial participants were provided a standardized placebo response education strategy[1]
- Patient and site education focused on:
  - Accurate pain reporting (0–10 NRS)[1]
  - Neutral expectations and trial understanding[1]
- This approach aimed to strengthen assay sensitivity and clarify treatment effects[1]



[1]Treister R, et al. *PLoS ONE*. 2018;13(5):e0197844; [2]Erpelding N, et al. *Clin J Pain*. 2020;36(12):950–4.

PIVOTAL PHASE 3 STUDY

RESILIENT PHASE 3 STUDY DESIGN

Study Design	Phase 3, randomized, multicenter (34 sites), parallel group, double-blind, placebo-controlled 16-week trial (NCT05273749)	
Study Objectives	Evaluate the efficacy and safety of TNX-102 SL for treatment of adults with FM	
Study Population	457 participants with FM as defined by the ACR 2016 Revisions to the 2010/2011 FM Diagnostic Criteria (TNX-102 SL, n=231; Placebo, n=226)	
Primary Endpoint	Change from baseline to the Week 14 endpoint in the diary numerical rating scale (NRS) weekly average of daily self-reported average pain intensity scores	
Secondary Endpoints	• PGIC responder* analysis at Week 14 • Change from baseline in FIQR Symptoms and Function domain scores at Week 14 • Change from baseline in PROMIS Fatigue (8a) T-score at Week 14 • Change from baseline in PROMIS Sleep Disturbance (8a) T-scores at Week 14 • Change from baseline in weekly average of daily sleep quality NRS scores at Week 14	
Treatments Administered at Bedtime	TNX-102 SL First 2 weeks, 1 tablet; 2.8 mg/d dose Remaining 12 weeks, 2 tablets; 5.6 mg/d dose	Placebo First 2 weeks, 1 tablet Remaining 12 weeks, 2 tablets
Study Visits	Screening, baseline, and 4 treatment visits (Weeks 2, 6, 10, 14/ET)	

ACR, American College of Rheumatology; ET, early termination; FIQR, Fibromyalgia Impact Questionnaire (Revised); FM, fibromyalgia; PGIC, Patient Global Impression of Change; PROMIS, Patient-Reported Outcomes Measurement Information System; *Responders defined as a PGIC rating of '1' very much improved, or '2' much improved; missing PGIC data = nonresponder

Lederman S, et al. *Pain Med*. 2026; Jan 1;27(1):86-94.

RESILIENT: SUMMARY OF PRIMARY AND KEY SECONDARY OUTCOMES

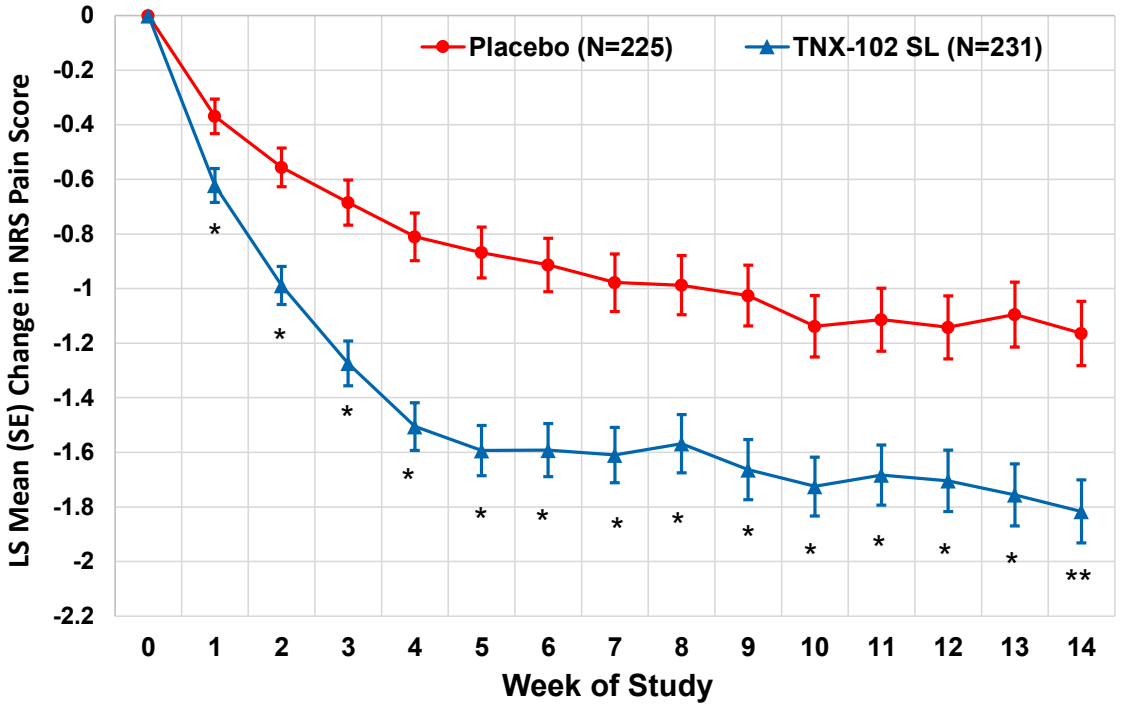
Endpoint	P-value	Effect Size (ES)[b]
Primary Endpoint		
Daily Diary Pain ratings	**p < 0.001**	ES = 0.38
Key Secondary Endpoints[a]		
Patient Global Impression of Change (PGIC), responders	p < 0.001	--
Fibromyalgia Impact Questionnaire – Symptoms domain	p < 0.001	ES = 0.44
Fibromyalgia Impact Questionnaire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

[a]In order of statistical serial gate-keeping hierarchy (or, "waterfall") to control overall Type 1 error.
[b]Effect size calculated as: effect size = (difference in LS means/standard error) x square root ($1/N_{placebo} + 1/N_{active}$)
PROMIS, Patient-Reported Outcomes Measurement Information System.

Lederman S, et al. *Pain Med*. 2026; Jan 1;27(1):86-94.

RESILIENT PRIMARY OUTCOME MEASURE: REDUCTION IN WIDESPREAD PAIN

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



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<0.001**[#]

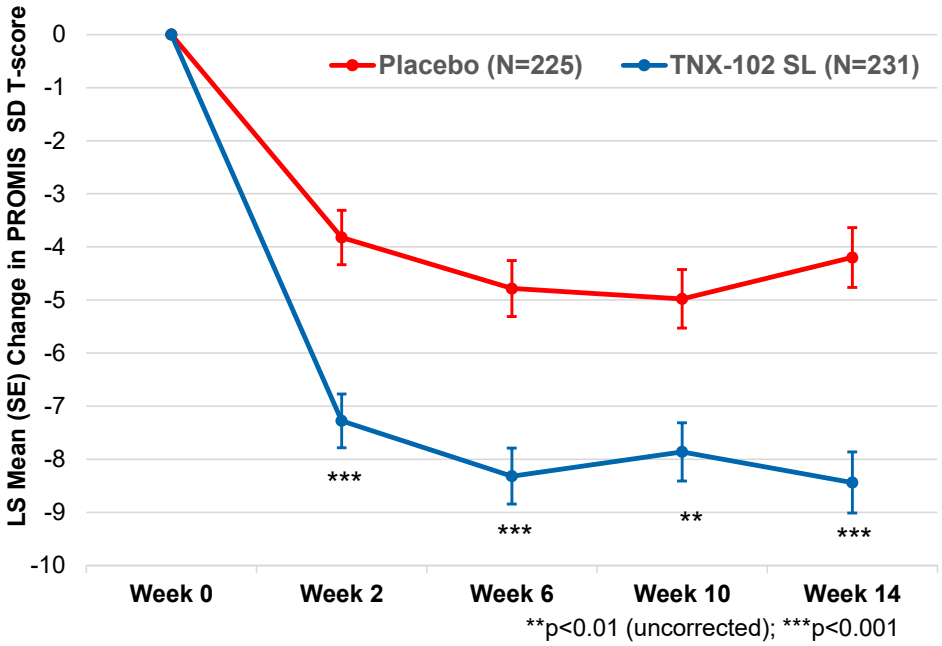
[#]Based on mixed model repeated measures with multiple imputation, with fixed categorical effects of treatment, center, study week, and treatment by study week interaction, as well as baseline value and baseline value-by-study week interaction. Weeks 1-13 represent exploratory endpoints, and p-values are uncorrected for multiplicity control. LS, least squares; LSMD, least-squares mean difference; NRS, numerical rating scale; SE, standard error.

*p<0.01 (uncorrected); **p<0.001.

Lederman S, et al. *Pain Med*. 2026 Jan 1;27(1)86-94.

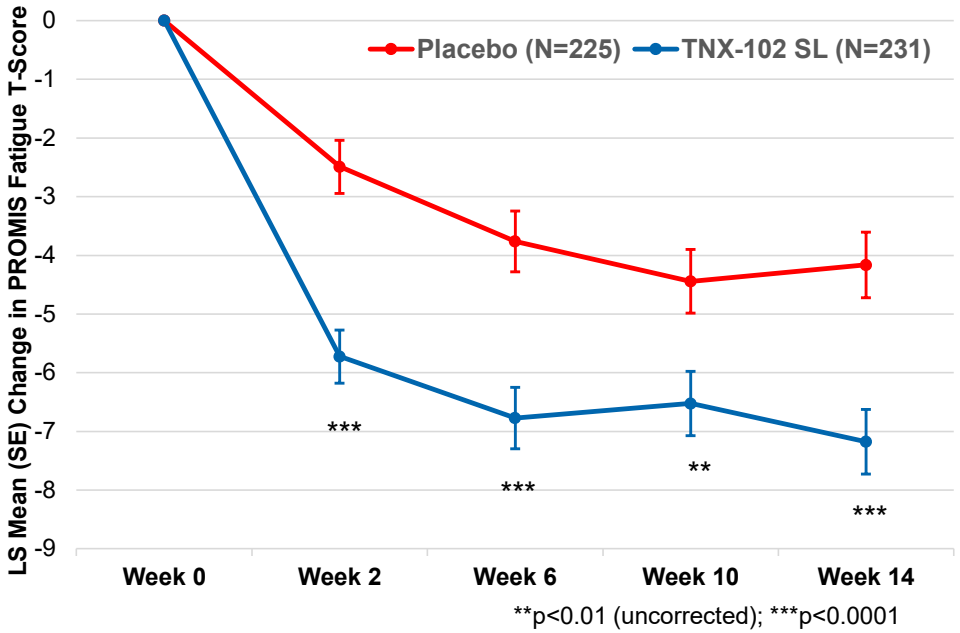
RESILIENT SECONDARY OUTCOME MEASURES: PROMIS SLEEP DISTURBANCE AND FATIGUE SCORES

PROMIS Sleep Disturbance



Week 14 LS mean (SE) change from baseline for TNX-102 SL, -8.4 (0.57) and for placebo, -4.2 (0.56); LSMD from placebo, -4.2 (0.79); **p<0.001**[a]

PROMIS Fatigue



Week 14 LS mean (SE) change from baseline for TNX-102 SL, -7.2 (0.55) and for placebo, -4.2 (0.56); LSMD from placebo, -3.0 (0.77); **p<0.001**[a]

[a]Based on mixed model for 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. Weeks 2-10 represent exploratory endpoints, and p-values are uncorrected for multiplicity control.
LS, least squares; LSMD, least squares mean difference; PROMIS, patient-reported outcomes measurement information system; SD, sleep disturbance; SE, standard error.

Lederman S, et al. *Pain Med*. 2026; Jan 1;27(1):86-94.

RESILIENT: SAFETY

Treatment-Emergent Adverse Events (TEAEs) at Rate of ≥3% in Any 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%)

- No new safety signals were observed
- There were no clinically meaningful changes from baseline in systolic or diastolic blood pressure or weight between groups
- Serious adverse events (SAEs) occurred in 3 participants taking placebo and 2 participants taking TNX-102 SL
- The majority of events were mild or moderate in severity; severe AEs occurred in 1.3% of participants in each group (3 of 231 on active)
- TEAE-related study discontinuations occurred in 6.1% of TNX-102 SL participants and 3.5% of placebo participants

Lederman S, et al. *Pain Med*. 2026 Jan 1;27(1)86-94.

RESILIENT: CONCLUSIONS

Efficacy: TNX-102 SL provides "broad spectrum, syndromal activity" in fibromyalgia

- TNX-102 SL provides significant pain reduction in patients with fibromyalgia
- TNX-102 SL improves core symptoms of fibromyalgia, including sleep disturbance and fatigue
- Thus, broad-spectrum activity across triad of pain, nonrestorative sleep, and fatigue

Safety: TNX-102 SL was generally well tolerated, with an AE profile comparable to that observed in prior TNX-102 SL fibromyalgia studies

- No new or previously unknown safety signals were observed
- Most AEs were mild or moderate in severity; severe AEs occurred in 1.3% of participants
- Systemic AEs, including somnolence and headache, were infrequent (excepting COVID, ≤3%)
  - Oral AEs were most common but were transient, self-limited and uncommonly led to discontinuation
- There were no clinically meaningful changes in blood pressure or weight between groups

AE, adverse event.

CURRENT FDA-APPROVED FIBROMYALGIA DRUGS[1]

Improvement in fibromyalgia pain was primary endpoint for approval

- No other current approved products address the triad of pain, poor sleep, and fatigue
- Tolerability issues limit long-term use for many patients

Drug		Pregabalin	Duloxetine Milnacipran
Class		Gabapentinoid	SNRI
Fibromyalgia Activity	**Pain Reduction**	**YES**	**YES**
	Sleep Improvement	**YES**	**-**
	Fatigue Reduction	**-**	**YES**
Tolerability Issues	Fatigue increase	**YES**	**-**
	Sleep problems	**-**	**YES**
	Weight gain	**YES**	-
	Blood pressure increase	**-**	**YES**
	Sexual impairment	**-**	**YES**
	GI issues	**-**	**YES**
	Hip fractures[2]	**YES**	**-**
	DEA scheduled	**YES**	**-**

[1]The three drugs with FDA approval for the management of fibromyalgia are Pregabalin (Lyrica®); Duloxetine (Cymbalta®); and Milnacipran (Savella®)
[2]Leung MTY, et al. *JAMA Netw Open*. 2024;7(11):e2444488.

CONCLUSIONS

- TONMYA™ (TNX-102 SL) is a newly approved, centrally-acting, non-opioid treatment designed to improve pain, sleep, and daytime fatigue and function

Pathophysiology

- Central hyperarousal and sensory sensitivity, e.g., pain
- Non-restorative sleep

Design

- Bedtime sublingual dosing
- ↑ relative parent drug exposure during sleep
- ↓ active metabolite exposure during sleep relative to parent and during daytime

Clinical Outcomes

- ✓ Pain reduction
- ✓ Favorable tolerability
- ✓ Non-opioid therapeutic option

COMBINED SAFETY FROM ALL 3 PHASE 3 TRIALS

Treatment-Emergent Adverse Events (TEAEs) at Rate of ≥ 2% in Either Treatment Group

Adverse Reactions	Placebo (N = 739)	Cyclobenzaprine HCl Sublingual Tablets (N = 735)
Oral hypoesthesia[a]	0.7%	23%
Oral discomfort[b]	0.7%	9%
Abnormal product taste	0.7%	9%
Somnolence[c]	2%	6%
Oral paresthesia[d]	0.4%	6%
Oral pain[e]	1%	5%
Fatigue[f]	2%	4%
Dry mouth[g]	2%	3%
Aphthous ulcer	0.5%	2%

[a]Oral hypoesthesia includes hypoesthesia and teeth hypoesthesia
[b]Oral discomfort includes tongue discomfort
[c]Somnolence includes hypersomnia, lethargy, and sedation
[d]Oral paresthesia includes paresthesia and teeth paraesthesia
[e]Fatigue includes asthenia and lethargy
[g]Dry mouth includes dry throat

TONMYA (cyclobenzaprine HCl sublingual) [prescribing information]. Chatham, NJ: Tonix Medicines, Inc.; 2025.

CYCLOBENZAPRINE HCL SUBLINGUAL TABLETS: SAFETY PROFILE

Contraindications:

- Hypersensitivity to cyclobenzaprine or any inactive ingredient in cyclobenzaprine HCl sublingual tablets
- Concomitant use of monoamine oxidase inhibitors or within 14 days after their discontinuation
- During acute recovery phase of myocardial infarction and in patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure
- Hyperthyroidism

Warnings and Precautions:

- Embryofetal toxicity: Cyclobenzaprine HCl sublingual tablets may cause neural tube defects when used 2 weeks prior to conception and during the first trimester of pregnancy (animal data). Advise female patients of reproductive potential of the potential risk and to use effective contraception during treatment and for 2 weeks after the final dose. Perform a pregnancy test prior to initiation of treatment
- Serotonin syndrome: Concomitant use of serotonergic drugs with cyclobenzaprine HCl sublingual tablets increases the risk of serotonin syndrome, which may be life threatening. Treatment with cyclobenzaprine sublingual HCl tablets and serotonergic drugs should be closely monitored, particularly during treatment initiation and dosage increases, and should be immediately discontinued if serotonin syndrome symptoms occur, including mental status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms
- Tricyclic antidepressant-like adverse reactions: Given the structural similarity of cyclobenzaprine to tricyclic antidepressants (TCAs), discontinuation of cyclobenzaprine HCl sublingual tablets should be considered for patients experiencing clinically significant central nervous system (CNS) symptoms, such as arrythmia, sinus tachycardia, myocardial infarctions, or stroke, and caution is advised for patients with a history of seizure disorder, as TCAs may lower the seizure threshold
- Atropine-like adverse reactions: Caution is advised for patients with a history of urinary retention, angle-closure glaucoma, increased intraocular pressure, and those taking anticholinergic drugs
- CNS depression and risk of operating a motor vehicle or hazardous machinery: Cyclobenzaprine HCl sublingual tablets may cause CNS depression, which may be exacerbated by concomitant use of alcohol, barbiturates, or other CNS depressants. Patients should not operate motor vehicles/heavy machinery until they are reasonably certain that cyclobenzaprine HCl sublingual tablets will not impair their ability to operate them
- Oral mucosal adverse reactions: The risk of oral sensory changes can be reduced by moistening the mouth with sips of water prior to administration of cyclobenzaprine HCl sublingual tablets

TONMYA (cyclobenzaprine HCl sublingual) [prescribing information]. Chatham, NJ: Tonix Medicines, Inc.; 2025.

CYCLOBENZAPRINE HCL SUBLINGUAL TABLETS: SAFETY PROFILE (CONTINUED)

Drug Interactions:

- **Monoamine oxidase inhibitors:** Life-threatening interactions may occur
- **Other serotonergic drugs:** Serotonin syndrome has been reported
- **CNS depressants:** CNS depressant effects of alcohol, barbiturates, and other CNS depressants may be enhanced
- **Tramadol:** Seizure risk may be enhanced
- **Guanethidine or other similar acting drugs:** The antihypertensive action of these drugs may be blocked

Use in Specific Populations:

- **Pregnancy:** Based on animal data, cyclobenzaprine HCl sublingual tablets may cause fetal harm when administered to a pregnant patient; pregnant women should be advised of the potential risk to the fetus and avoid use of cyclobenzaprine HCl sublingual tablets two weeks prior to conception and through the first trimester of pregnancy
- **Lactation:** There are no data on the effects of cyclobenzaprine on a breastfed infant or the effects on milk production
- **Pediatric use:** The safety and effectiveness of cyclobenzaprine HCl sublingual tablets have not been established
- **Geriatric patients:** Clinical trials of cyclobenzaprine HCl sublingual tablets did not include sufficient numbers of patients ≥65 years of age to determine whether they respond differently from younger adult patients
- **Hepatic impairment (HI):** The recommended dose of cyclobenzaprine HCl sublingual tablets in patients with mild HI (Child Pugh A) is 2.8 mg daily. The use of cyclobenzaprine HCl sublingual tablets is not recommended in patients with moderate or severe HI (Child Pugh B and C, respectively) due to increased adverse reaction risk

To report suspected adverse reactions, contact Tonix Medicines, Inc. at 1-888-869-7633, or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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QUESTIONS?