TNX-102 SL, Cyclobenzaprine HCl Sublingual Tablets, Demonstrates Pain Reduction and Favorable Tolerability in Participants With Fibromyalgia

Poster #37

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INTRODUCTION

- Fibromyalgia (FM) is a chronic condition characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive and somatic complaints[1,2]
 - FM has recently been described as the prototypic nociplastic syndrome[3]
 - Nociplastic pain is distinct from nociceptive or neuropathic pain and is characterized by pain arising from altered nociception in the absence of peripheral nociceptor or somatosensory system pathology[3,4]
 - Disruptions to the deep, restorative stages of sleep occur in patients with FM[5]
 - Poor sleep quality is highly associated with an amplification of nociplastic pain[4]
- In the US, FM affects an estimated 2%-8% of adults, 75%-90% of whom are female[6,7]
- FDA-approved treatments for FM have historically been limited by intolerable side effects that often lead to poor adherence[8]
- Tonmya™ (TNX-102 SL, cyclobenzaprine HCl sublingual tablets) is FDA approved for the treatment of FM in adults[9-11]
 - TNX-102 SL treatment has shown statistically significant reductions in daily pain in two pivotal phase 3 studies, RELIEF (NCT04172831) and RESILIENT (NCT05273749)
 - TNX-102 SL also improved sleep quality, fatigue, and cognitive function and was well tolerated, with a favorable safety profile
 - The demonstrated efficacy and tolerability of TNX-102 SL may support its addition to the existing therapeutic landscape

OBJECTIVE

- To report pain, sexual function, and tolerability outcomes for TNX-102 SL in the treatment of FM from RESILIENT, a phase 3, randomized, placebo-controlled study

METHODS

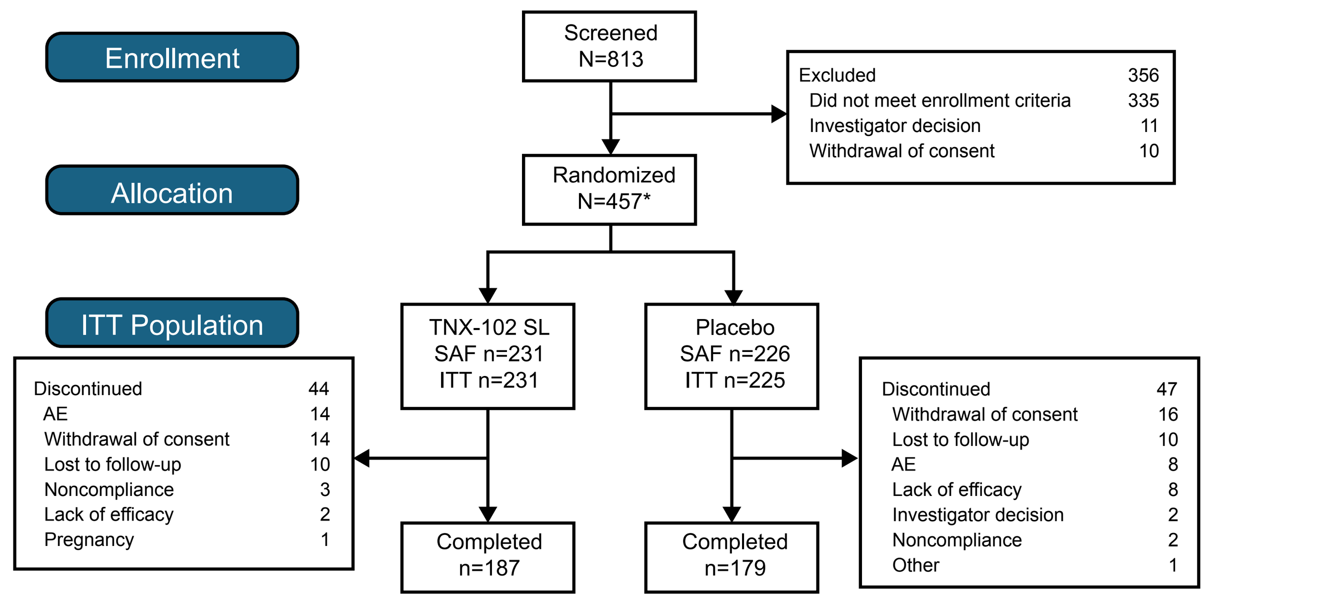
- RESILIENT was a 14-week, randomized, parallel-group, double-blind, placebo-controlled trial conducted at 34 sites in the US and was designed to evaluate the efficacy and safety of TNX-102 SL in participants with FM
 - Participants 18-65 years of age were randomized 1:1 to receive 2.8 mg TNX-102 SL (1 tablet) sublingually at bedtime for 2 weeks followed by 5.6 mg (2 tablets) for 12 weeks or matching placebo for 14 weeks
- The prespecified primary endpoint was change from baseline to Week 14 in the weekly average of daily self-reported average pain intensity scores (11-point numerical rating scale [NRS]), analyzed using a mixed model for repeated measures (MMRM) with multiple imputation for missing data
- Exploratory efficacy endpoints included changes in sexual function, as measured by the Changes in Sexual Functioning Questionnaire short form (CSFQ-14)
 - The CSFQ-14 was analyzed by ANCOVA, and significance testing was based on least-squares (LS) means using a 2-sided α=0.05 test. Two-sided 95% confidence intervals (CIs) were generated.
- Safety evaluations included changes in blood pressure, adverse events (AEs), other vital signs, weight, physical exams, Columbia-Suicide Severity Rating Scale (C-SSRS), and Beck Depression Inventory (BDI-II)

RESULTS

Participants

- A total of 813 participants were screened for eligibility, with 456 in the intent-to-treat (ITT) population receiving TNX-102 SL (n=231) or placebo (n=225) (**Figure 1**)
 - 81.0% of the TNX-102 SL group and 79.2% of the placebo group completed the study
- Participant demographics and baseline characteristics were generally comparable between groups (**Table 1**)

Figure 1: CONSORT Diagram


Enrollment
Allocation
ITT Population
Screened N=813
Excluded 356
Did not meet enrollment criteria 335
Investigator decision 11
Withdrawal of consent 10
Randomized N=457*
TNX-102 SL SAF n=231 ITT n=231
Placebo SAF n=226 ITT n=225
Discontinued 44
AE 14
Withdrawal of consent 14
Lost to follow-up 10
Noncompliance 3
Lack of efficacy 2
Pregnancy 1
Discontinued 47
Withdrawal of consent 16
Lost to follow-up 10
AE 8
Lack of efficacy 8
Investigator decision 2
Noncompliance 2
Other 1
Completed n=187
Completed n=179

*One placebo subject who was randomized in error (did not meet safety criteria) is included in Safety population (SAF) but not in ITT population.
AE, adverse event; ITT, intent-to-treat; SAF, safety.

Table 1: Participant Demographics and Baseline Characteristics (Safety Population)

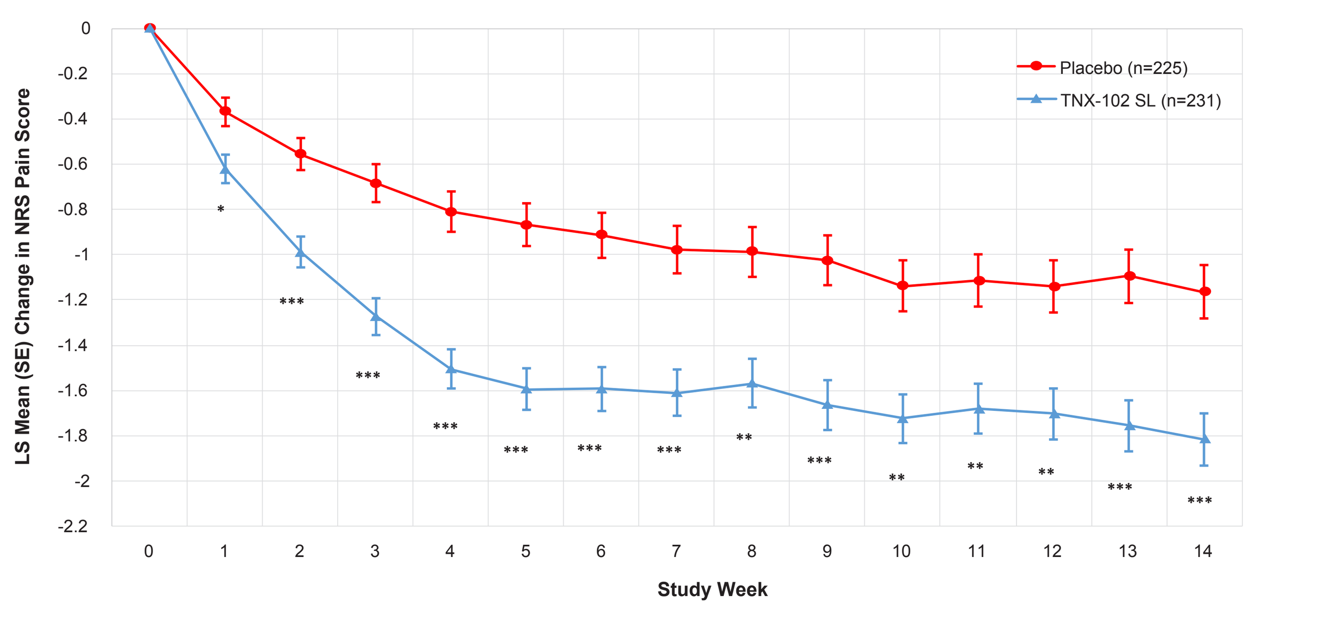
	TNX-102 SL (n=231)	Placebo (n=226)	Total (N=457)
Age, years, mean (SD)	49.3 (10.5)	49.5 (11.3)	49.4 (10.9)
Female, n (%)	224 (97.0)	212 (93.8)	436 (95.4)
Race, n (%)			
White	194 (84.0)	192 (85.0)	386 (84.5)
Black/African American	32 (13.9)	27 (11.9)	59 (12.9)
Asian	1 (0.4)	5 (2.2)	6 (1.3)
Ethnicity, n (%)			
Hispanic or Latino	36 (15.6)	35 (15.5)	71 (15.5)
Weight, kg, mean (SD)	83.7 (17.8)	84.0 (17.4)	83.8 (17.8)
Employed currently, n (%)	147 (63.6)	150 (66.4)	297 (65.0)
Unable to work due to FM symptoms, n (%)	13 (5.6)	12 (5.3)	25 (5.5)
Education, some college or beyond, n (%)	187 (81.0)	193 (85.4)	380 (83.2)
Duration of FM disease in years, mean (SD)	8.6 (8.4)	9.9 (9.5)	9.2 (9.0)
Pain at baseline, NRS, mean (SD)*	5.9 (1.1)	5.9 (1.1)	—

*Pain reported for ITT population.
FM, fibromyalgia; ITT, intent to treat; NRS, numerical rating scale; SD, standard deviation.

Efficacy

- TNX-102 SL demonstrated significant improvement vs placebo (P<0.0001) in the primary endpoint of change in weekly pain scores at Week 14 (**Figure 2**)
 - At Week 14, the LS mean weekly average of daily pain scores was 4.1 (95% CI: 3.8, 4.3) for TNX-102 SL vs 4.7 (95% CI: 4.5, 5.0) for placebo
 - LS mean changes from baseline were -1.8 (95% CI: -2.0, -1.6) for TNX-102 SL vs -1.2 (95% CI: -1.4, -0.9) for placebo
 - The difference in LS means between TNX-102 SL and placebo was 0.7 (-1.0, -0.3) NRS units. The difference in the LS means (i.e., -0.7) was due to a rounding effect: the change from baseline was -1.82 in the TNX-102 group and -1.16 in the placebo group, and the difference in LS means between the groups was -0.66.

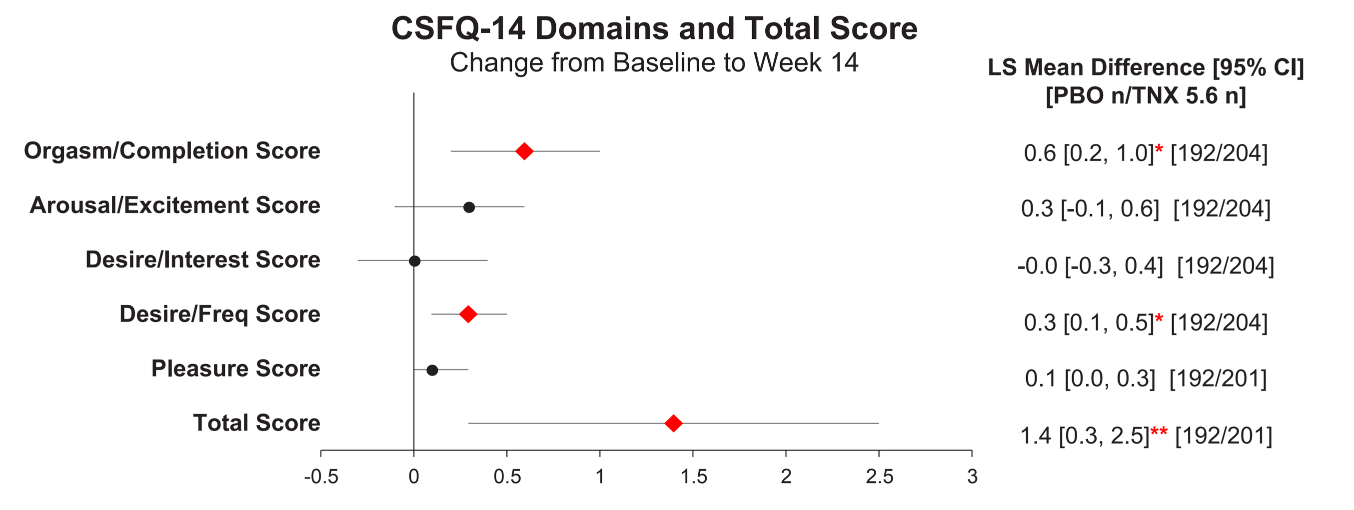
Figure 2: Mean (SE) Change From Baseline in Weekly Averages of Daily NRS Pain Scores


LS Mean (SE) Change in NRS Pain Score
Study Week
Placebo (n=225)
TNX-102 SL (n=231)
0
-0.2
-0.4
-0.6
-0.8
-1
-1.2
-1.4
-1.6
-1.8
-2
-2.2
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14

*P<0.01; **P<0.001; ***P<0.0001. P-values for weeks 1-13 were not corrected for multiple comparisons.
LS, least-squares; NRS, numerical rating scale; SE, standard error.

- Female participants receiving TNX-102 SL showed larger mean improvements from baseline in total CSFQ-14 score at Week 14 vs those receiving placebo, reflecting improvements in sexual function (**Figure 3**).
 - Compared to placebo-treated participants, female participants treated with TNX-102 SL had similar or greater improvement in all domains. Treatment effects on desire/frequency (P=0.010), orgasm/completion (P=0.007), and total sexual function scores (P=0.010) were all nominally significant.
- The small number of male participants did not allow meaningful assessment of sexual functioning between treatment groups on the CSFQ-14

Figure 3: Mean (SE) Change From Baseline in CSFQ-14 Domains and Total Score in Females


CSFQ-14 Domains and Total Score
Change from Baseline to Week 14
LS Mean Difference [95% CI]
[PBO n/TNX 5.6 n]
Orgasm/Completion Score
Arousal/Excitement Score
Desire/Interest Score
Desire/Freq Score
Pleasure Score
Total Score
0.6 [0.2, 1.0]* [192/204]
0.3 [-0.1, 0.6] [192/204]
-0.0 [-0.3, 0.4] [192/204]
0.3 [0.1, 0.5]* [192/204]
0.1 [0.0, 0.3] [192/201]
1.4 [0.3, 2.5]** [192/201]
-0.5
0
0.5
1
1.5
2
2.5
3

*P<0.05; **P<0.01.
Red diamonds indicate treatment differences with P<0.05; not corrected for multiple comparisons.
CI, confidence interval; CSFQ-14, Changes in Sexual Functioning Questionnaire short form; LS, least-squares; PBO, placebo; SE, standard error; TNX 5.6, TNX-102 SL 5.6 mg.

Safety

- No clinically meaningful differences in change from baseline in systolic or diastolic blood pressure or weight were observed between the TNX-102 SL and placebo groups at Week 14 (**Table 2**)

Table 2: Change From Baseline in Vital Sign Measurements

	TNX-102 SL (n=231)	Placebo (n=226)
Systolic blood pressure, mmHg		
n	185	180
Change from baseline to Week 14, mean (SD)	0.7 (12.4)	0.5 (10.4)
Diastolic blood pressure, mmHg		
n	185	180
Change from baseline to Week 14, mean (SD)	1.1 (8.6)	0.2 (8.2)
Weight, kg		
n	185	179
Change from baseline to Week 14, mean (SD)	0.02 (2.9)	0.20 (2.9)

- Treatment-emergent AEs (TEAEs) occurring in ≥3% of participants are shown in **Table 3**
 - A total of 47.9% of participants overall experienced at least one TEAE
 - Three (1.3%) participants each in both treatment groups experienced a severe TEAE. All other participants experiencing a TEAE rated the severity of their event as mild or moderate (57.6% of participants in the TNX-102 SL group and 35.4% of participants in the placebo group).
- The most commonly reported TEAEs were oral cavity administration site reactions that were mild-to-moderate, self-limited, and rarely led to discontinuations
 - Treatment-related discontinuations occurred in 6.1% and 3.5% of participants in the TNX-102 SL and placebo groups, respectively
 - Systemic TEAE rates, excluding COVID-19, remained below 4.0%

Table 3. TEAEs Occurring in ≥3% of Participants in Either Treatment Group

	TNX-102 SL (n=231)	Placebo (n=226)	Total (N=457)
Systemic adverse events, n (%)			
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, n (%)			
Hypoesthesia oral	55 (23.8)	1 (0.4)	56 (12.3)
Product taste abnormal	27 (11.7)	2 (0.9)	29 (6.3)
Paresthesia oral	16 (6.9)	2 (0.9)	18 (3.9)
Tongue discomfort	16 (6.9)	0 (0.0)	16 (3.5)

CONCLUSIONS

- TNX-102 SL significantly reduced pain and showed a favorable tolerability profile, including minimal impact on weight and blood pressure
- Among females, TNX-102 SL was associated with improvements in sexual functioning compared with placebo and did not cause weight gain, an adverse effect often observed with other treatments
- Along with its unique mechanism targeting sleep disturbances, these results support TNX-102 SL as a new treatment option for FM
- The availability of a well-tolerated treatment may also encourage clinicians to make the diagnosis of FM earlier, thereby improving participant outcomes through timely intervention

References

1. Kang JH, et al. *J Rheum Dis.* 2022;29(1):4-13.
2. Theadom A, et al. *J Psychosom Res.* 2007;62(2):145-51.
3. Clauw DJ. *Ann Rheum Dis.* 2024;83(11):1421-7.
4. Kaplan CM, et al. *Nat Rev Neurol.* 2024;20(6):347-63.
5. Moldofsky H, et al. *Psychosom Med.* 1975;37(4):341-51.
6. Arout CA, et al. *J Womens Health (Larchmt).* 2018;27(8):1035-44.
7. Clauw DJ. *JAMA.* 2014;311(15):1547-55.
8. Robinson RL, et al. *Pain Med.* 2012;13(10):1366-76.
9. Lederman S, et al. *Pain Med.* 2025:pnaf089.
10. Lederman S, et al. *Arthritis Care Res (Hoboken).* 2023;75(11):2359-68.
11. Lederman S, et al. PainConnect 2025, April 3-6, 2025, Austin, TX.

Disclosures

GS, MK, JE, SE: Employee of and stock ownership in Tonix Pharmaceuticals, Inc.
EG: Employee of Tonix Medicines, Inc.

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