

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

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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 syndrome³
- 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 FM⁵
- Poor sleep quality is highly associated with an amplification of nociplastic pain⁴
- 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 adherence⁸
- Tonmya[™] (TNX-102 SL, a sublingual formulation of cyclobenzaprine) is FDA approved for the treatment of FM in adults⁹⁻¹¹
- 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

AE, adverse event; ITT, intent-to-treat; SAF, safety.

- 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**)

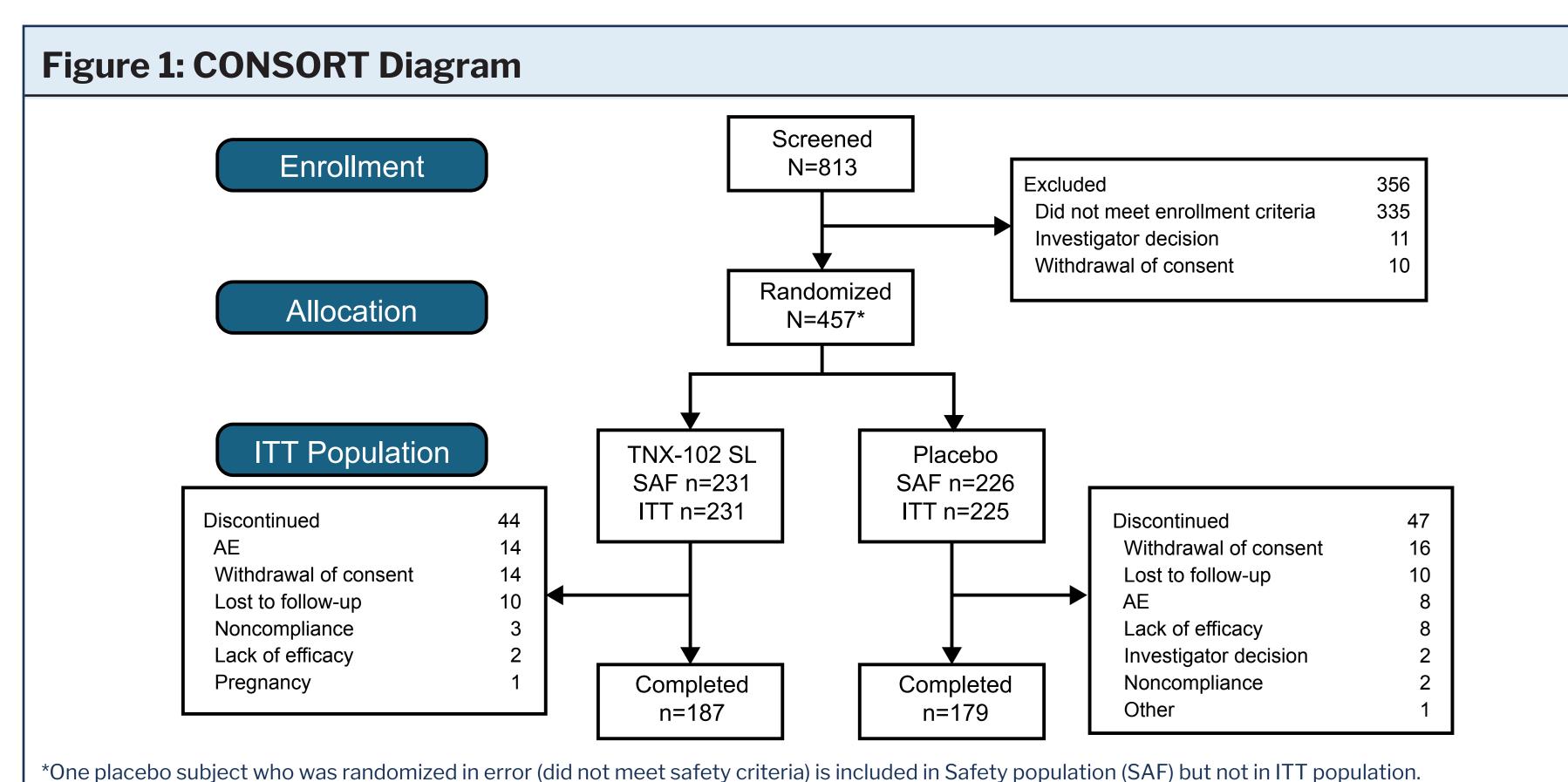
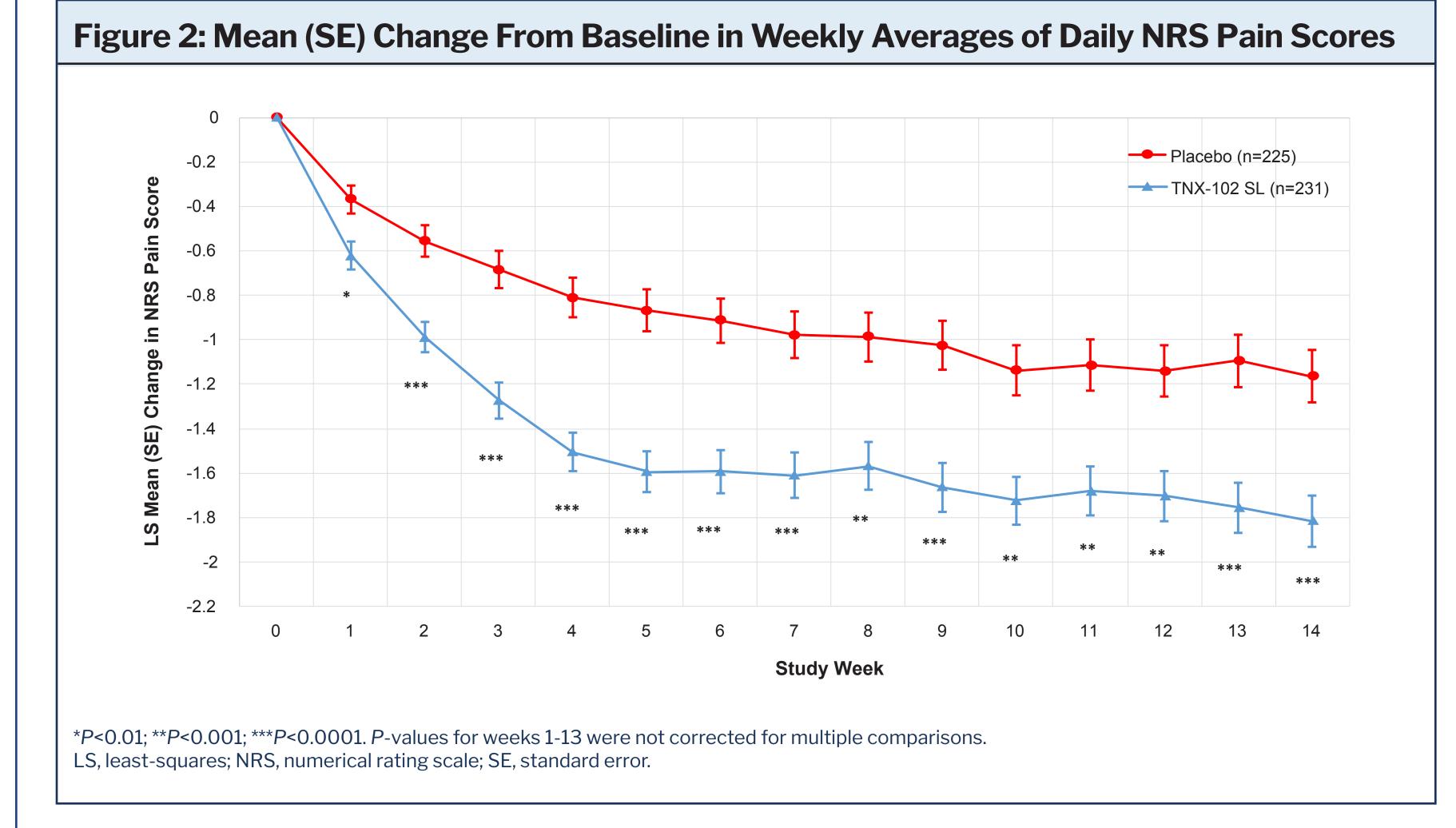


Table 1: Participant Demographics and Baseline Characteristics (Safety Population)				
	TNX-102 SL (n=231)	Placebo (n=226)	Total (N=457)	
Age, years, mean (SD)	49.3 (10.5)	49.5 (11.3)	49.4 (10.9)	
Female, n (%)	224 (97.0)	212 (93.8)	436 (95.4)	
Race, n (%)				
White	194 (84.0)	192 (85.0)	386 (84.5)	
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)	_	

FM, fibromyalgia; ITT, intent to treat; NRS, numerical rating scale; SD, standard deviation.

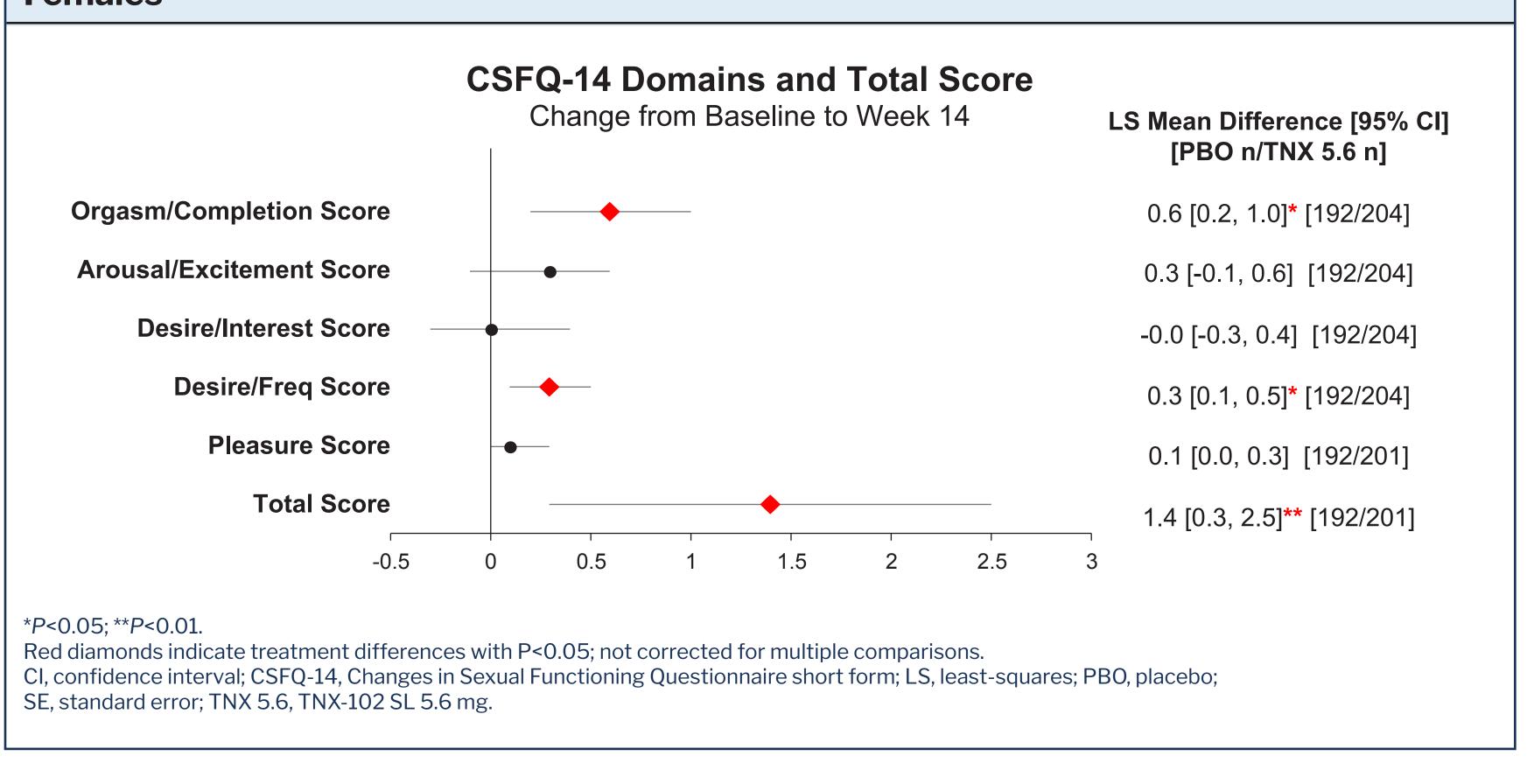
Efficacy

- 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.



- 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



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**)

References

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- Table 2: Change From Baseline in Vital Sign Measurements Placebo (n=226) Systolic blood pressure, mmHg 180 185 Change from baseline to Week 14, mean (SD) 0.5 (10.4) 0.7 (12.4) Diastolic blood pressure, mmHg 180 Change from baseline to Week 14, mean (SD) 0.2 (8.2) 1.1 (8.6) | Weight, kg 0.20 (2.9) Change from baseline to Week 14, mean (SD)
- 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 mildto-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)	O (O.O)	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
- 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

Disclosures

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

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