Poster #: 50

Treatment with TNX-102 SL Produces Clinically Meaningful Improvements in Patient-Centered Outcomes in Fibromyalgia

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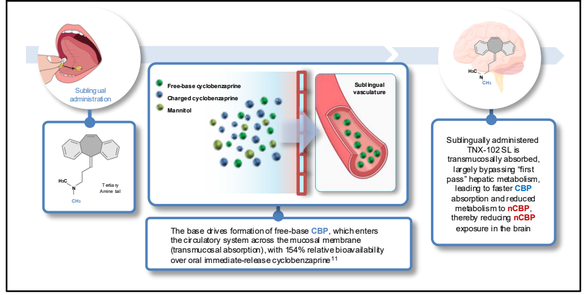
INTRODUCTION

- Fibromyalgia (FM) is a chronic pain disorder that affects ~2 to 4% of US adults, occurs predominantly in women, and is characterized by widespread pain, nonrestorative sleep, fatigue, cognitive dysfunction, and functional impairment[1-3]
- FM is the prototypic nociplastic pain syndrome, with pain arising from abnormal processing in the central nervous system (CNS), not from tissue or nerve injury, resulting in amplified and widespread pain[4,5]
- Disruptions to deep restorative sleep are common in FM, and poor sleep quality is strongly associated with greater nociplastic pain[6]
- Standard analgesics (NSAIDs, opioids) are typically ineffective because they do not target the CNS mechanisms driving nociplastic pain[4,5]
- Other FDA-approved therapies for FM are often limited by side effects, including dizziness, drowsiness, nausea, weight gain, sexual dysfunction, and cognitive impairment, which can lead to poor adherence and high discontinuation rates[7]
- TNX-102 SL (Tonmya™, cyclobenzaprine HCl sublingual tablets) is recently FDA-approved for adults with FM, based in part on the Phase 3 RESILIENT trial results[8]
  - Cyclobenzaprine (CBP) antagonizes the 5-HT_{2A}-serotonergic, α1-adrenergic, M1-muscarinic, and H1-histaminergic receptors, influencing sleep architecture and potentially alleviating core FM symptoms[9]
  - TNX-102 SL rapidly disintegrates, dissolves, and releases stabilized CBP into the saliva, which enters the circulatory system across the mucosal membrane and then directly enters the brain (**Figure 1**)
  - Compared with oral immediate-release CBP, TNX-102 SL undergoes transmucosal absorption and reduced first-pass hepatic metabolism, resulting in higher bioavailability of the parent compound[9]
    - By largely bypassing first-pass hepatic metabolism, TNX-102 SL administration results in reduced formation of the active, long half-life metabolite norcyclobenzaprine (nCBP) relative to oral IR CBP, which may minimize next-day sedation and support restorative sleep[10]

Figure 1. TNX-102 SL Bypasses First-Pass Metabolism



- Although ≥30% pain reduction with treatment is recognized as clinically meaningful in FM, considering pain outcomes in isolation may not thoroughly capture TNX-102 SL's broader treatment benefits[12]

OBJECTIVE

- To assess pain reduction in combination with additional patient-reported outcomes to further establish the clinical meaningfulness of TNX-102 SL's efficacy

METHODS

- The RESILIENT trial assessed the efficacy and safety of TNX-102 SL vs placebo in adults with FM (2016 ACR diagnostic criteria) over 14 weeks
- The RESILIENT trial's primary efficacy endpoint evaluated the change from baseline in the weekly average of daily self-reported NRS pain scores (0-10) at Week 14 for TNX-102 SL vs placebo, analyzed by mixed model for repeated measures with multiple imputation for missing data
- Key secondary endpoints, all assessed at Week 14, included:
  - Proportion of subjects with a Patient Global Impression of Change (PGIC) rating of "very much improved" or "much improved"
  - Change from baseline in the Fibromyalgia Impact Questionnaire – Revised (FIQR) Symptoms domain score
  - Change from baseline in the FIQR Function domain score
  - Change from baseline in the Patient-Reported Outcomes Measurement Information System (PROMIS) 8a score for sleep disturbance
  - Change from baseline in the PROMIS 8a score for fatigue
  - Change from baseline in the weekly average of the daily diary assessment of sleep quality
- Clinically meaningful pain reduction was a prespecified endpoint assessing the proportion of participants with ≥30% reduction in the primary pain endpoint scores from baseline to Week 14
- The proportion of participants achieving ≥50% improvement in FIQR total scores was assessed
- In a post hoc analysis, the proportion of participants achieving a composite response criterion (≥30% pain reduction + PGIC response of "very much" or "much" improved) was analyzed
- Binary endpoints were analyzed with the Pearson chi-squared test; missing data were treated as non-response
- Safety assessments included reporting of adverse events (AEs)

RESULTS

- A total of 457 adults with FM were randomized 1:1 to receive either TNX-102 SL (2.8 mg tablets at bedtime for 2 weeks, followed by 5.6 mg at bedtime for 12 weeks) or placebo
- Baseline characteristics and demographics were well-balanced between TNX-102 SL (n=231) and placebo (n=225) groups (**Table 1**)

Table 1. Baseline Characteristics and Demographics of the RESILIENT Trial

	TNX-102 SL (n = 231)	Placebo (n =225[a])
Age, years, mean (SD)	49.3 (10.5)	49.5 (11.4)
Female, n (%)	224 (97.0)	212 (93.8)
Diary pain score, 0-10 NRS, mean (SD)	5.9 (1.1)	5.9 (1.1)
Duration of FM, years, mean (SD)	8.6 (8.4)	9.9 (9.5)
BMI, kg/m^2, mean (SD)	31.1 (6.3)	31.1 (6.3)
FIQR Symptoms domain score, mean (SD)	53.1 (14.9)	54.1 (14.6)
FIQR Function domain score, mean (SD)	38.5 (19.9)	37.9 (19.1)
PROMIS Sleep Disturbance 8a score, mean (SD)	59.2 (6.0)	59.4 (7.2)
PROMIS Fatigue 8a score, mean (SD)	63.7 (5.9)	63.9 (7.1)
Diary sleep score, mean (SD)	5.8 (1.3)	5.7 (1.3)
Prior (lifetime) FDA-approved FM treatments, n (%)		
Duloxetine	47 (20.3)	52 (23.0)
Pregabalin	46 (19.9)	45 (19.9)
Milnacipran	5 (2.2)	10 (4.4)

[a]Does not include 1 patient who was inadvertently randomized and received placebo.
BMI, body mass index; FIQR, Fibromyalgia Impact Questionnaire Revised; FM, fibromyalgia; NRS, numeric rating scale; PROMIS, Patient-Reported Outcomes Measurement Information System; SD, standard deviation.

RESULTS

- The primary and all key secondary endpoints were statistically significant in favor of TNX-102 SL over placebo, as shown in **Table 2**

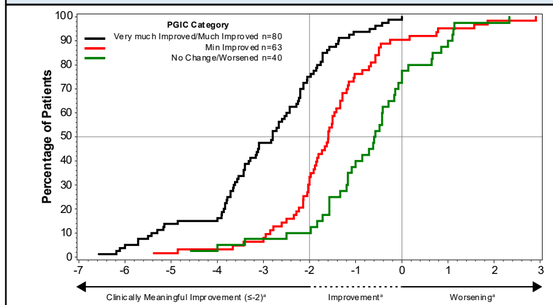
Table 2. Efficacy Summary[a]: Primary and 6 Key Secondary[b] Endpoints at Week 14

	TNX-102 SL n=231	Placebo n=225	LS Mean (SE) Difference	P-value
Primary Endpoint				
Daily diary pain ratings, LS Mean (SE)	-1.82 (0.116)	-1.16 (0.118)	-0.65 (0.161)	<0.001
Key Secondary Endpoints				
PGIC responders, %	35.1	19.1	16.0[c] (7.9, 24.0)	<0.001
FIQR–Symptoms domain score, LS Mean CFB (SE)	-16.02 (1.166)	-8.36 (1.173)	-7.67 (1.619)	<0.001
FIQR–Function domain score, LS Mean CFB (SE)	-12.22 (1.190)	-6.81 (1.207)	-5.41 (1.661)	0.001
PROMIS Sleep Disturbance score, LS Mean CFB (SE)	-8.44 (0.575)	-4.20 (0.564)	-4.24 (0.789)	<0.001
PROMIS Fatigue score, LS Mean CFB (SE)	-7.18 (0.550)	-4.16 (0.559)	-3.01 (0.768)	<0.001
Diary Sleep Quality ratings, LS Mean CFB (SE)	-1.77 (0.119)	-1.20 (0.121)	-0.57 (0.168)	<0.001

[a]Data derived from intention-to-treat (ITT) population. [b]In order of statistical serial gate-keeping hierarchy to control overall type 1 error. [c]Difference in proportions [95% CI]. CFB, change from baseline; FIQR, Fibromyalgia Impact Questionnaire – Revised; LS, least-squares; PGIC, Patient Global Impression of Change; PROMIS, Patient-Reported Outcomes Measurement Information System; SE, standard error.

- At Week 14, 45.9% of TNX-102 SL-treated participants and 27.1% of placebo-treated participants achieved ≥30% reduction in pain intensity (p<0.001, uncorrected) from baseline
- PGIC responders taking TNX-102 SL experienced a median pain score reduction of 2.8 points, and those reporting minimal improvement had a median pain score reduction of 1.6 points (**Figure 2**)
- Participants reporting no change or worsening had a median increase in pain score of 0.67 points (**Figure 2**)
- 75% of PGIC responders treated with TNX-102 SL achieved a reduction in pain score of ≥2 points (**Figure 2**)

Figure 2. Cumulative NRS Pain Change from Baseline Scores by PGIC Categories for TNX-102 SL at Week 14

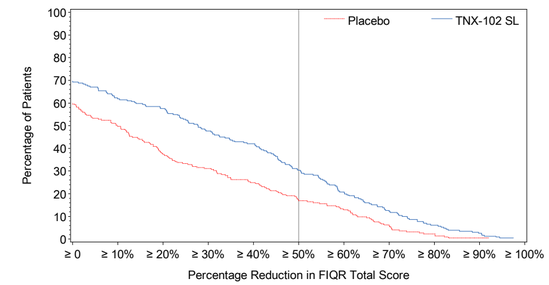


[a]Negative values indicate improvement in NRS pain scores, with reductions of ≥2 points representing clinically meaningful improvement; positive values indicate worsening. Figure does not include participants with missing data at Week 14. NRS, Numeric Rating Scale; PGIC, Patient Global Impression of Change.

- More participants treated with TNX-102 SL vs placebo experienced ≥50% reduction in FIQR total score (30.3% vs 17.3%, respectively; p=0.001, uncorrected) (**Figure 3**)
- Similarly, TNX-102 SL treatment was associated with a higher percentage of participants meeting the composite response criteria vs placebo (28.6% vs 15.1%, respectively; p<0.001, uncorrected)

RESULTS

Figure 3. Continuous Responder Graph of Percentage Change from Baseline Scores at Week 14 on the FIQR



FIQR, Fibromyalgia Impact Questionnaire – Revised.

- TNX-102 SL was generally well tolerated, with an AE profile consistent with previous studies and no new safety signals observed
- In total, 6.1% of participants discontinued TNX-102 SL due to AEs
- The most commonly reported treatment-emergent adverse events (TEAEs) for TNX-102 SL were mild, transient, and self-limited local oral administration site reactions site reactions that infrequently led to study discontinuation (**Table 3**)

Table 3. TEAEs Reported by ≥2% of Patients in Either Treatment Group

	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)
Fatigue	6 (2.6)	5 (2.2)	11 (2.4)
Upper respiratory tract infection	6 (2.6)	1 (0.4)	7 (1.5)
Oral Cavity Adverse Events			
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	16 (3.5)
Oral mucosal erythema	6 (2.6)	2 (0.9)	8 (1.8)
Glossodynia	5 (2.2)	1 (0.4)	6 (1.3)
Tongue disorder	5 (2.2)	0	5 (1.1)

TEAEs, treatment-emergent adverse events.

CONCLUSIONS

- TNX-102 SL treatment provided clinically meaningful improvements in pain (≥30%), FIQR total score (≥50%), and the composite endpoint of ≥30% pain reduction and PGIC response
- TNX-102 SL treatment significantly improved sleep disturbance, fatigue and FIQR symptoms and function domain scores vs placebo
- TNX-102 SL shows a low systemic adverse-event (AE) burden, with prominent but generally self-limited oral local AEs; in contrast, oral IR cyclobenzaprine is limited by classic tricyclic systemic AEs such as somnolence and anticholinergic effects at commonly prescribed doses
- Although study designs and methodologies differ, AE-related discontinuation rates observed with TNX-102 SL were lower than those observed in registrational studies supporting previous US FDA-approved therapies (6.1% vs 14.7-32.6%) in FM, corroborating TNX-102 SL as a well-tolerated, patient-centered therapy for adults with FM[9,13-16]
- This analysis highlights the patient-centered and clinically meaningful effects of TNX-102 SL across multiple symptom domains in adults with FM

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DISCLOSURES

GMS, JH: Employee of Tonix Pharmaceuticals, Inc. and owns stock and/or stock options in Tonix Pharmaceuticals Holding Corp. **CB**: Consultant to Tonix Pharmaceuticals, Inc. **EG**: Employee of Tonix Medicines, Inc. and owns stock and/or stock options in Tonix Pharmaceuticals Holding Corp.

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