Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results from the Phase 3 Randomized, Double-Blind, Placebo-Controlled RESILIENT Trial

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*Tonmya™ (TNX-102 SL) is an investigational drug and has not been approved for any indication

INTRODUCTION

Fibromyalgia (FM) is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system. Fibromyalgia afflicts an estimated 6 million to 12 million adults in the U.S., the majority of whom are women. Symptoms of fibromyalgia include chronic widespread pain, nonrestorative sleep, fatigue, and morning stiffness. Other associated symptoms include cognitive dysfunction and mood disturbances, including anxiety and depression. Individuals suffering from fibromyalgia struggle with their daily activities, have impaired quality of life, and frequently are disabled. Physicians and patients report common dissatisfaction with currently marketed products. Tonmya™ (TNX-102 SL) is an innovative sublingual tablet formulation of cyclobenzaprine HCl (CBP) which is distinct from oral immediate-release (CBP) in providing rapid sublingual transmucosal absorption, greater bioavailability, and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. CBP potently binds and antagonizes 5-HT_{2A}-serotonergic, α_1-adrenergic, M_1-muscarinic acetylcholine, and H_1-histaminergic receptors, each of which impacts aspects of sleep architecture. Tonmya is believed to work in FM by targeting improvement in sleep quality.

METHODS

Across 33 U.S. sites, RESILIENT enrolled 457 fibromyalgia patients; the intent-to-treat (ITT) population received TNX-102 SL 2.8 mg for 2 weeks, followed by 5.6 mg for 12 weeks (N=231) or matching placebo (N=225). The primary endpoint was change from baseline at Week 14 in the weekly averages of daily diary pain numeric rating scale (NRS) scores. Secondary endpoints included Patient Global Impression of Change (PGIC), Fibromyalgia Impact Questionnaire - Revised (FIQR) Symptoms and Function domains, PROMIS Sleep Disturbance and Fatigue, and daily diary sleep quality ratings. Safety was assessed by adverse events, vital signs/weight, physical exams, and Changes in Sexual Functioning Questionnaire short form (CSFQ-14).

RESULTS

Figure 1: CONSORT Diagram

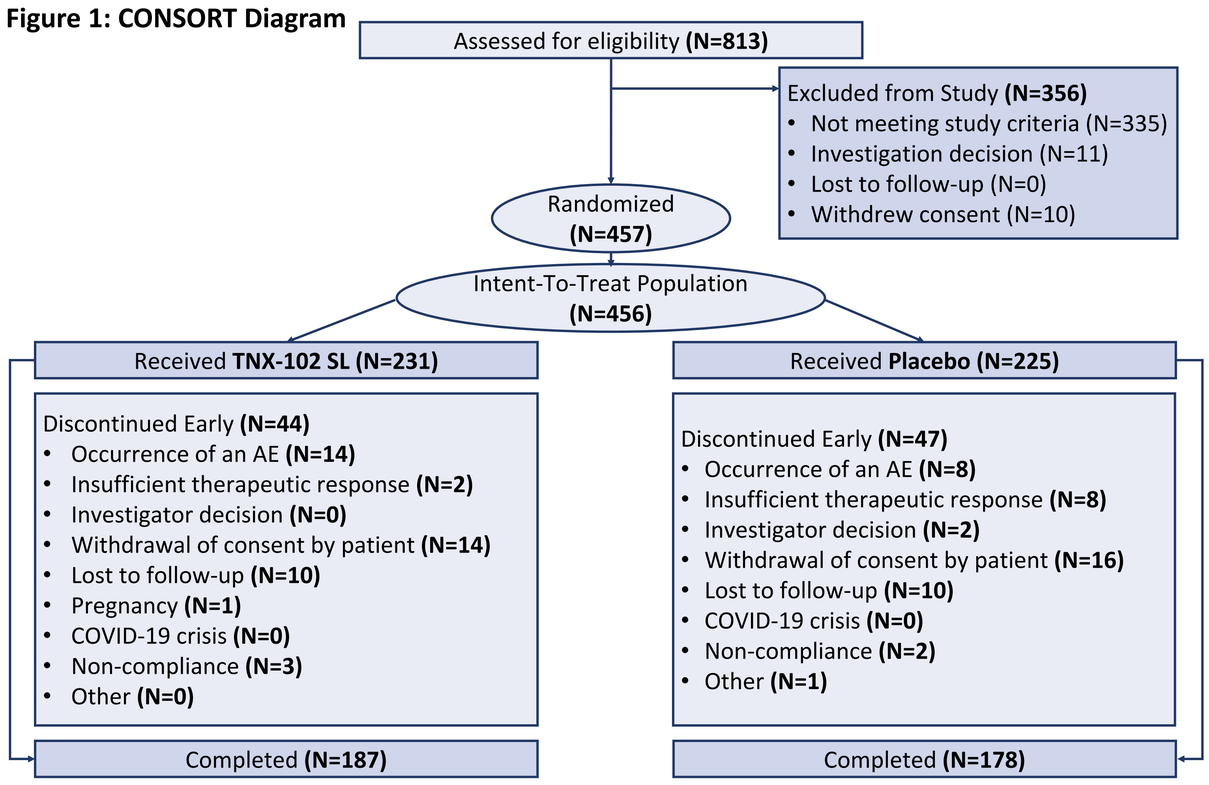


Table 1: Demographics and Baseline Characteristics in Safety Population

	TNX-102 SL (N=231)	Placebo (N=226)	Total (N=457)
Females, n (%)	224 (97.0%)	212 (93.8%)	436 (95.4%)
Age in years, mean (SD)	49.3 (10.45)	49.5 (11.32)	49.4 (10.88)
Race, n (%)			
White/Caucasian	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%)
BMI, kg/m², mean (SD)	31.1 (6.34)	31.1 (6.32)	31.1 (6.33)
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 (8.44)	9.9 (9.52)	9.2 (9.00)
Pain at baseline, NRS, mean (SD)	5.9 (1.05)	5.9 (1.08)	

As seen in **Table 2**, Tonmya demonstrated highly statistically significant improvement in primary endpoint of mean weekly pain scores over placebo at Week 14 (p = 0.00005). Furthermore, all six key secondary endpoints were statistically significant (all p-values ≤ 0.001). Cohen's d effect size for primary endpoint was 0.38 and all five continuous key secondaries in range of 0.30 – 0.50. PGIC was a responder analysis.

Table 2: Summary of Results of the Primary and 6 Key Secondary Endpoints at Week 14

	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

TOPLINE RESULTS

Figure 2: Mean Change from Baseline in Weekly Averages of Daily NRS Pain Scores

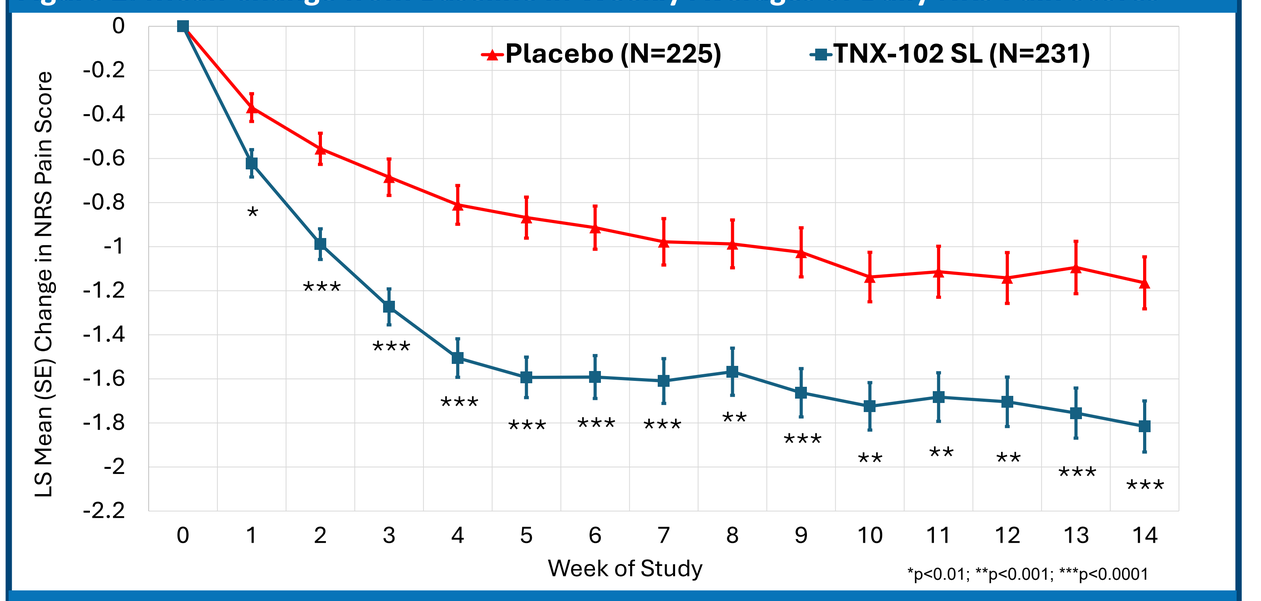
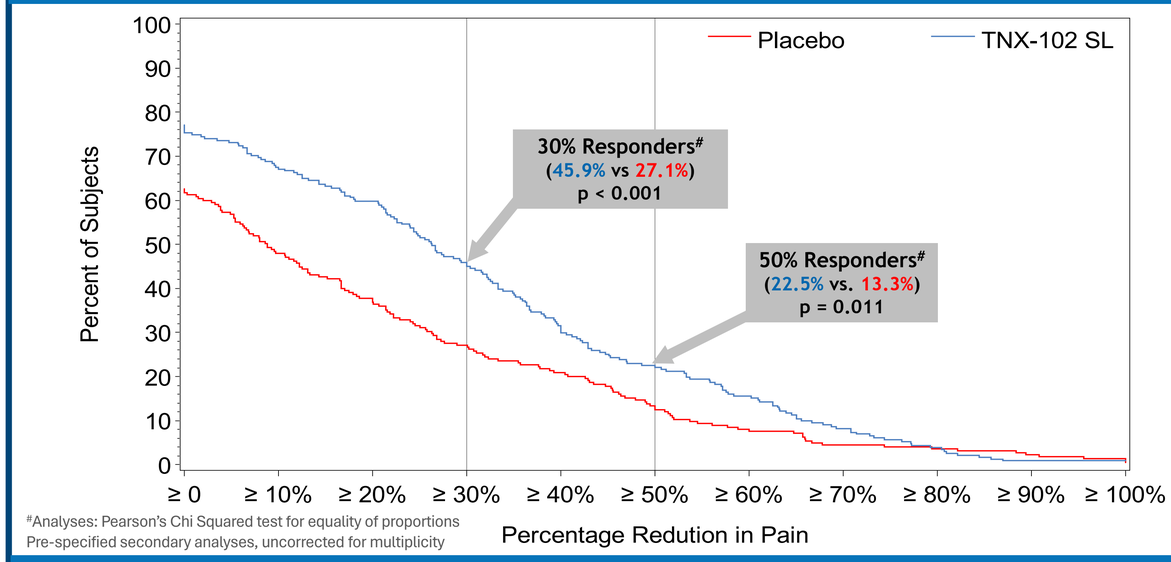
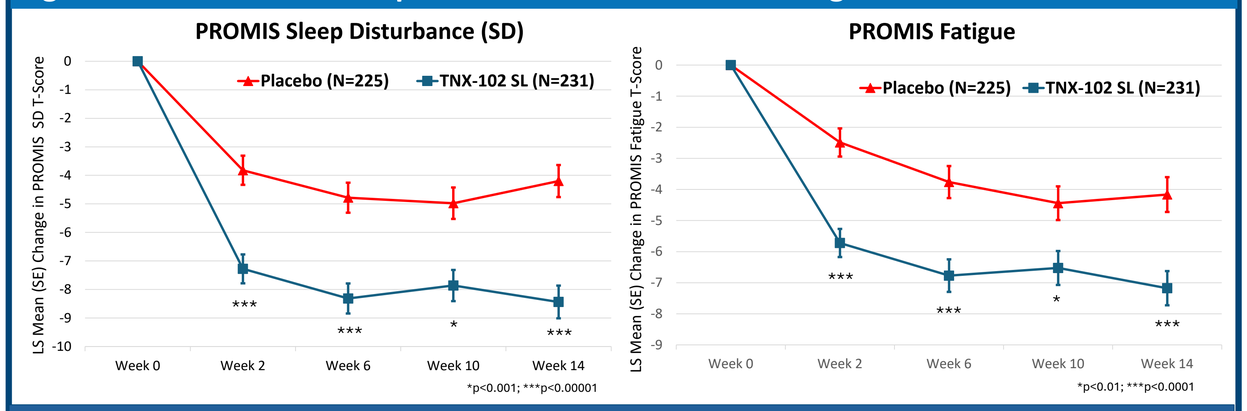


Figure 3: Continuous Responder Analysis Graph



#Analyses: Pearson's Chi Squared test for equality of proportions
Pre-specified secondary analyses, uncorrected for multiplicity

Figures 4 & 5: PROMIS Sleep Disturbance and PROMIS Fatigue



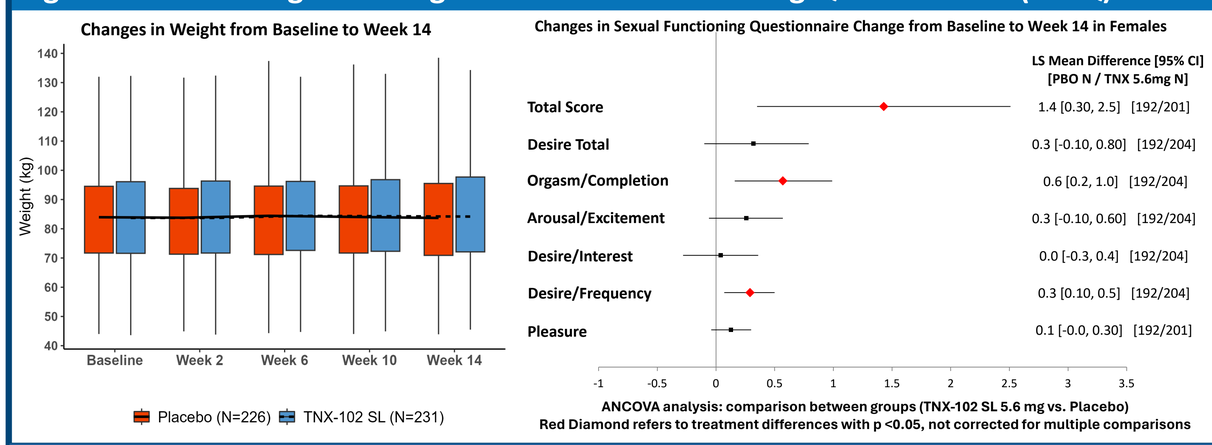
SAFETY

Table 3: Treatment-Emergent Adverse Events 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

Figures 6 & 7: Changes in Weight and Sexual Functioning Questionnaire (CSFQ)



DISCUSSION

- Treatment with Tonmya significantly reduced daily pain and demonstrated broad FM symptom improvement, as demonstrated by significant improvement on all six key secondary endpoints
- Tonmya demonstrated a favorable safety and tolerability profile, avoiding common side effects associated with currently approved products such as increase in weight and decrease in sexual functioning

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