Cyclobenzaprine HCl sublingual tablets (CBP SL) provide rapid pain relief in adults with fibromyalgia

Errol Gould, PhD[1]; Jean Heilman, MS[2]; Gregory M. Sullivan, MD[2]

[1]Tonix Medicines, Inc., Berkeley Heights, NJ, USA; [2]Tonix Pharmaceuticals, Inc., Berkeley Heights, NJ, USA

INTRODUCTION

- Fibromyalgia (FM) is a chronic nociplastic pain disorder that affects ~2 to 4% of US adults, mostly women, and is characterized by widespread pain, nonrestorative sleep, fatigue, cognitive dysfunction, and functional impairment[1-5]
- Cyclobenzaprine HCl sublingual tablets (CBP SL) are the first FDA-approved treatment for adults with FM in over 15 years[6-8]

OBJECTIVE

- To evaluate the initial onset of pain improvement with CBP SL in adults with fibromyalgia

METHODS

- RESILIENT was a 14-week, randomized, placebo-controlled phase 3 trial evaluating the efficacy and safety of CBP SL in adults with FM as defined by 2016 American College of Rheumatology (ACR) criteria
- The primary endpoint was the change from baseline to Week 14 in the weekly average of daily numeric rating scale (NRS, 0-10) pain scores for CBP SL vs placebo
- This post hoc mixed-model repeated-measures analysis assessed the treatment differences in pain between CBP SL and placebo during the first 2-7 days of study treatment
- Safety assessments included reporting of adverse events (AEs)

RESULTS

- Adults with FM (N=457) were randomized 1:1 to receive either CBP SL (2.8 mg tablets at bedtime for 2 weeks, followed by 5.6 mg at bedtime for 12 weeks) or placebo (**Table 1**)

Table 1. Baseline Demographics and Patient Characteristics of the RESILIENT Trial

	CBP 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)

[a]Does not include 1 patient who was inadvertently randomized and received placebo.
FM, fibromyalgia; NRS, numeric rating scale; SD, standard deviation.

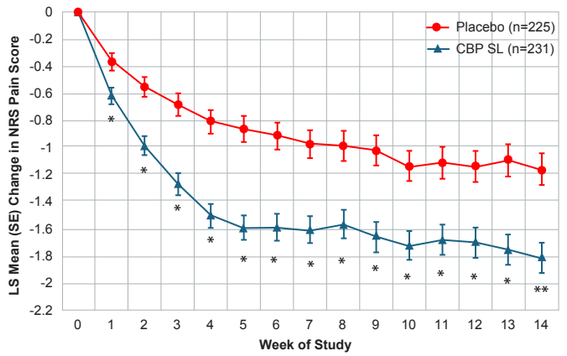
- The primary and all key secondary endpoints were statistically significant in favor of CBP SL over placebo (**Figure 1** and **Table 2**)
- CBP SL showed an improvement in pain vs placebo at every day in the first week of the study (**Figure 2**)

Table 2. Primary and Key Secondary Endpoints at Week 14[a,b]

	CBP 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[c], %	35.1	19.1	16.0[d] (7.9, 24.0)	<0.001
FIQR–Symptoms domain score, LS mean CFB (SE)	-16.0 (1.17)	-8.4 (1.17)	-7.7 (1.62)	<0.001
FIQR–Function domain score, LS mean CFB (SE)	-12.2 (1.19)	-6.8 (1.21)	-5.4 (1.66)	0.001
PROMIS Sleep Disturbance score, LS mean CFB (SE)	-8.4 (0.57)	-4.2 (0.56)	-4.2 (0.79)	<0.001
PROMIS Fatigue score, LS mean CFB (SE)	-7.2 (0.55)	-4.2 (0.56)	-3.0 (0.77)	<0.001
Diary Sleep Quality ratings, LS mean CFB (SE)	-1.8 (0.12)	-1.2 (0.12)	-0.6 (0.17)	<0.001

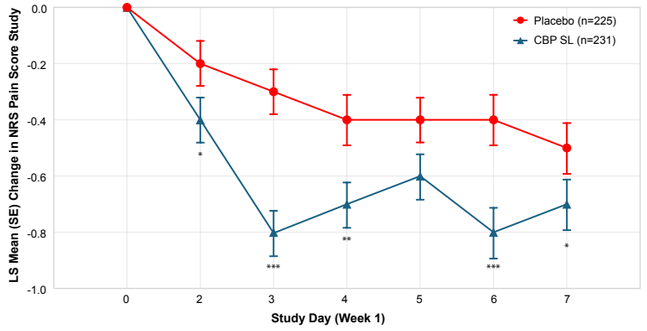
[a]Data derived from intention-to-treat (ITT) population. [b]In order of statistical serial gate-keeping hierarchy to control overall type 1 error. [c]PGIC response defined as "much" or "very much" improved. [d]Difference in proportions [95% CI]. CFB, change from baseline; FIQR, Fibromyalgia Impact Questionnaire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

Figure 1. Mean Change from Baseline in Weekly Averages of Daily NRS Pain Scores[a]



[a]Based on a mixed model for repeated measures with multiple imputation, with treatment, center, study week, and treatment by study week interaction as fixed categorical effects, as well as baseline value and baseline value-by-study week interaction. Weeks 1-13 represent exploratory endpoints, and reported *P* values are uncorrected for multiplicity control.
*$P<0.01$; **$P<0.001$.
LS, least squares; NRS, numeric rating scale; SE, standard error.

Figure 2. Mean Change from Baseline in Daily NRS Pain Scores Over Treatment Days 2-7[a]



[a]LS mean, differences, SEs and *P* values are based on a mixed model for repeated measures with treatment, center, study day and treatment by study day interaction as fixed categorical effects as well as baseline value and baseline value-by-study day interaction as continuous fixed covariates. An unstructured covariance matrix was used.
*$P<0.05$; **$P=0.01$; ***$P\leq0.001$. All *P* values were uncorrected.
LS, least squares; NRS, numeric rating scale; SE, standard error.

Safety and tolerability

- CBP SL was generally well tolerated (**Table 3**)
  - Overall, 6.1% of participants discontinued CBP SL due to AEs vs 3.5% with placebo

Table 3. TEAEs Reported by ≥3% of Participants[a]

	CBP 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			
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)

[a]Outcome data for CBP SL and placebo are presented as n (%).
TEAEs, treatment-emergent adverse events.

CONCLUSION

- CBP SL produced rapid reduction in pain as early as Day 2; significant pain relief vs placebo was observed at each week over Weeks 1-14
- Early and sustained pain reduction was accompanied by significant improvements in all key secondary endpoints
- CBP SL demonstrated a low systemic AE burden with prominent but generally self-limited oral local AEs

REFERENCES

1. Bhargava J, Goldin J. StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2025.
2. Kang JH, et al. *J Rheum Dis*. 2022;29(1):4-13.
3. Theadom A, et al. *J Psychosom Res*. 2007;62(2):145-51.
4. Clauw DJ. *Ann Rheum Dis*. 2024;83(11):1421-7.
5. Kaplan CM, et al. *Nat Rev Neurol*. 2024;20(6):347-63.
6. TONMYA™ (cyclobenzaprine hydrochloride sublingual tablets) [prescribing information]. Chatham, NJ: Tonix Medicines, Inc.;2025.
7. Lederman S, et al. *Pain Med*. 2026;27(1):86-94.
8. Lederman S, et al. *Arthritis Care Res (Hoboken)*. 2023;75(11):2359-68.

ACKNOWLEDGMENTS

This study was supported by Tonix Pharmaceuticals, Inc. (Berkeley Heights, NJ). Medical writing and editorial assistance were provided by Tanmaya Phanda, PharmD, and Anthony DiLauro, PhD, ELS, of the Sensified Division of Woven Health Collective, LLC (New York, NY), and were funded by Tonix Medicines, Inc.

DISCLOSURES

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

Presented at the 8th International Congress on Controversies in Fibromyalgia, March 9-10, 2026, Krakow, Poland