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A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) for the Treatment of Fibromyalgia (FM):

Evidence for a Broad Spectrum of Activity on the FM Syndrome

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Chief Medical Officer
Tonix Pharmaceuticals Inc
presenting at
American College of Rheumatology
Annual Meeting, Atlanta, GA
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The preliminary prospectus, dated October 18, 2019, is available on the SEC Web site at www.sec.gov/Archives/edgar/data/.

Alternatively, we or any underwriter participating in the offering will arrange to send you the preliminary prospectus and, when available, the final prospectus and/or any supplements thereto if you contact A.G.P./Alliance Global Partners, 590 Madison Avenue, 36th Floor, New York, NY 10022 or via telephone at 212-624-2006 or email: presentation@allianceg.com.

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Disclosure Statements

- Gregory Sullivan MD is an employee of Tonix Pharmaceuticals Inc and owns stock and stock options in the company
- The co-authors on this work are employees or consultants of Tonix Pharmaceuticals Inc
- TNX-102 SL is an investigational new drug and has not been approved for any indication

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TNX-102 SL for the Treatment of Fibromyalgia
Rationale for Targeting Sleep Quality

- Inter-relationship between poor sleep quality and fibromyalgia (FM) described almost 50 years ago[1]
  - Moldofsky & Smythe identified anomalous alpha-rhythms in stage 4 NREM EEG delta wave sleep in patients with "fibrositis syndrome" (a former name for fibromyalgia)
  - In healthy volunteers, stage 4 sleep deprivation results in temporary appearance of myalgia, tenderness, and fatigue comparable to that in fibromyalgia (FM)
    - Suggests sleep disturbance in FM may not only be a consequence of pain but also pathogenic in the disorder
- Sleep deprivation impairs descending pain inhibition pathways involved in controlling/coping with pain[2]
  - Poor sleep quality is a risk factor for the development of widespread pain through central sensitization
  - Reduced slow wave sleep (SWS) in FM may indicate impairment in homeostatic mechanisms of pain control
  - Serotonergic (5-HT) and noradrenergic (NA) systems mediate descending inhibitory pain pathways in FM
    - Dysfunction in descending inhibitory activity plays a role in central sensitization in FM and the maladaptive pain expression
    - Enhancement of restorative sleep via modulation of 5-HT and NA pathways may allow homeostatic plastic changes in pain processing circuitry and recovery from FM
- Proof of concept study showed clinical and pharmacodynamic benefit of low dose cyclobenzaprine in FM[3]
  - 8-week RCT with polysomnography (PSG) demonstrated improvement in core FM symptoms
  - Cyclobenzaprine treatment associated with a decreased pathological arousal pattern in the SWS EEG

[1] Moldofsky & Smythe. *Psychosomatic Medicine*. 1975; **37**(4):341–351. [2] Choi EHS. *Nat Rev Rheumatol* 2015; **11**:513–520. [3] Moldofsky et al. *J Rheumatol* 2011; **38**:2653-63.
CNS, central nervous system; EEG, electroencephalogram; RCT, randomized clinical trial

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Non-restorative Sleep is Common in Fibromyalgia and May Contribute to Pain Symptoms[1]

Sleep problems and non-restorative sleep have been reported in >90% of fibromyalgia patients[2-5]

- Prolonged time to sleep onset (latency)

- Increased number of arousals leading to fragmented sleep

- Non-restorative sleep or waking feeling unrefreshed
  - Diffuse stiffness, aching and fatigue, even after 6-8 hours sleep

[1] Oswald I. *Proc R Soc Med.* 1962; 55:910-912; [2] Bigatti SM, et al. *Arthritis Rheum* 2008; 59:961-967; [3] Russell IJ & Bieber CS in *Wall and Melzack's Textbook of Pain* 5th edn Ch. 44 (eds McMahon SB & Koltzenburg M) 669-682, Elsevier, 2006. [4] Moldofsky H. *Joint Bone Spine* 2008; 75:397-402. [5] Yunus MB et al. *Arthritis Rheum* 1991; 34:15-21; Illustrations from: Stahl SM. *Stahl's Illustrated Chronic Pain and Fibromyalgia*. New York, NY: Cambridge University Press; 2009.

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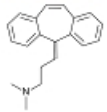
What is TNX-102 SL?

- **TNX-102 SL is a sublingual eutectic formulation[1] of cyclobenzaprine (CBP) for transmucosal absorption**
  - CBP is a tricyclic molecule with high affinity for target receptors that play key roles in sleep physiology and restorative sleep-related pain processing
  - *In vitro* studies[2] show potent binding and functional antagonism at each of
    - 5-HT_{2A}
    - α_1-adrenergic
    - Histamine-H_1
  - Non-narcotic, centrally-acting analgesic with no recognized risk of addiction



[1] Notice of Allowance for Eutectic Proprietary Protectic™ Formulation Patent issued by the U.S. Patent and Trademark Office; [2] Daugherty et al. Society of Biological Psychiatry (SOBP) 70th Annual Scientific Convention, May 14-16, 2015 Toronto, Ontario, Canada.

- **TNX-102 SL is designed for bedtime administration with desirable nighttime pharmacokinetic profile and pharmacodynamics effects[3]**
  - Rapid systemic exposure and increased plasma concentration and AUC during sleep period
  - Avoids first-pass metabolism reducing exposure to long-lived active metabolite, norcyclobenzaprine (nCBP)
    - $t_{1/2}$~72 hours
    - Less selective for target receptors -> undesirable off-target functional activities
    - Exposure (AUC_{0-48}) for CBP/nCBP of 1.9 for TNX-102 SL vs. 1.2 for oral IR tablet[2]
    - Multi-dose (20-day) PK of TNX-102 SL compared to simulated multi-dose oral IR CBP shows flipped nighttime exposure ratio: higher CBP to nCPB with TNX-102 SL; higher nCBP to CBP with oral IR CBP[4]

[3] Lederman et al. European Congress of Rheumatology, June 2015, , Rome, Italy; 4 Sullivan et al. American Society of Clinical Psychopharmacology (ASCP), May 28-31, 2019, Scottsdale, AZ; IR, immediate-release;

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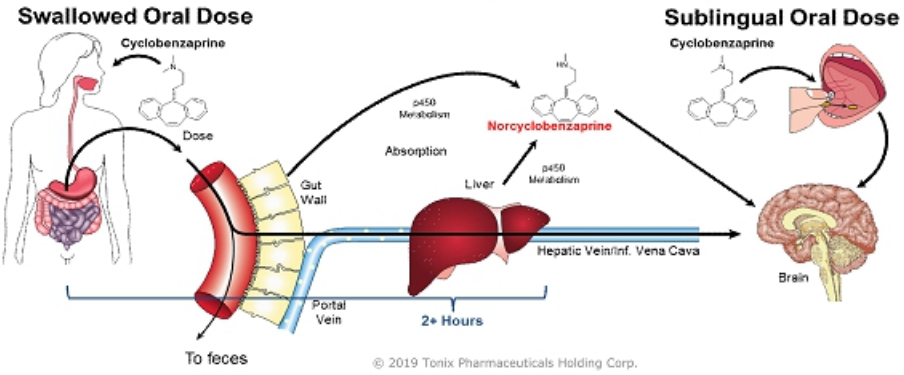
TNX-102 SL: Sublingual Cyclobenzaprine Tablet

- **Faster Absorption**
- **Bypasses "First-Pass" Hepatic Metabolism**
  - **Reduced metabolism of parent CBP to active metabolite nCBP**



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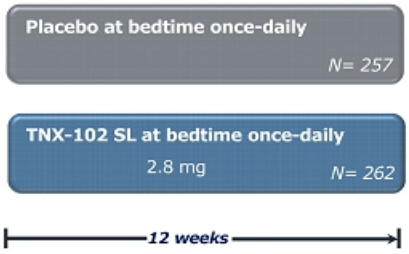
Phase 3 AFFIRM Study of TNX-102 SL 2.8 mg in Fibromyalgia

General Study Characteristics:

- 12-week, randomized, double-blind, placebo-controlled study in fibromyalgia conducted at 45 U.S. sites
- TNX-102 SL 2.8 mg at bedtime nightly for 12 weeks
- Daily diary reporting of average pain severity over prior 24 hours



Primary Endpoint

- Response defined as a ≥ 30% improvement from baseline to Week 12 in the weekly average of the daily self-reported average NRS pain severity (Logistic Regression[1])

Key Secondary Endpoints

- Patient's Global Impression of Change (PGIC) responder analysis at Week 12
- Fibromyalgia Impact Questionnaire - Revised (FIQR) Symptom Domain score at Week 12
- FIQR Function Domain score at Week 12
- Weekly average of the daily diary assessment of sleep quality at Week 12
- Patient Reported Outcomes Measurement Information System (PROMIS) Short Form score for sleep disturbance at Week 12
- PROMIS Short Form score for fatigue at Week 12
- Weekly average of the daily self-reported average pain severity score at Week 12

[1] subject's with missing data considered non-responders

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AFFIRM Study Results:
Primary Analysis

- Primary Analysis of Pain Response in FM (TNX-102 SL N=262; Placebo N=257)
  - Logistic regression (LR) responder analysis (≥30% pain reduction); all discontinuations considered non-responders
  - TNX-102 SL **28.6%**; Placebo **22.6%**; Odds Ratio (95% CI) of 1.41 (0.94, 2.10), p=0.095, **NS**
  - AFFIRM Study did not meet its primary endpoint

CI, confidence interval; LR, logistic regression; N, number; NS, not significant; OR, odds ratio

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AFFIRM Study Results:
Pre-Planned Sensitivity Analyses Assessed Impact of Missing Data Handling on Primary Efficacy Outcome

- **Sensitivity Analysis 1 – Treatment of missing data** (TNX-102 SL N=262; Placebo N=257)
  - Responder analysis by LR; discontinuations due to LOE/AE treated as non-responders, all others as LOCF
  - TNX-102 SL **33.6%**; Placebo **23.7%**; OR (95% CI) of 1.65 (1.12, 2.42), **p=0.012**
  - **Conclusion: treating non-LOE/non-AE discontinuations as non-responders in the primary analysis reduced response rate more for TNX-102 SL (by 5%) than for placebo (by 1.1%), compared to LOCF**

- **Sensitivity Analysis 2 – Treatment of missing data** (TNX-102 SL N=262; Placebo N=257)
  - Responder analysis by LR; discontinuations due to LOE/AE treated as non-responders; all others with values imputed using quadratic fit on within-subject observed pain scores
  - TNX-102 SL **39.3%**; Placebo **26.1%**; OR (95% CI) of 1.87 (1.28, 2.72), **p=0.001**
  - **Conclusion: treating non-LOE/non-AE discontinuations as non-responders in primary analysis reduced response rate more for TNX-102 SL (by 10.7%) than for placebo (by 3.5%), compared to within-subject quadratic fitting**

AE, adverse event; CI, confidence interval; LOCF, Last Observation Carried Forward; LOE, Lack of Efficacy; LR, logistic regression; N, number; OR, odds ratio

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AFFIRM Study Results:

Pre-Planned Sensitivity Analyses Indicated Treatment of Missing Data May Have Had Adverse Impact on Primary Efficacy Outcome

- Unexpected imbalance in patient discontinuations for reasons unrelated to efficacy or tolerability (eg, patient relocating) created a negative bias in the primary responder analysis because any patient who left the study for any reason, prior to completion, was labeled a non-responder despite their results up to that point

- 'Withdrawal of Consent' utilized as discontinuation reason when a patient informs a site she/he can no longer participate due to moving away from site or starting school or job incompatible with study visits. Note imbalance in this reason in disposition table.

- AFFIRM disposition table:

Discontinuation Reason	TNX-102 SL	Placebo
Occurrence of an AE	20 (7.6%)	11 (4.3%)
Withdrawal of Consent	**15 (5.7%)**	**3 (1.2%)**
Investigator Decision	6 (2.3%)	0 (0.0%)
Lack of Efficacy	6 (2.3%)	5 (1.9%)
Lost to Follow-up	11 (4.2%)	15 (5.8%)
Other	1 (0.4%)	1 (0.4%)
Total	59 (22.5%)	35 (13.6%)

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AFFIRM Study Results:
Supporting Primary Efficacy Analyses

- Primary Analysis in Per Protocol (PP) Population (TNX-102 SL N=179; Placebo N=200)
  - Responder analysis in PP population; all discontinuations are non-responders (like primary analysis)
  - PP population includes all randomized patients with no major protocol violations who are at least 70% compliant with investigational product and who have non-missing Week 12 pain data
  - TNX-102 SL **38.5%**; Placebo **26.0%**; OR (95% CI) of 1.81 (1.17, 2.82), **p=0.008**
  - **Conclusions:**
    - **Compared with the ITT population, the PP population showed a higher response rate (by 9.9%) to TNX-102 SL than the higher rate to placebo (by 3.4%), and there was a positive (p<0.01) efficacy signal**
    - **Major protocol violations and/or poor compliance with IP also adversely affected efficacy signal in the ITT population**

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AFFIRM Study Results:
Primary Efficacy Analysis by an Additional Standard Statistical Approach to Pain and Overall Conclusions on the Negative Primary Outcome

- ≥50% Responder Analysis (all discontinuations treated as non-responders)
  - TNX-102 SL **14.5%**; Placebo **8.6%**; OR (95% CI) of 1.82 (1.04, 3.17), **p=0.035**

- Overall Conclusion On Negative Outcome of the Primary Efficacy Analysis:
  - Unexpected imbalance in discontinuations unrelated to efficacy or tolerability, i.e., in the 'withdrawal of consent' category
  - Imbalance created negative bias in primary responder analysis since any patient who left the study for any non-LOE/non-AE reason prior to completion was labeled a non-responder despite their results up to that point

MCFB, Mean Change from Baseline; MMRM, Mixed Models Repeated Measures; MAR, Missing-at-Random

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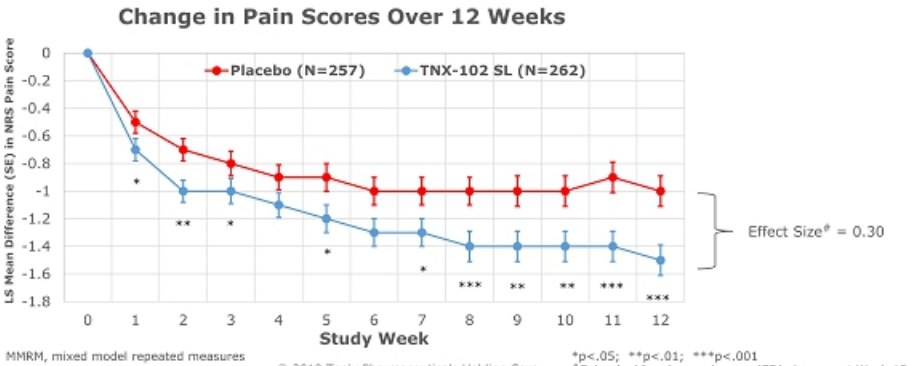
AFFIRM Study Results:
Graphical Display of Primary Endpoint Analyzed by Mean Pain MMRM

- Mean Pain Analysis (MMRM with no imputation) (TNX-102 SL N=262; Placebo N=257)
  - Difference in LS Mean (SE): **-0.6** (0.15); 95% CI (-0.8, -0.3); **p<0.001**



MMRM, mixed model repeated measures

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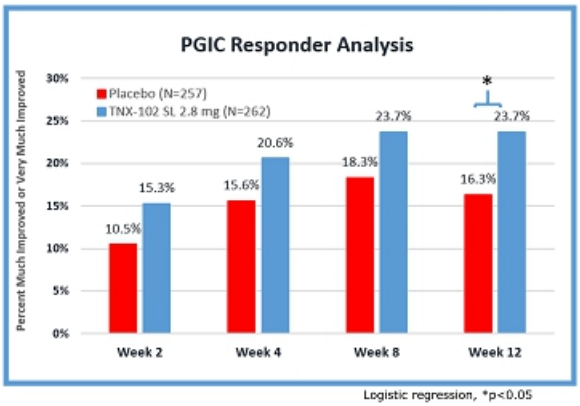
*p<.05; **p<.01; ***p<.001
#Cohen's *d* for observed mean (SD) changes at Week 12

AFFIRM Study Results:
Patient Global Impression of Change (PGIC)

- Responder status defined as a patient rating of 2 ('much improved') or 1 ('very much improved')
- Significantly greater percentage of responders to TNX-102 SL 2.8 mg than placebo at Week 12 (p=0.038)
- Activity of TNX-102 SL 2.8 mg in FM cross-validated by significant effect on Week 12 PGIC



Logistic regression, *p<0.05

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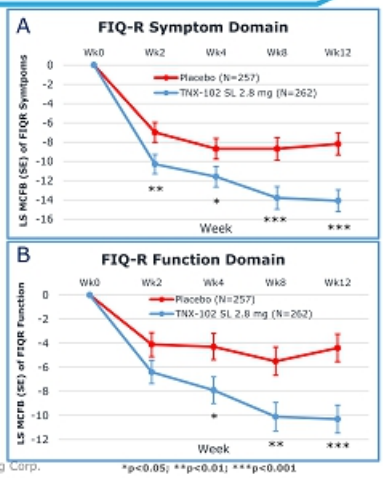
AFFIRM Study Results:
Fibromyalgia Impact Questionnaire – Revised (FIQ-R)

- Robust effect of TNX-102 SL 2.8 mg on FIQ-R Symptoms domain (see figure A)
  - Early onset significant by Week 2
- Similarly robust effect TNX-102 SL 2.8 mg on FIQ-R Function domain by Week 12 (see figure B)
  - Functional improvement trails onset of FM symptom improvement, with first significant function timepoint at Week 4
- FIQ-R Total score was significantly more improved at Week 2 (p=0.023), Week 8 (p<0.001) and Week 12 (p<0.001)
- Significant and clinically-meaningful effects of TNX-102 SL on FIQ-R symptom, function, and total score also cross-validate the activity in FM



*p<0.05; **p<0.01; ***p<0.001

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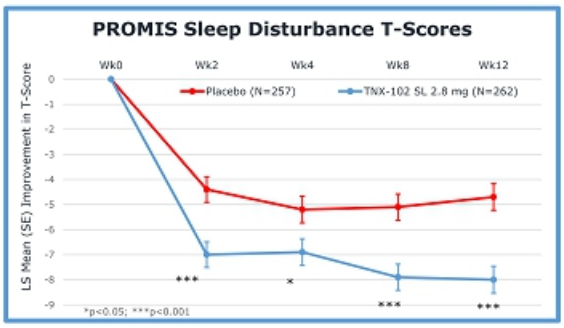
AFFIRM Study Results:
Early Effects on Sleep Quality of TNX-102 SL

PROMIS Sleep Disturbance

- Baseline Mean (SD) T-Scores:
  - Placebo group: 59.9 (6.8)
  - TNX-102 SL group: 59.0 (6.6)
- PROMIS Sleep Disturbance instrument showed positive effects on sleep quality that began separating early, by Week 2



Daily Sleep Quality Diary NRS

- Sleep quality on the daily diary showed greater improvement for TNX-102 SL 2.8 mg over placebo for every week of the study (all $p<0.001$; see figure on next slide)

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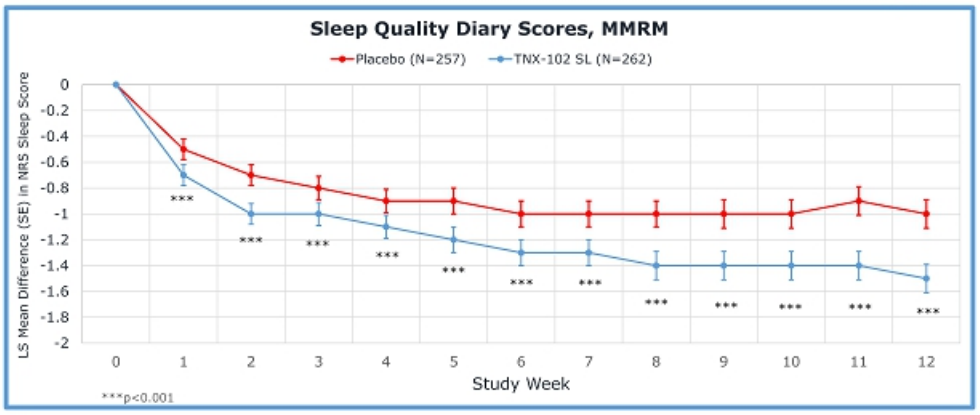
AFFIRM Study Results:
TNX-102 SL Effects on Sleep Quality as Recorded on Daily Diary



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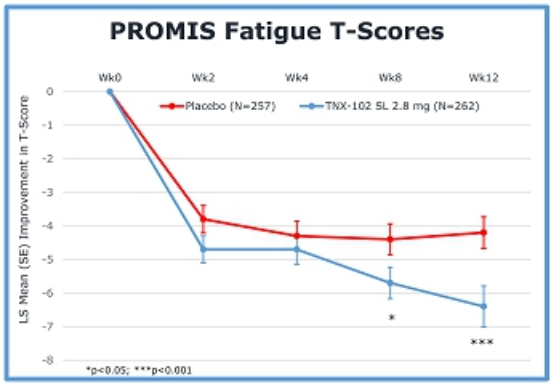
AFFIRM Study Results: TNX-102 SL Effects on Fatigue in FM

- Fatigue is a core FM symptom
  - Fatigue is 1 of 3 symptoms that, if experienced over the past week, can contribute up to 3 points to the symptom severity score for diagnosis[1]
- TNX-102 SL 2.8 mg had a statistically significant improvement on fatigue by Week 8 that continued through Week 12
- The steep slope down for the TNX-102 SL group for fatigue improvement from Week 4 onward contrasts with the relatively flat effect of placebo over the same period



[1]Wolfe et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Seminars in Arthritis and Rheumatism 2016; 46:319-329.

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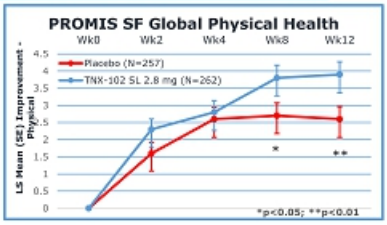
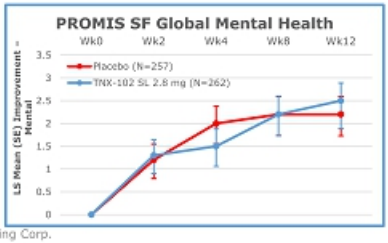
AFFIRM Study Results: PROMIS Global Health – Short Form

- Higher scores reflect improved health on PROMIS Global Health
- TNX-102 SL 2.8 mg improved Global Physical Health domain by last four weeks of study, at Weeks 8 and 12
- TNX-102 SL 2.8 mg had no effect on Global Mental Health domain





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AFFIRM Study Results:
Safety and Tolerability

- Trial Completion Rates: 86.4% Placebo; 77.5% TNX-102 SL 2.8 mg
- TNX-102 SL was well-tolerated in AFFIRM and AEs reported were similar to other TNX-102 SL studies
- Total of 7 serious adverse events (SAEs) were reported: 4 in placebo group and 3 in TNX-102 SL group. No new safety signals observed; multiple causal factors involved in each SAE, and all resolved quickly and without sequelae
- Table of systemic AEs and local administration site reactions (at rate of ≥3% in TNX-102 SL group:

Systemic Adverse Events	Placebo N=256	TNX-102 SL 2.8 mg N=262	Total N=518*
Fatigue	2.3%	5.7%	4.1%
Headache	3.9%	3.4%	3.7%
Somnolence	1.6%	3.1%	2.3%
Local Administration Site Reactions			
Hypoaesthesia oral*	0.8%	40.1%	20.7%
Glossodynia	1.6%	9.2%	5.4%
Paraesthesia oral	1.2%	7.6%	4.4%
Product taste abnormal	0.8%	6.1%	3.5%
Oral discomfort	0.0%	3.1%	1.5%

*Oral hypoaesthesia (tongue numbness) was most common AE, generally transient (<60 minutes), rated mild in 87% and moderate in 13% on TNX-102 SL, and rarely (0.8%) associated with discontinuation; *Safety Population (N=518)

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What was learned about dose and tolerability from studies of TNX-102 SL in PTSD?

- For overall PTSD symptoms, TNX-102 SL 5.6 mg showed an efficacy signal, whereas the 2.8 mg dose did not
- The most common AE with TNX-102 SL, oral hypoaesthesia, occurred at similar rates with 2.8 mg (39%) and 5.6 mg (36%) in AtEase, and 5.6 mg (37%) in HONOR.
  - Rate of oral hypoaesthesia does not appear to be dose dependent
- TNX-102 SL 5.6 mg was well tolerated with only systemic AE of somnolence at a consistently higher rate (at ~16%) than in 2.8 mg
- In-clinic Past 24-hr average NRS pain ratings were collected at each visit in the military PTSD study AtEase (P201; data on next slide)

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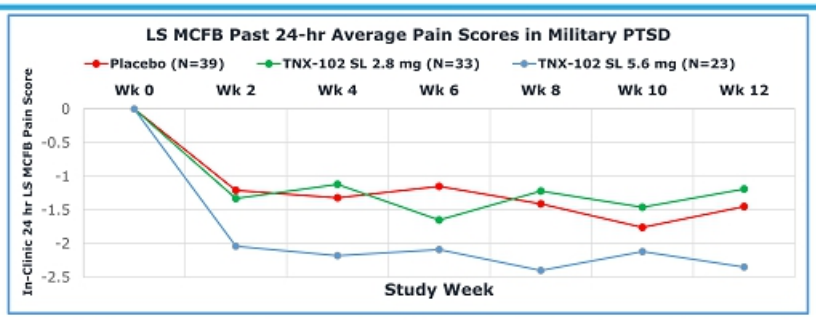
Evidence from Military PTSD Study of Higher Dose Requirement for Pain

Dose Effect on Past 24-hr Average Pain in PTSD Patient with Baseline Pain ≥4



- TNX-102 SL 5.6 mg dose with greater effect on pain in PTSD patients (with baseline pain ≥4) than 2.8 mg dose, which was similar to placebo on pain
- Cohen's *d* effect size for Week 12 (on observed mean [SD] differences from baseline) between 5.6 mg and placebo = 0.34
- At least for the types of pain experienced in this military PTSD population, only the 5.6 mg dose had numerically greater effect than placebo on pain (LS mean difference from placebo = 0.9 units at Week 12)

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LS, least squares; MCFB, mean change from baseline; PTSD, posttraumatic stress disorder

Conclusions

- The AFFIRM Study in fibromyalgia (FM) did not achieve significance on the primary endpoint
  - While the study was not significant base on the pre-specified pain responder analysis, it was significant by other standard pain analysis techniques
  - Results were highly sensitive to methods used to handle missing data
- Significant effects on PGIC and FIQ-R cross-validated the activity of TNX-102 SL in FM
- Improved effects on sleep quality, present within the 1st week and throughout treatment, support the mechanistic hypothesis that TNX-102 SL has positive effects on FM mediated by improvements in sleep quality
- Broad based effects on FM symptoms also evident from statistically significant effects on PROMIS Fatigue Scale and Global Physical Health domain
- Studies with TNX-102 SL at 2.8 mg and 5.6 mg in PTSD suggested higher dose more effective on pain, and the 5.6 mg dose is generally well-tolerated
- Therefore, the planned next phase 3 study of TNX-102 SL in FM will utilize the 5.6 mg dose with the expectation of a larger effect on FM pain and symptoms than the 2.8 mg dose used in AFFIRM

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Thank you!

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