



BIO and Solve M.E. Virtual Event

“Long Covid: What Will It Take To Accelerate Therapeutic Progress?”

NASDAQ: TNXP

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Role of Infections in Triggering Fibromyalgia or Chronic fatigue (CFS)-Like Illnesses

- Symptoms of Long COVID, like multi-site pain, fatigue and insomnia, are the hallmarks of chronic pain syndromes like fibromyalgia and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).
- Experts in chronic pain (Prof. Dan Clauw, Winfried Häuser et al.) predicted an epidemic of chronic pain would follow the COVID epidemic¹
- In August 2022, the HHS released the *National Research Action Plan on Long COVID*² which endorses the connection between Long COVID and CFS/ME.

Infection initiates an *unknown* process, which affects several functions, including brain and energy metabolism³⁻⁸

- Infections can trigger any of these conditions in approximately 10% of exposed individuals
- The initial location of the infection plays a role in determining the subsequent pain syndrome



¹Clauw DJ, et al. Pain. 2020 Aug;161(8):1694-1697.

²Department of Health and Human Services, Office of the Assistant Secretary for Health. 2022. National Research Action Plan on Long COVID, 200 Independence Ave SW, Washington, DC 20201.

³Blomberg J, et al. Front Immunol. 2018;9:229. Published 2018 Feb 15.

⁴Warren JW, et al. Urology. 2008;71(6):1085-1090.

⁵Buskila D, et al. Autoimmun Rev. 2008;8(1):41-43.

⁶Hickie I, et al. BMJ. 2006;333(7568):575.

⁷Parry SD, et al. Am J Gastroenterol. 2003;98(9):1970-1975.

⁸Halvorsen HA, et al. Am J Gastroenterol. 2006;101(8):1894-1942.



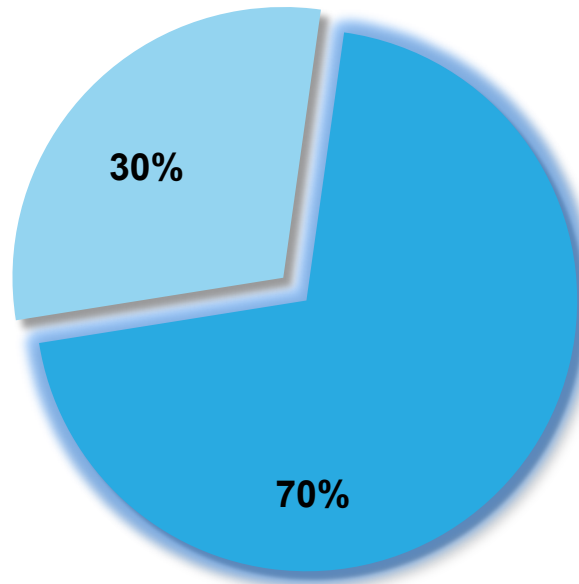
Rate of Central Sensitization (CS) in Long COVID and Comparability of Symptom Severity to CFS/ME and Fibromyalgia



~70% Prevalence of CS in Long COVID patients¹

70% of Long COVID participants had CS symptoms (CSI³ ≥ 40/100)

65% of Long COVID participants had severe CS symptoms



491 total participants

- Long COVID with CSI ≥ 40/100
- Long COVID with CSI < 40/100

Comparable symptom severity in Long COVID, CFS/ME and Fibromyalgia patients²

Recent survey² found comparable pain, fatigue, and function between post-COVID-19 condition, fibromyalgia, and chronic fatigue syndrome

¹Goudman, L, et al. *J of Clin Med*. 2021;10(23):5594.

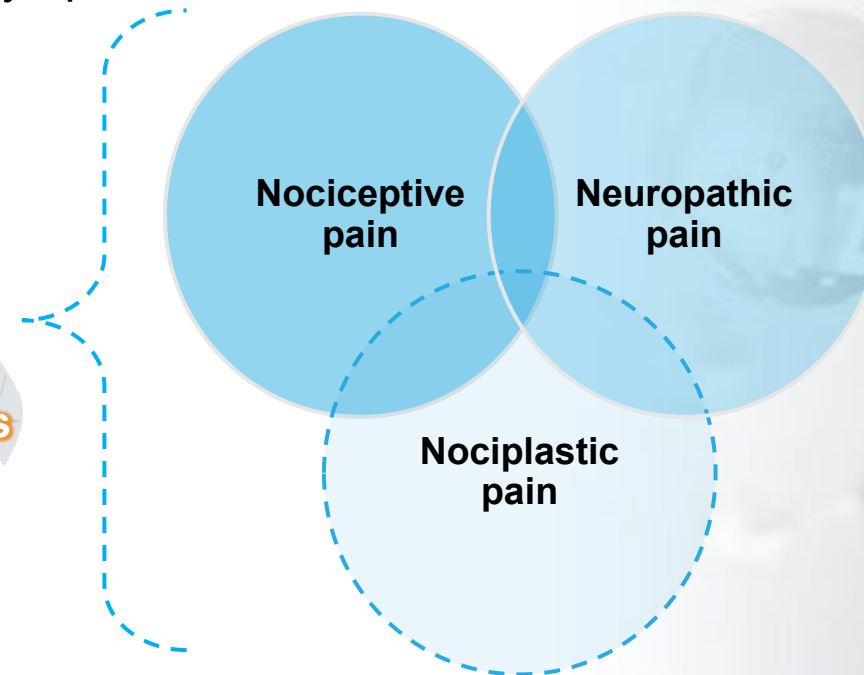
²Haider S, et al. *Pain*. 2023;164(2):385-401.

³CSI = Central Sensitization Inventory



Fibromyalgia-Type Long COVID

- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained symptoms¹⁻²



Symptoms (multi-site pain, fatigue, sleep disorders and cognitive dysfunction) overlap with the key symptoms of fibromyalgia

Nociceptive pain³: (*new term for “Central Sensitization”*) Pain due to the activation of nociceptors that arises from actual or threatened damage to non-neural tissue

¹Bierle DM, et al. Central Sensitization Phenotypes in Post Acute Sequelae of SARS-CoV-2 Infection (PASC): Defining the Post COVID Syndrome. J Prim Care Community Health 2021;12:21501327211030826. doi: 10.1177/21501327211030826.

²Moghimi, N. et al. The Neurological Manifestations of Post-Acute Sequelae of SARS-CoV-2 infection Curr Neurol Neurosci Rep. 2021;21(9):44. doi: 10.1007/s11910-02101130-1.

³Trouvin AP, et al. Best Pract Res Clin Rheumatol. 2019;33(3):101415.

TNX-102 SL*

Cyclobenzaprine (Protectic®) Pipeline in a Product

A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

Potent binding and antagonist activities at the serotonin-5-HT_{2A}, α₁-adrenergic, histaminergic-H₁, and muscarinic-M₁ receptors to facilitate restorative sleep

Innovative and proprietary PROTECTIC® Rapid drug exposure following nighttime administration

Differentiators:

Relative to Oral Cyclobenzaprine

- Lower daytime exposure
- Avoids first-pass metabolism
- Reduces risk of pharmacological interference from major metabolite

Relative to Standard of Care

- Potential for better tolerability while maintaining efficacy

Patents Issued

*TNX-102 SL has not been approved for any indication.



Fibromyalgia

Status: Mid-Phase 3

- One positive Phase 3 study (RELIEF) completed
- Second Phase 3 study (RALLY) missed primary endpoint
- Confirmatory Phase 3 study (RESILIENT) is currently enrolling
 - >50% enrolled

Next Steps: Interim analysis results expected 2Q 2023

Long COVID

Status: Phase 2

- Phase 2 study (PREVAIL) is currently enrolling

Next Steps: Trial enrollment is in process

Posttraumatic Stress Disorder (PTSD)

Status: Mid-Phase 2

- One Phase 2 study (AtEase) completed
- Two Phase 3 studies (HONOR, RECOVERY) conducted

Next Steps: Initiate Phase 2 trial 2Q 2023





Phase 2 Long COVID Study Design (PREVAIL)

Study characteristics:

- Randomized, double-blind, placebo-controlled study of TNX-102 SL in fibromyalgia-type Long COVID
- U.S. sites only, expected to enroll approximately 470 patients
- One unblinded interim analysis based on 50% of randomized participants

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
 - Weekly averages of the daily numerical rating scale scores
 - Analyzed by mixed model repeated measures with multiple imputation (MMRM with MI)

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

Placebo once-daily at bedtime

14 weeks

*Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

ClinicalTrials.gov Identifier: NCT05472090
“A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL in Patients With Multi-Site Pain Associated With Post-Acute Sequelae of SARS-CoV-2 Infection (PREVAIL)”



THANK YOU

