UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): April 20, 2022

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Main Street, Chatham,New Jersey 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company □

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. □

Item 7.01. Regulation FD Disclosure.

On April 20, 2022, Tonix Pharmaceuticals Holding Corp. (the "Company") announced the results of a retrospective observational database study in over 50,000 patients diagnosed with Long COVID. A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference.

On April 21, 2022, the Company will present certain information regarding the Company and its product candidates at the NobleCon18 Investor Conference (the "Presentation"). The Presentation, which may contain nonpublic information, is filed as Exhibit 99.02 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.01 and 99.02 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

On April 20, 2022, the Company issued a press release announcing the results of a retrospective observational database study in over 50,000 patients diagnosed with Long COVID. The goal of the retrospective database study, which was commissioned by the Company, was to assess the proportion of Long COVID patients who experience fibromyalgia-like multi-site pain and to measure their use of opiates. In the study, over 40% of patients with symptoms of Long COVID had fibromyalgia-like multi-site pain. The retrospective analysis was undertaken in part to determine the feasibility and representative nature of the Company's upcoming Phase 2 study of the Company's TNX-102 SL product candidate in patients with Long COVID who present with fibromyalgia-like multi-site pain. The Company believes that these findings suggest that the Company may be able to recruit a robust cohort of participants to test the effects of TNX-102 SL in treating this condition. Further, these findings suggest that the group of Long COVID patients with fibromyalgia-like multi-site pain represents a significant portion of this patient population. The primary efficacy endpoint of the upcoming Phase 2 study will be change from baseline in the weekly average of daily self-reported worst pain intensity scores.

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 9.01. Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press release of the Company, dated April 20, 2022
99.02	Presentation by the Company
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: April 20, 2022

By: /s/ Bradley Saenger
Bradley Saenger
Chief Financial Officer

Exhibit 99.01

Tonix Pharmaceuticals Announces Results of Retrospective Observational Database Study In Over 50,000 Long COVID Patients

Over 40% of Long COVID Patients Had Fibromyalgia-Like Multi-Site Pain Symptoms

Rate of Opioid Use in Long COVID Patients with Multi-Site Pain is a Potential Health Concern

CHATHAM, N.J., April 20, 2022 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, announced today the results of a retrospective observational database study in over 50,000 patients diagnosed with Long COVID[1-2]. Long COVID is known officially as Post-Acute Sequelae of COVID-19 (PASC[3]). Tonix recently announced that the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to support a Phase 2 clinical trial with TNX-102 SL[4] (cyclobenzaprine HCl tablets for sublingual administration) as a potential treatment for a subset of patients with Long COVID whose symptoms overlap with fibromyalgia, and expects to initiate this study in the second quarter. The goal of the retrospective database study was to assess the proportion of Long COVID patients who experience fibromyalgia-like multi-site pain and to measure their use of opiates.

In the study, over 40% of patients with symptoms of Long COVID had fibromyalgia-like multi-site pain [1,2]. In addition, the study reported on the rate of opioid use in Long COVID patients. Opioid use noted was in 36% of Long COVID patients with multi-site pain symptoms relative to 19% of Long COVID patients without multi-site pain. In patients with multisite pain, opiate use increased to 39% of patients when fatigue was present, and 50% of patients when insomnia was present.

“We undertook this retrospective analysis in part to determine the feasibility and representative nature of our upcoming Phase 2 study of TNX-102 SL in patients with Long COVID who present with fibromyalgia-like multi-site pain,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “The finding that more than 40% of Long COVID patients in this sample have fibromyalgia-like multi-site pain symptoms suggests that we should be able to recruit a robust cohort of participantsto test the effects of TNX-102 SL in treating this condition. Further, these findings suggest that the group of Long COVID patients with fibromyalgia-like multi-site pain represents a significant portion of this underserved population. Finally, the high level of opiate use reveals the urgency to provide effective non-opioid analgesia that is targeted toward widespread pain thought to be nociplastic in nature, meaning that augmented CNS pain and sensory processing, as well as altered pain modulation, play a role. The primary efficacy endpoint of the upcoming Phase 2 study will therefore be change from baseline in the weekly average of daily self-reported worst pain intensity scores.”

The study queried data from the TriNetX Dataworks USA Network. The network is a federated network of de-identified inpatient and outpatient electronic medical records from 48 U.S. healthcare organizations. From 75 million people in the network, approximately 1 million adults (18-65) had been diagnosed with acute COVID-19. Of these, approximately 260,000 followed up with a healthcare provider in the network within six months of having acute COVID-19. Of these, approximately 52,000 had Long COVID symptoms in the period between 3 and 6 months after acute COVID-19, which was the time-frame for the analysis for diagnostic codes consistent with multi-site pain, fatigue and insomnia.

[1]*Harris, H, et al. Tonix data on file. 2022*

[2]*TriNetX Analytics*

[3]*Feb. 24, 2021 - White House COVID-19 Response Team press briefing; Feb 25, 2021 - policy brief from the World Health Organization on long COVID.*

[4]*TNX-102 SL is an investigational new drug and has not been approved for any indication.*

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics and diagnostics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of immunology, rare disease, infectious disease, and central nervous system (CNS) product candidates. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500[1] which is a humanized monoclonal antibody targeting CD40-ligand being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second half of 2022. Tonix's rare disease portfolio includes TNX-2900[2] for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan-Drug Designation by the FDA. Tonix's infectious disease pipeline includes a vaccine in development to prevent smallpox and monkeypox called TNX-801[3], next-generation vaccines to prevent COVID-19, and an antiviral to treat COVID-19. Tonix's lead vaccine candidates for COVID-19 are TNX-1840 and TNX-1850[4], which are live virus vaccines based on Tonix's recombinant pox vaccine (RPV) platform. TNX-3500[5] (sangivamycin, *i.v.* solution) is a small molecule antiviral drug to treat acute COVID-19 and is in the pre-IND stage of development. TNX-102 SL, (cyclobenzaprine HCl sublingual tablets), is a small molecule drug being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix expects to initiate a Phase 2 study in Long COVID in the second quarter of 2022. The Company's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL, is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022. Finally, TNX-1300[6] is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial in the second quarter of 2022.

[1] *TNX-1500 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication.*

[2] *TNX-2900 is an investigational new drug at the pre-IND stage of development and has not been approved for any indication.*

[3] *TNX-801 is a live horsepox virus vaccine for percutaneous administration in development to protect against smallpox and monkeypox. TNX-801 is an investigational new biologic and has not been approved for any indication.*

[4] *TNX-1840 and TNX-1850 are live horsepox virus vaccines for percutaneous administration, in development to protect against COVID-19. TNX-1840 and TNX-1850 are designed to express the SARS-CoV-2 spike protein from the omicron and BA.2 variants, respectively. TNX-1840 and TNX-1850 are investigational new biologics at the pre-IND stage of development and have not been approved for any indication.*

[5] *TNX-3500 is an investigational new drug at the pre-IND stage of development and has not been approved for any indication.*

[6] *TNX-1300 is an investigational new biologic and has not been approved for any indication.*

This press release and further information about Tonix can be found at www.tonixpharma.com.

About TriNetX, LLC

TriNetX is a global health research network that connects the world of drug discovery and development from pharmaceutical company to study site, and investigator to patient by sharing real-world data to make clinical and observational research easier and more efficient. TriNetX combines real time access to longitudinal clinical data with state-of-the-art analytics to optimize protocol design and feasibility, site selection, patient recruitment, and enable discoveries through the generation of real-world evidence. The TriNetX platform is HIPAA and GDPR compliant.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate,” “expect,” and “intend,” among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the “SEC”) on March 14, 2022, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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Exhibit 99.02

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate" and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, the risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by Tonix on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the "SEC") on March 14, 2022, and periodic reports and current reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.

PIPELINE
CENTRAL NERVOUS SYSTEM (CNS) PORTFOLIO

CNS PORTFOLIO

CANDIDATES*	INDICATION	STATUS / NEXT MILESTONE
TNX-102 SL[1]	Fibromyalgia (FM) Posttraumatic Stress Disorder (PTSD) Long COVID (PASC[2])	Mid-Phase 3 Phase 2, Targeted 2Q 2022 Start Phase 2, Targeted 2Q 2022 Start[3]
TNX-1300[4]	Cocaine Intoxication / Overdose *FDA Breakthrough Designation*	Phase 2, Targeted 2Q 2022 Start
TNX-1900[5]	Migraine, Craniofacial Pain and Binge Eating Disorder	Phase 2, Targeted 2H 2022 Start[6]
TNX-601 CR	Depression, PTSD, Neurocognitive Dysfunction from Steroids	Phase 2, Targeted 1Q 2023 Start[7]
TNX-1600[8]	Depression, PTSD and ADHD	Preclinical

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*
[1]TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is also in development for Agitation in Alzheimer's Disease (AAD) and Alcohol Use Disorder (AUD) are Phase 2 ready.
[2]Post-Acute Sequelae of COVID-19.
[3]IND clearance granted by FDA. Company plans to start Phase 2 study in subset of patients whose symptoms overlap with fibromyalgia in 2Q 2022.
[4]TNX-1300 (double-mutant cocaine esterase) was licensed from Columbia University.
[5]Acquired from Trigemina; license agreement with Stanford University; IND cleared for the prevention of migraine indication; Planned Binge Eating Disorder study is expected to be investigator initiated.
[6]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900; Phase 2 for the prevention of migraine headache expected to start 2H 2022
[7]TNX-601 CR is in the pre-IND stage in the U.S.; a Phase 1 trial for formulation development was completed outside of the U.S; Phase 2 expected to start 1Q 2023
[8]Acquired from TRImaran Pharma; license agreement with Wayne State University

ADHD = attention-deficit hyperactivity disorder; FM = fibromyalgia; IND = investigational new drug; PASC = post-acute sequelae of COVID-19; PTSD = posttraumatic stress disorder.

TONIX PHARMACEUTICALS

PIPELINE
IMMUNOLOGY AND IMMUNO-ONCOLOGY PORTFOLIO

CANDIDATES*	INDICATION	STATUS / NEXT MILESTONE
TNX-1500[1]	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1, Targeted 2H 2022 Start
TNX-1700[2]	Gastric and colorectal cancers	Preclinical

IMMUNOLOGY PORTFOLIO

*All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.
[1]anti-CD40L humanized monoclonal antibody
[2]Recombinant trefoil factor 2 (rTFF2) based protein; licensed from Columbia University

TONIX PHARMACEUTICALS

PIPELINE
INFECTIOUS DISEASE PORTFOLIO

CANDIDATES*	INDICATION	STATUS / NEXT MILESTONE
TNX-801[1]	Smallpox and monkeypox vaccine	Preclinical
TNX-1840/TNX-1850[2]	COVID-19 Vaccine (horsepox-based live virus vaccine)	Preclinical
TNX-2100[3]	SARS-CoV-2 Diagnostic for T Cell Immunity	First-in-human study initiated 1Q 2022
TNX-2300[4]	COVID-19 Vaccine	Preclinical
TNX-3500[5]	COVID-19 Antiviral	Preclinical
TNX-3600[6]	COVID-19 Therapeutic Platform (monoclonal antibodies)	Preclinical
TNX-3700[7]	COVID-19 Vaccine (zinc nanoparticle mRNA technology)	Preclinical

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*
[1]Live attenuated vaccine based on horsepox virus
[2]Live attenuated vaccine based on horsepox virus vector, expressed SARS-CoV-2 spike protein. TNX-1840 is based on the omicron variant spike protein. TNX-1850 is based on the BA.2 variant spike protein.
[3]*In vivo* diagnostic: SARS-CoV-2 peptide epitope mixtures for intradermal administration to measure delayed-type hypersensitivity to SARS-CoV-2.
[4]Live attenuated vaccine based on bovine parainfluenza (BPI) virus
[5]Sangivamycin for injection; licensed from OyaGen, Inc.
[6]Fully human monoclonal antibody generated from COVID-19 convalescent patients
[7]anti-CD40LCOVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation

TONIX PHARMACEUTICALS

PIPELINE
RARE DISEASE PORTFOLIO

CANDIDATES*	INDICATION	STATUS / NEXT MILESTONE
TNX-2900[1]	Prader-Willi Syndrome *FDA Orphan Drug Designation*	Preclinical

*All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.
[1]Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)


TONIX
PHARMACEUTICALS
CNS:
KEY CANDIDATES
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TNX-102 SL*: FIBROMYALGIA
CYCLOBENZAPRINE PROTECTIC® SUBLINGUAL TABLETS

CNS PORTFOLIO

PROFILE

A unique formulation of cyclobenzaprine designed to optimize delivery and absorption

Innovative and proprietary PROTECTIC® Rapid drug exposure following nighttime administration

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

Clinical trial program designed to examine treatment of core Fibromyalgia symptoms

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia

Additional Indications: Long COVID, PTSD, Agitation in Alzheimer's, Alcohol Use Disorder

Status: One Positive Phase 3 study RELIEF Completed

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT (F307) is currently enrolling

Next Steps: Interim analysis results expected 1Q 2023

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

TONIX PHARMACEUTICALS

TNX-102 SL: FIBROMYALGIA
PROGRAM UPDATE

CNS PORTFOLIO

Phase 3 Study, RESILIENT (F307), will compare TNX-102 SL 5.6 mg and placebo

- First patient enrolled in April 2022
- Interim Analysis results expected 1Q 2023
- Parallel design, double-blind, randomized placebo-controlled study, all U.S. sites
- Primary endpoint is pain at week 14 analyzed by MMRM with MI
- Projecting adverse event related discontinuations to decrease towards rates in RELIEF and PTSD Studies

Phase 3 Study, RALLY (F306), comparison of TNX-102 SL 5.6 mg and placebo

- As expected from interim results published July 2021, RALLY Study missed primary endpoint
- Unexpected ~80% increase in adverse event-related discontinuations in both drug and placebo arms
- Multiple imputation approach on 'Missing Data' attenuated statistical significance of efficacy endpoints'
- TNX-102 SL was generally well tolerated with overall adverse event profile comparable to prior studies; no new safety signals observed

TONIX PHARMACEUTICALS

TNX-102 SL: RALLY STUDY
INCREASED ADVERSE EVENT-RELATED DISCONTINUATIONS

Increases in AE-Related discontinuations in RALLY study compared with RELIEF study in both placebo and TNX-102 SL groups

	RALLY (F306)	RELIEF (F304)	RALLY (F306)	RELIEF (F304)
	Placebo		TNX-102 SL	
Patients with at least one TEAE leading to early discontinuation	6.2%	3.5%	15.2%	8.5%
Ratio of patients with at least one TEAE leading to early discontinuation in F306 to F304 (F306/F304)	1.77		1.79	

TEAE = treatment-emergent adverse event

Adverse events in RALLY

- TNX-102 SL 5.6 mg was well tolerated.
- Among participants randomized to drug and placebo groups, 73.8% and 81.4%, respectively, completed the 14-week dosing period.
- As expected, based on prior TNX-102 SL studies, oral administration site reactions were higher in the drug treatment group, including rates of tongue/mouth numbness, pain/discomfort of tongue/mouth, and product taste abnormal (typically a transient bitter aftertaste)
- Tongue/mouth numbness or tingling and product aftertaste were local effects nearly always temporally related to dose administration and transiently expressed (<60 minutes) in most occurrences.
- Adverse events resulted in premature study discontinuation in TNX-102 SL and placebo groups at rates of 15.2% and 6.2%, respectively
- Approximately 95% of adverse events in both the drug treatment and placebo groups were rated as mild or moderate.

TNX-102 SL: RALLY STUDY
IMPACT OF MISSING DATA ON *P*-VALUES IN RALLY

Since 2010, FDA has generally required that "missing data" be accounted for by using a statistical method called "multiple imputation" or MI

- MI data approach can attenuate *p*-values in the setting of missing data

RALLY (F306) results without MI treatment for missing data are comparable to prior positive RELIEF (F304) study

- Efficacy results in the table without MI are labelled "MMRM"

MI missing data treatment attenuated *p*-values in RALLY

- At the current time, we expect MI will be part of the statistical analysis for the RESILIENT trial

	RALLY (F306)			
	MMRM+MI*		MMRM**	
Endpoints	LSMD (SE)	*p*-value	LSMD (SE)	*p*-value
Pain by Diary	-0.2 (0.16)	**0.115**#	-0.4 (0.16)	0.014
FIQR Symptom domain	-1.9 (1.52)	0.216	-3.4 (1.55)	0.030
FIQR Function domain	-0.4 (1.46)	0.797	-1.6 (1.48)	0.266
PROMIS Sleep Disturbance	-2.3 (0.80)	0.004	-3.3 (0.73)	<0.001
PROMIS Fatigue	-1.2 (0.74)	0.101	-2.0 (0.73)	0.007
Sleep Quality by Diary	-0.3 (0.16)	0.094	-0.4 (0.16)	0.008
	RELIEF (F304)			
	MMRM+MI*		MMRM**	
Endpoints	LSMD (SE)	*p*-value	LSMD (SE)	*p*-value
Pain by Diary	-0.4 (0.16)	**0.010**#	-0.5 (0.16)	0.004
FIQR Symptom domain	-4.3 (1.60)	0.007	-5.6 (1.60)	<0.001
FIQR Function domain	-4.4 (1.69)	0.009	-5.2 (1.63)	0.001
PROMIS Sleep Disturbance	-2.9 (0.82)	<0.001	-3.3 (0.82)	<0.001
PROMIS Fatigue	-1.8 (0.76)	0.018	-2.1 (0.79)	0.007
Sleep Quality by Diary	-0.6 (0.17)	<0.001	-0.7 (0.17)	<0.001

FIQR = Fibromyalgia Impact Questionnaire-Revised; LSMD = least squares mean difference (between TNX-102 SL and placebo); MMRM = mixed model repeated measures; MI = multiple imputation; PROMIS = Patient-Reported Outcomes Measurement Information System; SE = standard error

* MMRM with MI was the pre-specified primary analysis

**MMRM without MI was a pre-specified analysis

Primary efficacy endpoint: change from baseline in the weekly average of daily diary pain severity numerical rating scale scores

CNS PORTFOLIO

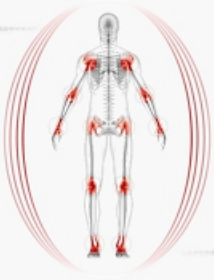
TONIX PHARMACEUTICALS

CHRONIC OVERLAPPING PAIN CONDITIONS (COPC) BELIEVED TO RESULT FROM SHARED BRAIN PROCESSES

CNS PORTFOLIO

- COPC is a set of disorders that coaggregate; these disorders can include but are not limited to[1,2]:

- Temporomandibular disorder
- Fibromyalgia
- Irritable bowel syndrome
- Vulvodynia
- CFS/ME[3]
- Interstitial cystitis/painful bladder syndrome



- Endometriosis
- Chronic tension-type headache
- Migraine headache
- Chronic lower back pain

- Similar central mechanisms play significant roles in all pain conditions, even those with known peripheral contributions[1,2]

[1]Maixner W, et al. *J Pain*. 2016;17(9 Suppl):T93-T107.
[2]Veasley C, et al. http://www.chronicpainresearch. org/public/CPRA_WhitePaper_2015-FINAL-Digital.pdf. Published May 2015. Accessed July 26, 2021.
[3]CFS/ME – chronic fatigue syndrome/myalgic encephalomyelitis

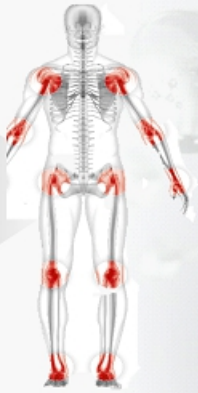
TONIX PHARMACEUTICALS

INFECTIONS MAY TRIGGER OR EXACERBATE CNS CONDITIONS FIBROMYALGIA OR CFS/ME[1] SHARE THIS CHARACTERISTIC

CNS PORTFOLIO

Infection initiates an autoreactive process, which affects several functions, including brain and energy metabolism[2-7]

- Infections can trigger any of these conditions in approximately 10% of exposed individuals
- The initial location of the infection determines the subsequent pain syndrome
- Any type of infectious diarrhea will trigger IBS in 10% to 20% of those exposed



[1]CFS/ME = chronic fatigue syndrome/myalgic encephalomyelitis
[2]Blomberg J, et al. Front Immunol. 2018;9:229. Published 2018 Feb 15.
[3]Warren JW, et al. Urology. 2006;71(6):1085-1090.
[4]Buskila D, et al. Autoimmun Rev. 2008;8(1):41-43.
[5]Hickie I, et al. BMJ. 2006;333(7568):575.
[6]Parry SD, et al. Am J Gastroenterol. 2003;98(9):1970-1975.
[7]Halvorson HA, et al. Am J Gastroenterol. 2006;101(8):1894-1942.

TONIX PHARMACEUTICALS

POTENTIAL INCREASE IN MYALGIA FOLLOWING THE COVID-19 PANDEMIC

Chronic pain increase due to COVID-19 could be nociplastic, neuropathic, or nociceptive

The specific causes may be due to:

Chronic pain as part of a post viral syndrome or the result of viral-associated organ damage

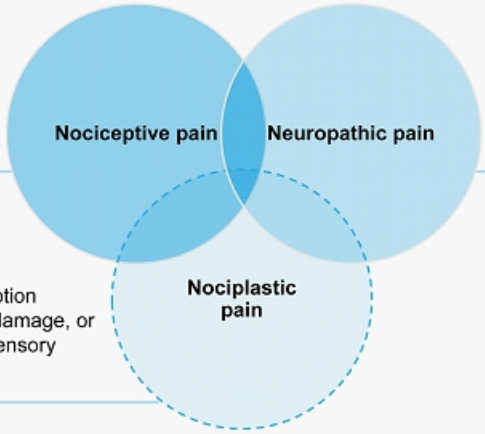
Worsening of chronic pain due to exacerbation of preexisting pain physical or mental complaints

Chronic pain newly triggered in individuals without SARS-CoV-2 infection by exacerbation of risk factors (poor sleep, inactivity, fear, anxiety, and depression)

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

NEW CLASSIFICATION OF PAIN TYPES
NOCIPLASTIC PAIN (f.k.a. "CENTRAL NEUROPATHIC PAIN")

Pain due to the activation of nociceptors that arises from actual or threatened damage to non-neural tissue



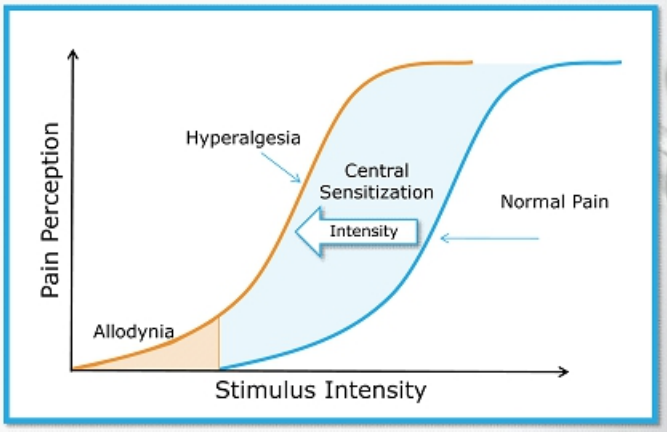
Pain caused by a lesion or disease of the somatosensory nervous system

Pain that arises from altered nociception despite no clear evidence of tissue damage, or for disease or lesion of the somatosensory system causing the pain

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

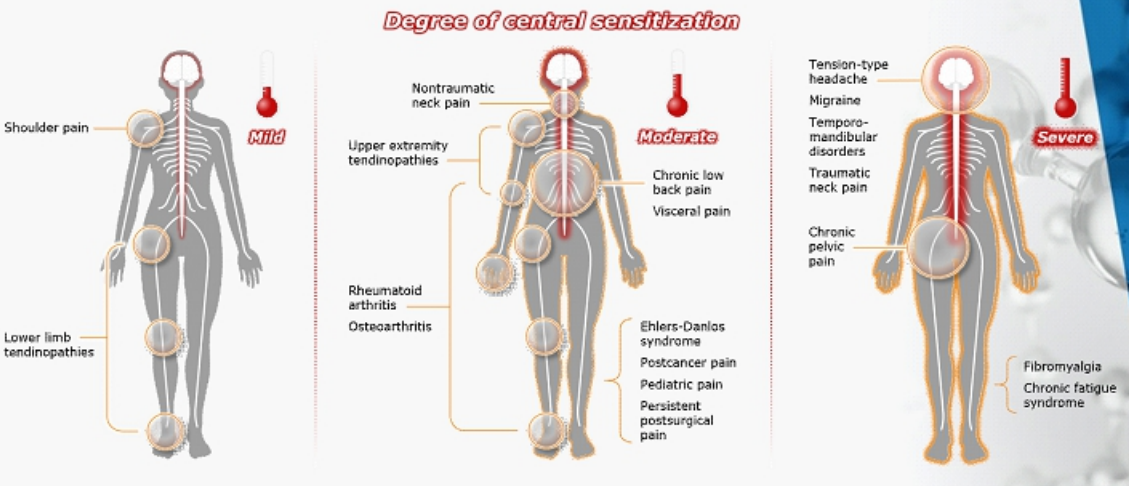
CENTRAL SENSITIZATION (CS)
A FEATURE OF MANY NOCIPLASTIC PAIN SYNDROMES

- CS is caused by amplified neural signaling in CNS pain circuits[1-3]
- Patients with CS perceive higher pain to a slightly noxious stimuli than in non-CS individuals (hyperalgesia)[1]
- Severe CS can lead to hypersensitivity to stimuli that are not typically painful (allodynia)[2]
- CS varies in severity and is observed in syndromes including FM and ME/CFS[1,3]



[1]CFS/ME – chronic fatigue syndrome/myalgic encephalomyelitis
[2]FM - fibromyalgia
[3]Nijs J, et al. *Lancet*. 2021;3(5):e383-e392.
[4]Lolignier, S, et al. *Pflugers Arch*. 2015;467(1):133-139.
[5]Harte, SE, et al. *J of Appl Biobehav Res*. 2018;23(2):e12137.

CENTRAL SENSITIZATION (CS)
CAN OCCUR IN A RANGE OF DISEASES AND CONDITIONS



Nijs J, et al. *Lancet*. 2021;3(5):e383-e392.

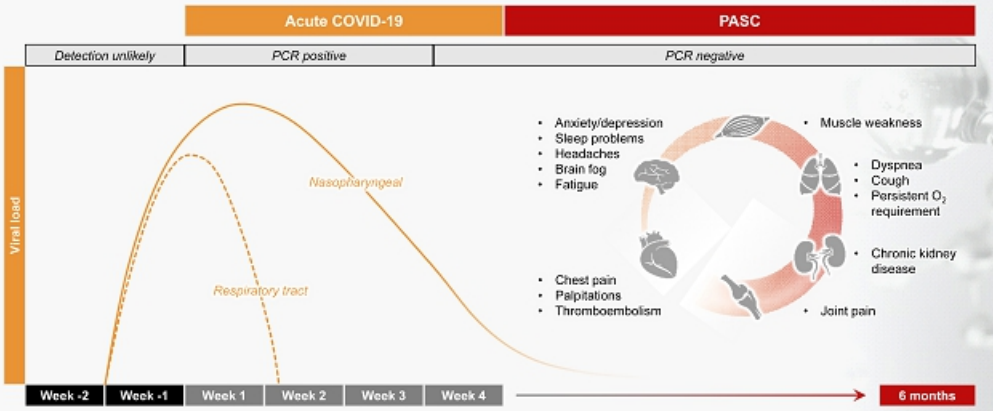
TNX-102 SL: LONG COVID
a.k.a POST-ACUTE SEQUELAE OF SARS-COV-2 INFECTION (PASC[1])

- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained[2-3]:

- Symptoms (multi-site pain, fatigue, sleep disorders and cognitive dysfunction) overlap with the key symptoms of fibromyalgia
- The primary outcome measure for fibromyalgia-type Long COVID will be decrease in multi-site pain measured by a daily diary

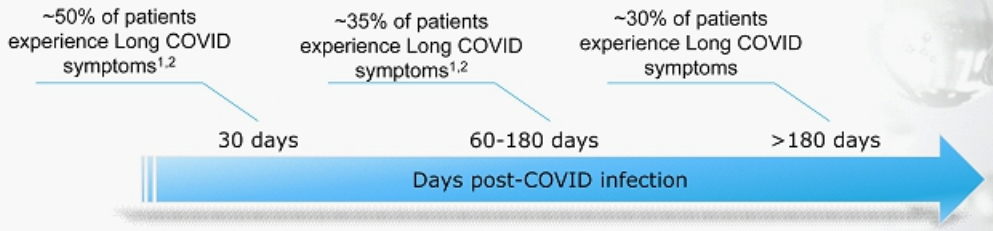
[1]NIH Feb 24, 2021 – White House COVID-19 Response Team press briefing; Feb 25, 2021 - policy brief from the World Health Organization on Long COVID
[2]Bierle DM, et al. *J Prim Care Community Health*. 2021;12:21501327211030826.
[3]Moghimi N, et al. *Curr Neurol Neurosci Rep*. 2021;21(9)44.

TIMELINE OF LONG COVID AFTER ACUTE COVID-19
POST-INFECTIOUS SYNDROME



[1]Hirschtick JL, et al. *Clinical Infectious Diseases*. 2021;73(11):2055-2064.
[2]Taquet, M, et al. *PLOS Medicine*. 2021;18(9):e1003773.
[3]Sørensen, AL, et al. *medRxiv*. 2022:2022.2002.2027.22271328.

PREVALENCE OF LONG COVID
~30% OF RECOVERED SARS-CoV-2 PATIENTS AFTER 6 MONTHS



Long COVID (PASC) is more prevalent among patients[1,2]:

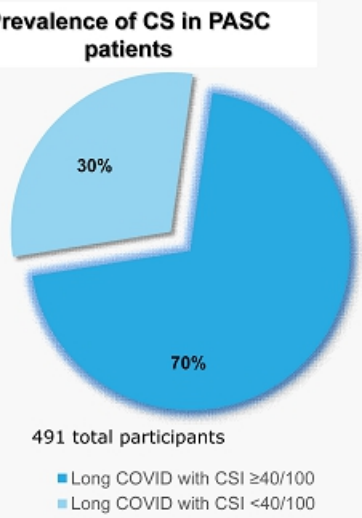
- Requiring hospitalization (93% vs 23% for those not requiring hospitalization)
- With severe symptoms (2.25 times higher prevalence vs those with mild symptoms)

[1]Hirschtick JL, et al. *Clinical Infectious Diseases*. 2021;73(11):2055-2064.
[2]Taquet, M, et al. *PLOS Medicine*. 2021;18(9):e1003773.
[3]Sørensen, AL, et al. *medRxiv*. 2022:2022.2002.2027.22271328.

RATE OF CENTRAL SENSITIZATION (CS) IN LONG COVID SURVEY
CS SYMPTOMS REPORTED IN 70%

70% of Long COVID participants had CS symptoms

65% of all participants had severe symptoms

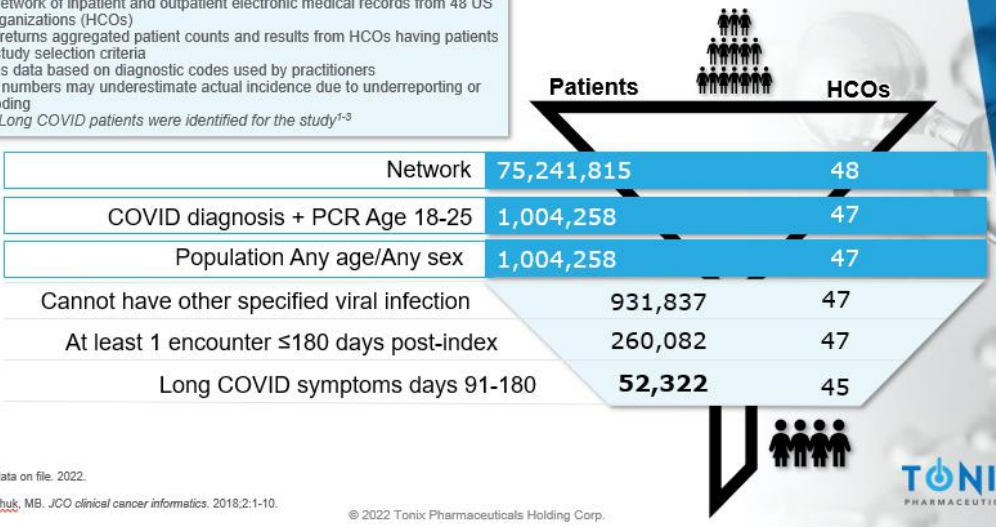


Goudman, L, et al. *J of Clin Med.* 2021;10(23):5594.

LONG COVID PATIENTS IN TriNetX STUDY[1]
RETROSPECTIVE OBSERVATIONAL DATABASE STUDY

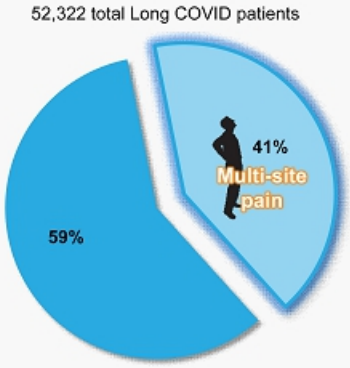
TriNetX Dataworks USA Network[2]:

- A federated network of inpatient and outpatient electronic medical records from 48 US healthcare organizations (HCOs)
- The platform returns aggregated patient counts and results from HCOs having patients meeting the study selection criteria
  - Claims data based on diagnostic codes used by practitioners
  - Case numbers may underestimate actual incidence due to underreporting or miscoding
- *Over 50,000 Long COVID patients were identified for the study[1-3]*

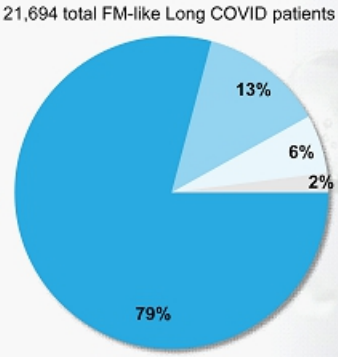


[1]Harris, H, et al. Tonix data on file. 2022.
[2]TriNetX Analytics
[3]Topaloglu, U, and Palchuk, MB. *JCO clinical cancer informatics*. 2018;2:1-10.

LONG COVID PATIENTS IN TriNetX STUDY[1]
FM-LIKE SYMPTOMS (MULTI-SITE PAIN) IN OVER 40% PATIENTS[1,2]



Multi-site Pain	-	+



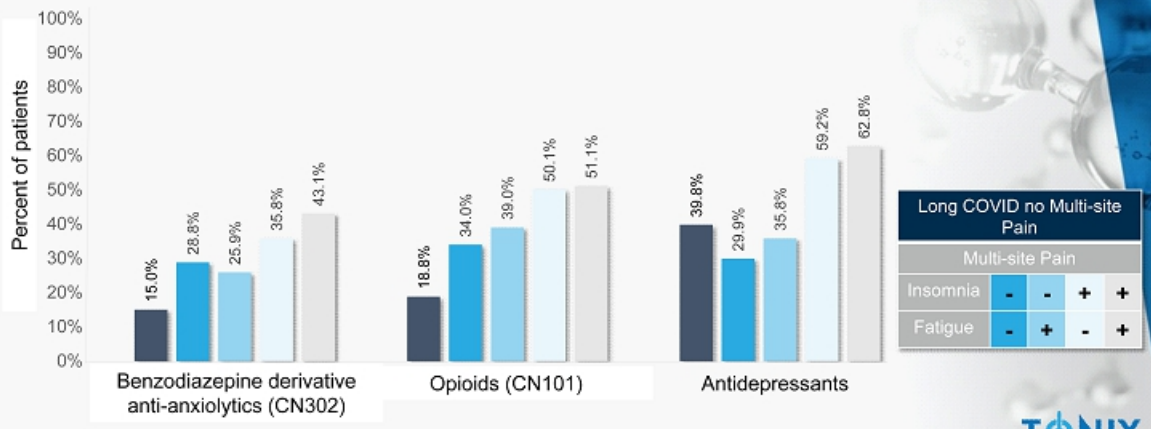
Multi-site Pain	+	+	+	+
Insomnia	-	-	+	+
Fatigue	-	+	-	+

[1]Harris, H, et al. Tonix data on file. 2022.
[2]TriNetX Analytics

LONG COVID PATIENTS IN TriNetX STUDY[1]
RECORDED MEDICATION USE, DAYS 91-180

CNS PORTFOLIO

Patients with compounding nociplastic symptoms are medicating with opioids, antidepressants and anti-anxiolytics at higher rates than those with only multi-site pain or without pain[1-2]



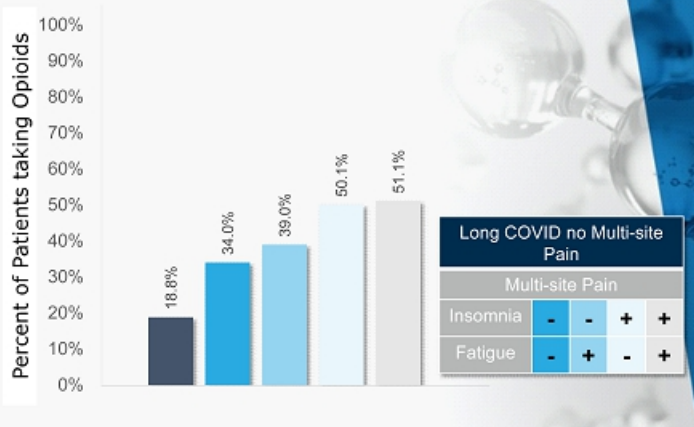
Long COVID no Multi-site Pain				
Multi-site Pain				
Insomnia	-	-	+	+
Fatigue	-	+	-	+

[1]Harris, H, et al. Tonix data on file. 2022.
[2]TriNetX Analytics

TONIX PHARMACEUTICALS

THE RATE OF OPIOID USE IN LONG COVID PATIENTS POTENTIAL HEALTH CONCERN

- In only a few days some people can develop a physical dependence and addiction to opioids[1-2]
- The USA Department of Labor estimates that **1 in 4 patients prescribed opioids long term will struggle with opioid addiction** adding to the already growing opioid crisis[1-4]



[1]Shah, A, et al. *MMWR Morb Mortal Wkly Rep.* 2017;66:265–269.
[2]U.S. Department of Labor
[3]Harris, H, et al. Tonix data on file. 2022.
[4]TriNetX Analytics

SIGNIFICANT FINANCIAL IMPACT OF LONG COVID FOR HOUSEHOLDS AND ECONOMIES

25% of Long COVID patients are unable to return to work[1]

Over 250,000 Quality Adjusted Life-Years (QUALYS) will be lost due to Long COVID in the UK[2]

$23.3 billion is estimated to be paid by the UK government to avoid QUALY losses due to Long COVID[2]

[1]Davis, HE, et al. *eClinicalMedicine*. 2021;38.
[2]Martin, C, et al. *PloS one*. 2021;16(12):e0260843-e0260843.

LONG COVID PRESIDENTIAL MEMORANDUM
PRESIDENT BIDEN – APRIL 5, 2022[1]

CNS PORTFOLIO

Policy

- Commits to redoubling efforts to address the long-term effects of COVID-19

Organizing Government Wide Response

- Harnesses the full potential of the Federal Government, in coordination with public- and private-sector partners, to mount a full and effective response

National Research Action Plane

- Coordinates efforts across the public and private sectors
- Orders establishment of the first-ever interagency national research agenda to, among other things, foster development of new treatments based on a better understanding of the pathophysiological mechanisms of the SARS-CoV-2 virus

Previously, Congress awarded NIH $1.15 billion to study Long COVID.[2]

- Funded among other things the RECOVER Initiative implemented by the National Institutes of Health.

[1]April 5, 2022 President Biden. "Memorandum on Addressing the Long-Term Effects of COVID-19 - www.whitehouse.gov/briefing-room/presidential-actions/2022/04/05/memorandum-on-addressing-the-long-term-effects-of-covid-19/
[2]The NIH provision of Title III Health and Human Services, Division M--Coronavirus Response and Relief Supplemental Appropriations Act, 2021, of H.R. 133, The Consolidated Appropriations Act of 2021. The bill was enacted into law on 27 December 2020, becoming Public Law 116-260.

TONIX PHARMACEUTICALS

TNX-102 SL*: LONG COVID (PASC)
CYCLOBENZAPRINE PROTECTIC® SUBLINGUAL TABLETS

CNS PORTFOLIO

PROFILE

Long COVID or Post-acute Sequelae of COVID-19 (PASC[1])

- Symptoms can include fatigue, sleep disorders, pain, fevers, shortness of breath, cognitive impairment described as "brain fog", gastrointestinal symptoms, anxiety, and depression[1]
- Can persist for months and can range in severity from mild to incapacitating
- Occurs in 30% of recovered COVID-19 patients
- Typically associated with moderate or severe COVID-19, Long COVID can occur after mild COVID-19 or even after asymptomatic SARS-CoV-2 infection

DEVELOPMENT PROGRAM

Market Entry: Long COVID (PASC)

Status: Clinical – IND clearance granted

Next Steps: Start Phase 2 study for treating subset of Long COVID patients whose symptoms overlap with fibromyalgia in 2Q 2022

Patents Issued

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

[1]Nalbandian, Ani, et al. "Post-acute COVID-19 syndrome." Nature Medicine (2021): 1-15.

TONIX PHARMACEUTICALS

TNX-1300*: COCAINE INTOXICATION
COCAINE ESTERASE (CocE)

CNS PORTFOLIO

PROFILE

Cocaine is the main cause for drug-related ED visits[1]

Cocaine use can cause irreversible structural damage to the heart and accelerate cardiovascular disease[2]

- In one survey of 94 long-term cocaine users, 71% had some form of cardiovascular disease[3]

CocE is a recombinant protein that degrades cocaine in the bloodstream

- Rapidly reverses physiologic effects of cocaine
- Drops plasma exposure by 90% in 2 minutes

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Cocaine Intoxication

Additional Indications: Cocaine Overdose

Status: Phase 2 Open Label

Next Steps: 2Q 2022 Initiate Trial

FDA Breakthrough Therapy Designation

*TNX-1300 has not been approved for any indication.

[1]Havakuk O et al. *J Am Coll Cardiol*. 2017;70:101-113.
[2]Phillips K et al. *Am J Cardiovasc Drugs*. 2009;9:177-196.
[3]Maceira AM et al. *J Cardiovasc Magn Reson*. 2014;16:26.
ED = emergency department.

TONIX PHARMACEUTICALS

TNX-1900*: MIGRAINE
INTRANASAL POTENTIATED OXYTOCIN (OT) WITH MAGNESIUM

CNS PORTFOLIO

PROFILE

Intranasal OT has potential utility in treating migraine[1]

- Intranasal OT reaches the trigeminal ganglion
- Preclinical evidence of OT blocking CGRP release and suppressing pain
- Association of low OT levels during and preceding migraine episodes
- Novel non-CGRP antagonist approach to treatment

Magnesium is known to potentiate the binding of OT to its receptor[2,3]

One billion individuals worldwide suffer from migraines

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Chronic Migraine

Additional Indications: Acute Migraine, Craniofacial Pain, Insulin Resistance, Binge Eating Disorder

Status: Clinical – IND cleared for prevention of migraine headache[4]

Next Steps: 2H 2022 Initiate Phase 2 Trial and Investigator Initiated Phase 2 Trial in Binge Eating Disorder

*TNX-1900 has not been approved for any indication.
CGRP = calcitonin gene-related peptide.

[1]Tzabazis A, et al. Oxytocin and Migraine Headache. Headache. 2017 May;57 Suppl 2:64-75. doi: 10.1111/head.13082. PMID: 28485846.
[2]Antoni FA, Chadio SE. Essential role of magnesium in oxytocin-receptor affinity and ligand specificity. Biochem J. 1989 Jan 15;257(2):611-4. doi: 10.1042/bj2570611. PMID: 2539090; PMCID: PMC1135623.
[3]Meyerowitz, J.G., *et al.* The oxytocin signaling complex reveals a molecular switch for cation dependence. *Nat Struct Mol Biol* (2022). (https://doi.org/10.1038/s41594-022-00728-4)
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900.

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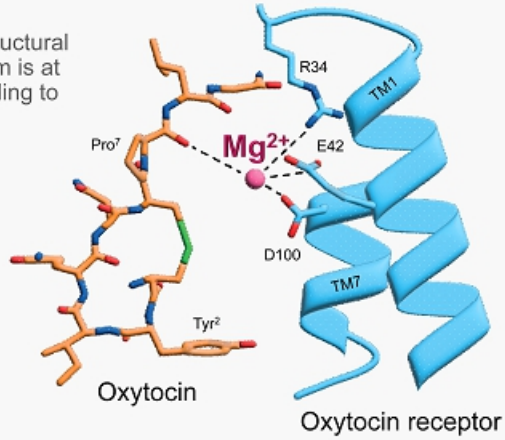
TNX-1900* FOR MIGRAINE
MAGNESIUM (Mg^{2+}) IS AT THE CORE OF OXYTOCIN BINDING[1]

TNX-1900 contains magnesium: Recent structural studies show magnesium is at the core of oxytocin binding to oxytocin receptor[1]



[1]Adapted from Meyerowitz, J.G., Robertson, M.J., Barros-Álvarez, X. *et al.* The oxytocin signaling complex reveals a molecular switch for cation dependence. *Nat Struct Mol Biol* 29, 274–281 (2022). https://doi.org/10.1038/s41594-022-00728-4

TNX-601 CR*: DEPRESSION
TIANEPTINE OXALATE AND NALOXONE

CNS PORTFOLIO

PROFILE

A novel, oral, controlled release once-daily tablet

Mechanistically different from traditional monoaminergic treatments for depression

Indirectly modulates the glutamatergic system

- No direct binding to NMDA, AMPA, or kainate receptors

Naloxone added to deter parenteral abuse

Treatment effect of tianeptine in depression is well-established

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder

Additional Indications: PTSD, Neurocognitive Disorder From Corticosteroids

Status: pre-IND

Next Steps: 1Q 2023 Initiate Phase 2 Trial

Patents Issued

*TNX-601 CR is in the pre-IND stage of development and has not been approved for any indication.

AMPA=α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; MAOI=monoamine oxidase inhibitors; NMDA=N-methyl-D-aspartate.

TONIX PHARMACEUTICALS


FUTURE OUTLOOK
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KEY DEVELOPMENT PARTNERS

Massachusetts General Hospital
Harvard Medical School

TNX-1500: ALLOGRAFT REJECTION

Stanford University
Université de Genève

TNX-1900: MIGRAINE & OTHER INDICATIONS

InsermTransfert
CHU de Toulouse
Aix Marseille université

TNX-2900: PRADER-WILLI SYNDROME

Columbia University

TNX-1300: COCAINE INTOXICATION
TNX-1700: GASTRIC AND COLORECTAL CANCERS
TNX-3600: MONOCLONAL ANTIBODIES FOR COVID-19 TREATMENT

University of Alberta
SR Southern Research

TNX-801: SMALLPOX AND MONKEYPOX VACCINE
TNX-1840 and TNX-1850: COVID-19 VACCINES

Kansas State University

TNX-3700: COVID-19 VACCINE (ZINC NANOPARTICLE mRNA TECHNOLOGY)
TNX-2300: BOVINE PARAINFLUEZNA VIRUS

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MILESTONES:
RECENTLY COMPLETED AND UPCOMING*

- ☑ 1st Quarter 2021 Non-human primate positive efficacy data from TNX-1800 in COVID-19 models reported
- ☑ 1st Quarter 2022 First-in-human study of TNX-2100 initiated for skin test to detect T cell immunity to SARS-CoV-2
- ☑ 1st Quarter 2022 Topline data from Phase 3 F306/RALLY study of TNX-102 SL for the management of fibromyalgia
- ☑ 2nd Quarter 2022 Phase 3 F307/RESILIENT study start of TNX-102 SL for the management of fibromyalgia

Expected Data

- ❑ 1st Quarter 2023 Interim analysis results of Phase 3 F307/RESILIENT study of TNX-102 SL in fibromyalgia

Expected Clinical Trial Initiations

- ❑ 2nd Quarter 2022 Phase 2 OL safety study start of TNX-1300 in ED setting for cocaine intoxication
- ❑ 2nd Quarter 2022 Phase 2 study start of TNX-102 SL for the treatment of PTSD in Kenya
- ❑ 2nd Quarter 2022 Phase 2 study start of TNX-102 SL for the treatment of Long COVID
- ❑ 2nd Half 2022 Phase 2 study start of TNX-1900 for the treatment of migraine
- ❑ 2nd Half 2022 Phase 1 study start of TNX-1500 for prevention of allograft rejection
- ❑ 1st Quarter 2023 Phase 2 study start of TNX-601 CR for the treatment of major depressive disorder

* We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones.

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MANAGEMENT TEAM

Seth Lederman, MD
Co-Founder, CEO & Chairman

TARGENT · Fusilev (levoleucovorin) for injection · vela

Gregory Sullivan, MD
Chief Medical Officer

Columbia University Department of Psychiatry · New York State Psychiatric Institute

Bradley Saenger, CPA
Chief Financial Officer

Shire · VERTEX · Steward · pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank · svb Silicon Valley Bank · American Capital

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THANK YOU
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