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): September 22, 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 September 22, 2022, Tonix Pharmaceuticals Holding Corp. (the "Company") announced data from a retrospective observational database study in patients diagnosed with Long COVID at the International Association for the Study of Pain (IASP) 2022 World Congress on Pain, being held September 20-23, 2022 (the "Presentation"). A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference. 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 Exhibit 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 September 22, 2022, the Company announced data from the Presentation entitled, "*Retrospective Observational Database Study of Patients with Long COVID with Multi-site Pain, Fatigue, and Insomnia: A Real-World Analysis of Symptomatology and Opioid Use*."

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 September 22, 2022
99.02	Retrospective Observational Database Study of Patients with Long COVID with Multi-site Pain, Fatigue, and Insomnia: A Real-World Analysis of Symptomatology and Opioid Use
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: September 22, 2022

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

Exhibit 99.01

Tonix Pharmaceuticals Presents Data from Retrospective Observational Database Study on the Incidence of Multi-Site Pain Symptoms in Long COVID Patients at IASP 2022 World Congress on Pain

Approximately 40% of Long COVID Patients Experience Multi-Site Pain Similar to Overlapping Chronic Pain Syndromes Fibromyalgia and ME/CFS

Approximately 50% of Long COVID Patients with Multi-Site Pain and Sleep Disturbance Use Opiates

CHATHAM, N.J., September 22, 2022 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced data from a retrospective observational database study in patients diagnosed with Long COVID at the International Association for the Study of Pain (IASP) 2022 World Congress on Pain, being held September 20-23, 2022, in Toronto, Canada. The study was motivated to identify the frequency of symptoms of multi-site pain, fatigue and insomnia in Long COVID patients because these are the hallmarks of Overlapping Chronic Pain Syndromes like fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). A copy of the poster is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

The poster presentation titled, "*Retrospective Observational Database Study of Patients with Long COVID with Multi-site Pain, Fatigue, and Insomnia: A Real-World Analysis of Symptomatology and Opioid Use*," include data from the study showing that:

- Approximately 40% of patients with symptoms of Long COVID had fibromyalgia-like multi-site pain.
- The rate of opioid use in Long COVID patients with multi-site pain was 34%, compared to 19% of Long COVID patients without multi-site pain.
- In patients with multi-site pain, opioid use increased to approximately 50% of patients when sleep disturbance was also present.

"The recently released U.S. HHS *National Research Action Plan on Long COVID*[1] repeatedly addresses the overlap of Long COVID with ME/CFS, which, like fibromyalgia is one of the overlapping chronic pain syndromes with central sensitization," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Previously, central sensitization had been observed in approximately two-thirds of Long COVID patients[2]. The data from the new retrospective study revealed that U.S. Long COVID patients are turning to opioids for symptomatic relief, revealing the urgency to provide effective non-opioid, non-addictive analgesics that address multi-site pain. Currently, there is no therapy approved by the U.S. Food and Drug Administration for the treatment of multi-site pain associated with Long COVID."

In August 2022, the Company announced that the first participant was enrolled in the Phase 2 PREVAIL study of TNX-102 SL as a potential treatment for patients with Long COVID syndrome (Long COVID) whose symptoms overlap with fibromyalgia. Long COVID is known officially as Post-Acute Sequelae of COVID-19 (PASC).

Dr. Lederman added, "TNX-102 SL is a centrally-acting non-opioid analgesic with no recognized abuse potential that has shown to decrease daily pain in a Phase 3 study of fibromyalgia. The finding that approximately 40% of Long COVID patients have fibromyalgia-like multi-site pain symptoms in the retrospective observational database study suggests that we should be able to recruit a robust cohort of participants to test the effects of TNX-102 SL in treating multi-site pain in Long COVID in our ongoing Phase 2 study."

Citations

[1]U.S. Department of Health and Human Services, August 9, 2022. "National Research Action Plan on Long COVID".www.covid.gov/assets/files/National-Research-Action-Plan-on-Long-COVID-08012022.pdf.

[2]Goudman, L, et al. *J of Clin Med.* 2021;10(23):5594. https://doi.org/10.3390/jcm10235594

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix'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 (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022 and interim data expected in the second quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix initiated a Phase 2 study in Long COVID in the third quarter of 2022 and expects interim data in the first half of 2023. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the first quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is expected to enter the clinic with a Phase 2 study in the fourth quarter of 2022. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) 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 first half of 2023. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. TNX-801, Tonix's vaccine in development to prevent smallpox and monkeypox, also serves as the live virus vaccine platform or recombinant pox vaccine (RPV) platform for other infectious diseases. A Phase 1 study of TNX-801 is expected to be initiated in Kenya in the first half of 2023. Tonix's lead vaccine candidate for COVID-19 is TNX-1850, a live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform. A Phase 1 study of the COVID-19 vaccine is expected to be initiated in the second half of 2023.

** All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*

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

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

Retrospective Observational Database Study of Patients with Long COVID with Multi-Site Pain, Fatigue, and Insomnia: A Real-World Analysis of Symptomatology and Opioid Use

Herb Harris, MD, PhD[1], Daniel Clauw, MD[2], Rachel Bergmans, MPH, PhD[2], Gregory Sullivan, MD[1], Annie Iserson, MA[1], Candace Flint[1], and Seth Lederman, MD[1]
[1]Tonix Pharmaceuticals, Inc., Chatham, NJ, [2]University of Michigan, Ann Arbor, MI

INTRODUCTION

Post-Acute sequelae of SARS-CoV-2 infection (PASC), or Long COVID, includes a broad constellation of symptoms that persist after resolution of acute COVID-19 infection. Descriptions of pain reported in PASC patients include diffuse myalgias, arthralgias, musculoskeletal pain, headaches, chest pain, abdominal pain, and generalized "body ache." In many patients, multiple sources/sites of pain are reported (Lambert et al., 2021). The prevalence of persistent pain (i.e., at 8 to 12 weeks) reported in PASC patients has been shown to vary from 20% to 64% with an overall average of approximately 30% (Lambert et al., 2021; Jiang et al., 2021). The co-occurrence of multi-site pain, fatigue, and sleep disturbance is similar to central sensitization symptoms found in other post-viral pain syndromes, which may reflect a common underlying nociplastic mechanism (Clauw et al., 2020, Goudman et al., 2021). Fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) are examples of such chronic overlapping pain syndromes. Much remains to be learned about the prevalence and overlaps of these symptoms, particularly multi-site pain, fatigue, and insomnia, which characterize these nociplastic pain syndromes. The present study retrospectively evaluated the prevalence, clinical features, demographics, and use of opioid analgesics in PASC patients with chronic complex multi-site pain, fatigue, and insomnia.

METHODS

We conducted a retrospective observational electronic health record (EHR) database study based on data from a federated network of linked electronic health records from 68 healthcare organizations, totaling 75.2 million patients since 2010. The analysis sample included patients aged 18-65 years with confirmed COVID-19 diagnosis or positive PCR test in any setting of care (January, 2020 to November, 2021), a PASC diagnosis based on the identification algorithm developed by Taquet, at least one healthcare encounter ≥ 180 days following the first COVID-19 diagnosis code or positive PCR test (index date), at least one PASC symptom as defined by Topaloglu (Topaloglu et al., 2018), and multi-site pain present over days 91-180 post-index (Taquet et al., 2021). Diagnostic codes (Figure 1, Table 2) were used to capture centrally-mediated, nociplastic pain components. An algorithm for patient selection included diagnoses associated with diffuse pain or more than two anatomically distinct sources of pain (i.e., multi-site pain). Patients with multi-site pain were further divided into four non-overlapping groups: (1) pain only, (2) pain with fatigue, (3) pain with insomnia, and (4) pain with fatigue and insomnia.

Figure 1: Diagnostic Codes

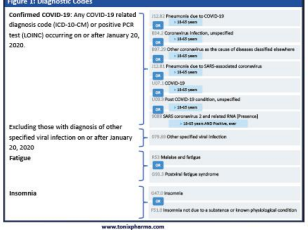


Table 1: Demographics

Measure	COVID-19	All PASC	PASC No Multi-site Pain	PASC Multi-site Pain
N	260,082	52,322	30,628	21,694
Age	43.7±13.7	43.8±13.2	43.6±13.5	47.3±12.4
Female	62.2%	69.4%	69.2%	69.7%
Race				
Caucasian	62.3%	66.6%	68.9%	62.9%
Black	22.0%	20.3%	18.5%	24.8%
Other	2.7%	2.1%	2.1%	2.1%
Unknown	13.0%	10.0%	10.5%	10.2%

RESULTS

- 21,694 patients met the criteria for PASC and multi-site pain (41.5% of the sample) (Figure 2).
- Patients with PASC were similar in age to patients with acute COVID (43.7 years versus 43.8 years, respectively).
- PASC symptoms were present in a predominantly female population (69.2% female among PASC patients with no multi-site pain and 69.7% female among PASC patients with multi-site pain) (Table 1).
- Somatic symptoms of PASC involving the respiratory and gastrointestinal systems occur in approximately equal frequencies 12.2-12.7% (respiratory) and 15.6-17.5% (abdominal) whether or not multisite pain is present. Patients with insomnia or fatigue generally had increased prevalence of respiratory (31.5-38.6%) and GI symptoms (23.4-36.5%).
- Anxiety and depression were present in almost 70% of the PASC study population. However, patients with multi-site pain reported lower symptoms of depression and anxiety (29.7%) (Figure 3).
- Opioid use in PASC patients without multi-site pain was approximately 19% and in patients with multi-site pain was 34.0%. Increased opioid use was observed in patients with multi-site pain and fatigue (38%) or insomnia (50%) and both fatigue and insomnia (51%) (Figure 4).

Figure 2: Multi-Site Pain in Approximately 40% of Patients

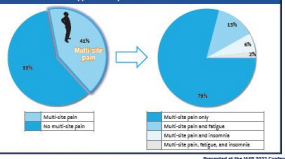


Table 2: Pain-Related Diagnoses for Multi-site Pain

	PASC Multi-site Pain Cohort			
Pain Diagnosis (ICD-10-CM)	- Fatigue - Insomnia	+ Fatigue - Insomnia	- Fatigue + Insomnia	+ Fatigue + Insomnia
N	17,160	2,782	1, 314	438
Migraine (G43)	14.9%	18.4%	21.4%	25.8%
Other headache syndromes (G44)	4.9%	6.1%	6.5%	7.1%
Pain, not elsewhere classified (G89)	50.5%	42.3%	59.6%	54.8%
Chronic pain not elsewhere classified (G89.2)	40.4%	33.1%	47.3%	44.7%
Chronic pain syndrome (G89.4)	6.6%	6.6%	10.4%	9.1%
Pain in joint (M25.5)	39.1%	37.6%	37.3%	41.3%
Lumbago with sciatica (M54.4)	6.1%	4.6%	7.1%	8.0%
Lower back pain (M54.5)	17.2%	15.6%	17.2%	20.8%
Other dorsalgia (M54.89)	0.9%	1.2%	1.5%	N/A
Myositis (M60)	2.3%	3.1%	2.8%	N/A
Other and unspecified soft tissue disorders, not elsewhere classified (M79)	42.0%	50.2%	39.5%	53.4%
Myalgia (M79.1)	12.3%	20.5%	9.9%	26.5%
Pain in hand, foot, fingers and toes (M79.7)	22.7%	22.6%	19.5%	19.4%
Fibromyalgia (M79.7)	9.6%	11.9%	13.7%	15.1%
Pain in throat and chest (R07)	18.5%	27.5%	19.6%	29.7%
Headache (R51)	14.3%	24.1%	15.3%	26.0%
Pain, unspecified (R52)	8.6%	12.3%	6.6%	13.0%

^^ Indicates absence of symptom; "+" Indicates presence of symptom

Figure 3: Prevalence of Core Symptoms in Patients with PASC

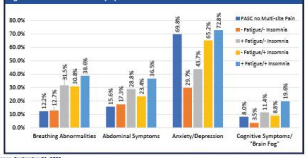
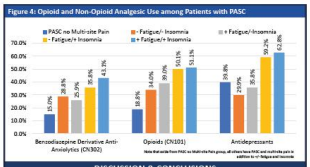


Figure 4: Opioid and Non-Opioid Analgesic Use among Patients with PASC



DISCUSSION & CONCLUSIONS

- PASC has been reported in approximately 30% of patients who recover from the acute infection.
- Complex multi-site pain symptoms are prevalent among patients with PASC (41.5%) and are often cited as most affecting quality of life and the ability to return to full-time work.
- Other symptoms commonly reported in patients with PASC are fatigue, sleep disturbances, and cognitive/memory issues. This cluster of symptoms is reminiscent of central sensitization syndromes, including fibromyalgia and ME/CFS (U.S. HHS National Research Action Plan on Long COVID August 9, 2022).
- PASC patients with multi-site pain had relatively low anxiety, which may relate to central processing of distress signals being differentially interpreted.
- The co-occurrence of fatigue and/or insomnia with multi-site pain symptoms was associated with greater medication burden including benzodiazepines, anti-inflammatory drugs, and analgesics.
- Opioid use noted was 34% in patients with multi-site pain only, further increased to 39% in patients with multi-site pain and fatigue, and exceeded 50% in patients with multi-site pain, fatigue, and insomnia. The high rate of opioid use in this large, growing and vulnerable population is a potentially significant emerging public health concern.
- Currently, there is no therapy approved by the FDA for the treatment of multi-site pain associated with PASC. The central sensitization (or nociplastic) characteristics of multi-site pain in PASC suggest classes of drugs such as opioids should be used with caution or avoided in this subset of patients.

References

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Conflict of Interest Statement: Dr. Clauw and Dr. Bergmans are consultants to Tonix. Tonix provided a gift to UMic of MI to support PASC patient education in 2021.